Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Virus Research 323 (2023) 198950

Contents lists available at ScienceDirect

Virus Research

journal homepage: www.elsevier.com/locate/virusres

Short communication

Temporal dynamics of RSV shedding and genetic diversity in adults during the COVID-19 pandemic in a French hospital, early 2021

Romain Coppée [a,#,*], Houssem Redha Chenane [a,#,*], Antoine Bridier-Nahmias [a], Colas Tcherakian [c], Emilie Catherinot [c], Gilles Collin [a,b], Samuel Lebourgeois [a], Benoit Visseaux [a,b], Diane Descamps [a,b], Marc Vasse [d], Eric Farfour [d]

[a] Université Paris Cité and Sorbonne Paris Nord, Inserm, IAME, F-75018 Paris, France
[b] Laboratoire de Virologie, Hôpital Bichat-Claude Bernard, AP-HP, F-75018 Paris, France
[c] Service de Pneumologie, Hôpital Foch, F-92150 Suresnes, France
[d] Service de Biologie Clinique, Hôpital Foch, F-92150 Suresnes, France

ARTICLE INFO

Keywords:
Human respiratory syncytial virus
RSV
Whole-genome sequencing
Temporal dynamics
RT-PCR

ABSTRACT

Human respiratory syncytial virus (RSV) is responsible of lower respiratory tract infections which may be severe in infants, elderly and immunocompromised adults. Europe and North-American countries have observed a massive reduction of RSV incidence during the 2020–2021 winter season. Using a systematic RSV detection coupled to SARS-CoV-2 for all adult patients admitted at the Foch hospital (Suresnes, France) between January and March 2021 (n = 11,324), only eight RSV infections in patients with prolonged RNA shedding were diagnosed. RSV whole-genome sequencing revealed that six and two patients were infected by RSV groups A and B, respectively. RSV carriage lasted from 7 to at least 30 days disregarding of RSV lineage. The most prolonged RSV shedding was observed in an asymptomatic patient. We detected novel patient-specific non-synonymous mutations in the G glycoprotein gene, including a double identical mutation in the repeated region for one patient. No additional mutation occurred in the RSV genome over the course of infection in the four patients tested for. In conclusion, our results suggest that the temporal shift in the RSV epidemic is not likely to be explained by the emergence of a high frequency, unreported variant. Moreover, prolonged RSV carriages in asymptomatic patients could play a role in virus spread.

Human respiratory syncytial virus (RSV) is considered as a major cause of lower respiratory tract infections amongst young children, elderly and immunocompromised adults worldwide (Falsey et al., 2005; Shi et al., 2017). RSV infections mostly occur seasonally from November to March in the Northern hemisphere and from April to October in the Southern hemisphere (Obando-Pacheco et al., 2018). No effective therapy or approved vaccine is available to date, but vaccine candidates and monoclonal antibodies are in late clinical development (Domachowske et al., 2021). RSV is a non-segmented, single-stranded, negative-sense RNA human Orthopneumovirus of ~15.2 kb in length encoding 11 viral proteins, including the G and F surface glycoproteins that mediate viral entry and are major targets of human immune responses (Levine et al., 1987; McLellan et al., 2013; Yin et al., 2006). RSV infections fall into two co-circulating groups which diverged approximately 350 years ago, named A and B (Mufson et al., 1985). Several RSV A and B sublineages are disseminated in human populations with some periodic shifts in predominance that are supposedly explained by the dynamics of population immunity (Botosso et al., 2009; Goya et al., 2020). In the late '90 s, a G glycoprotein gene variant was detected in RSV group B isolates from Buenos Aires (Argentina) harboring an exact duplication of 60 nucleotides in the second hypervariable region (2HR) of the G glycoprotein (Trento et al., 2003). In 2010, a similar duplication event of 72 nucleotides was identified in RSV group A isolates from Ontario province (Canada) (Eshaghi et al., 2012). These G-duplicated RSV lineages have largely spread worldwide and are now fixed in populations.

In the context of COVID-19 pandemic with resulting quarantine and barrier measures, a drastic reduction of RSV infections has been observed in Europe and North America during the 2020–2021 late winter season (Casalegno et al., 2021; Hodjat et al., 2021). Here, we

* Corresponding author.
# Authors contributed equally to this work.

https://doi.org/10.1016/j.virusres.2022.198950
Received 20 June 2022; Received in revised form 3 September 2022; Accepted 27 September 2022
Available online 29 September 2022
0168-1702/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

performed a systematic RSV detection coupled to SARS-CoV-2 by RT-PCR on nasopharyngeal swab (NPS) for patients (n = 11.324) admitted at Foch hospital (Suresnes, France) between January 1st and March 31st, 2021. NPS were processed with the Alinity M RESP-4-Plex (Abbott Molecular, Des Plaines, United States) assay which allows the detection of SARS-CoV-2, RSV, influenza A and B viruses. RSV detection was considered positive following manufacturer's recommendations, and a CT value ≤ 40. Only eight RSV infections in adults (named patients A to H), later transferred to the intensive care unit, were detected (Table 1). The median age of the RSV-positive patients was 65 [range: 36–72]. Two patients (C and D) were asymptomatic (both tested before admission for planned surgery), while the symptomatic patients exhibited at least one other respiratory disease except one. All symptomatic patients recovered from the infection. The CT value of the first RSV-positive RT-PCR ranged from 15 to 27, then decreased over the infection (Fig. 1). The median duration of RSV detection was 13 days [range: 7–30]. Four patients (B, D, G and H) were still RSV-positive on discharge, including an asymptomatic RSV-positive patient after 30 days of follow-up, leading to under-estimated RSV carriage duration. Previous studies already reported prolonged RSV carriages but in symptomatic patients, reaching 50 days in a symptomatic allogeneic bone marrow transplant recipient (de Lima et al., 2014; Richardson et al., 2016). Such prolonged RSV carriages in asymptomatic patients, as it is the case here, may likely have a role in virus spread. In this study, although we cannot discard viral transmission between the two asymptomatic patients and their respective families or other individuals during hospital visits, a transmission with other patients and hospital staff was however unlikely because *i*) a systematic test for all patients was done on days 2 and 7 of hospital stay and then every 7 days; and *ii*) we did not identify hospital transmission around the RSV-positive patients.

Next-generation sequencing (NGS) was used to retrieve the genome sequence of RSV through a hybrid capture-based approach. For that, viral RNA was first extracted using a MagNA Pure LC 2.0 system (Roche, Mannheim, Germany) with the MagNA Pure LC Total Nucleic Acid Kit-Large Volume reagent kit following supplier's recommendations. Up to 100 ng of RNA was taken for the preparation of libraries using the Illumina RNA Prep with Enrichment (L) Tagmentation kit (Illumina, Inc). Purified cDNA was tagmented using Enrichment Bead-Linked Transposomes, then the fragments were purified and amplified to add P7 and P5 adapters for dual indexing. Amplified samples were enriched as single-plex reactions using the Respiratory Virus Oligos Panel v2 (Illumina, Catalog no.20044311). Products were sequenced on a Miseq system (Illumina, Inc). From NGS data, we first looked for the RSV groups and sublineages (using the genotype definition proposed by Goya et al. (2020)). Raw sequence reads were mapped on RSV A (GenBank accession: NC_001803.1) and B (AY353550.1) reference genomes using the BWA-MEM algorithm (default parameters) (Li and Durbin, 2009). Note that we manually edited these reference genomes to include the duplication of 72 and 60 nucleotides in the 2HR region of the G glycoprotein gene in RSV groups A and B, respectively. Aligned reads were processed using SAMtools v.1.434 (Danecek et al., 2021). Coverage statistics using BEDtools v.2.26.0 (Quinlan and Hall, 2010) revealed that six patients were infected by RSV group A, and two patients carried RSV group B infection (Table 1). A maximum-likelihood phylogenetic tree based on the ectodomain of G glycoprotein, sufficient to elucidate the

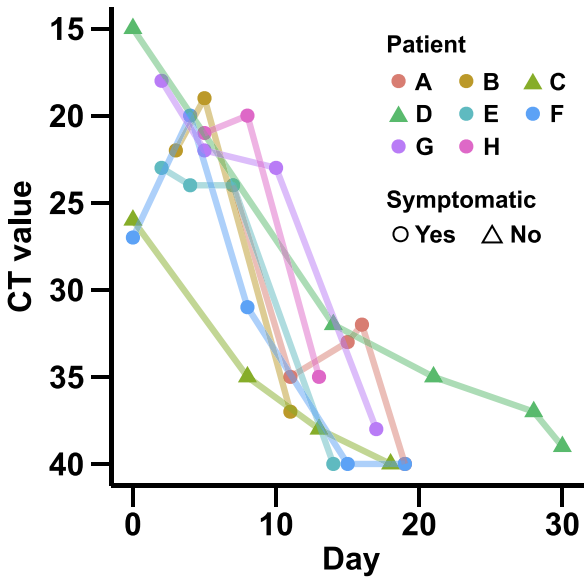

Fig. 1. CT values for detection of RSV over hospital stay for each adult patient. A CT > 40 was considered as RSV-negative. Each color is associated to a patient. The shape indicates whether the patient was symptomatic or asymptomatic.

Table 1
Clinical characteristics of the eight patients.

Patient	Age	Sex	Predisposing condition	Respiratory disease	Other predisposing conditions	Symptomatic	Follow-up (days)*	Duration of positive PCR (days) **	RSV lineage
A	62	F	Yes	Diffuse interstitial lung disease Obstructive sleep apnea syndrome	Epilepsie	Yes	19	16	A
B	68	F	Yes	None	Colorectal cancer Ventricular extrasystole	Yes	11	11	A
C	71	F	Yes	None	Glioblastoma	No	18	13	A
D	61	M	Yes	None	Multiple tumor-like brain lesions	No	30	30	A
E	36	F	Yes	Smoking-related desquamative interstitial pneumonia	Gastroesophageal reflux disease Autoimmune pancreatitis and thyroiditis	Yes	14	7	A
F	81	M	Yes	Smoking-related chronic obstructive pulmonary disease	Ischemic heart disease Atrial fibrillation	Yes	19	8	B
G	58	M	Yes	Smoking-related chronic obstructive pulmonary disease	Ischemic heart disease	Yes	18	18	A
H	72	F	Yes	Smoking-related chronic obstructive pulmonary disease Bronchiectasis	Rheumatoid arthritis	Yes	13	13	B

* From symptom onset to hospital discharge.
** After symptom onset in symptomatic individual or after first positive PCR in asymptomatic individual.

RSV sublineage (Goya et al., 2020), with already published sublineage-annotated sequences was produced (Supplementary Method 1). Mutational signatures showed that five patients (A, B, C, E and G) were infected by the sublineage GA2.3.6b of RSV group A, while the sixth RSV-positive group A patient (D) was infected by the lineage GA2.3.5 (Supplementary Fig. 1). For the two patients infected by RSV group B (patients F and H), the phylogeny clearly evidenced RSV belonged to the GB5.0.5a sublineage. All these sublineages circulated in human populations in recent years (Goya et al., 2020).

For four patients, two to three RSV samples were sequenced at different time points of the infection (two to five days interval; Supplementary Table 1). However, we did not detect acquisition of RSV mutations over the infection course.

We next compared the produced consensus sequences with the closest RSV whole-genome sequences available in the GenBank database and searched for mutations in the G and F surface glycoproteins. To ascertain that each consensus sequence we produced did not include mapping errors, raw reads were aligned on the consensus sequence, then the consensus was corrected if needed. We observed that the RSV group A genomes from this study were closely related to those collected during the 2017–2020 period across the United Kingdom, Spain and the Netherlands (Lin et al., 2021), with identity percentages ranging from 99.62% to 99.73%. All the amino acid positions that differed with the RSV group A reference genes are indicated in the Supplementary Fig. 2. RSV infection from the patient D harbored the R151H mutation in the G protein, close to its central conserved domain that interacts with neutralizing antibodies (Fedechkin et al., 2020), and commonly found in recent isolates of 2021 deposited on GenBank (on 24th August 2022). RSV infection from the patient A had an accumulation of additional mutations in the G protein compared to others (H67Y, V225A, and N273H). While H67Y and V225A have been previously reported in 2019 and 2021, the N273H mutation was not detected on GenBank-deposited sequences nor in the literature to date, and have the particularity to be also present in the G-duplicated insertion that appeared in 2010. Such double mutations in the duplication motif have been deposited on the GenBank database, but the cause and frequency of such events remain to be determined. Finally, all the samples harbored the mutation K209R, associated with a decreased G protein cleavage (Corry et al., 2016). In total, 46 distinct mutations were detected in the G protein (excluding the G-duplicated site). No unreported mutation than in the G protein ($n = 11$ mutations).

Following the same strategy for RSV group B sequences, our consensus sequences were closely related to those reported in Kilifi (Kenya, East Africa) during the 2015–2017 period (Kamau et al., 2020), sharing from 99.54 to 99.56% identity. As for RSV group A, all the amino acid positions that differed with the RSV group B reference genes are given in the Supplementary Fig. 3. By screening GenBank sequences and PubMed articles, we evidenced the presence of one novel non-synonymous mutation in the G protein for each patient, T92I and K224N, among a total of 42 non-synonymous mutations (excluding the G-duplicated site). The role of the newly identified mutations in the extracellular region of the protein requires further investigations, including concerning susceptibility to monoclonal antibodies. No novel mutations were observed in the F glycoprotein gene, which contained a total of 8 mutations.

This study presents two major impediments. First, we only worked on a very limited number of patients, therefore, we cannot ascertain if differences in viral shedding between viral lineages occurs. And second, since no sample was included from November and December 2020, we cannot directly address changes in RSV circulation frequency compared with the observed peak of RSV circulation in previous seasons, although this information was already reported in some other studies (Casalegno et al., 2021; Hodjat et al., 2021).

To conclude, genomic analyses did not detect any novel mutations present at high frequency in our samples, suggesting that the temporal shift in the RSV epidemic may not likely be explained by the emergence of unreported variants. Rather, we believe that non-pharmaceutical interventions due to the COVID-19 pandemic, including barrier gestures, the use of masks in public spaces and the national lockdowns introduced between November and December 2020 in most European countries, were able to strongly contribute in limiting the spread of the virus during the winter period. Additional RSV sequencings during the same period time are however required to confirm this observation.

Funding

This study was supported in part by the ANRS|MIE (Agence Nationale de la Recherche sur le SIDA et les hépatites virales – Maladies Infectieuses Emergentes) and the Inserm UMR1137 unit.

Data availability

All consensus sequences generated in this study have been submitted to NCBI GenBank (accession number OK500256 to OK500269). Next-generation sequence files obtained by Illumina are accessible on the European Nucleotide Archive (ENA) under the accession number ERR7013415 to ERR7013428.

CRediT authorship contribution statement

Romain Coppée: Conceptualization, Software, Methodology, Validation, Formal analysis, Investigation, Data curation, Visualization, Writing – original draft, Writing – review & editing. **Houssem Redha Chenane:** Validation, Investigation, Writing – review & editing. **Antoine Bridier-Nahmias:** Validation, Investigation, Supervision, Writing – review & editing. **Colas Tcherakian:** Investigation, Resources, Writing – review & editing. **Emilie Catherinot:** Investigation, Resources, Writing – review & editing. **Gilles Collin:** Writing – review & editing. **Samuel Lebourgeois:** Writing – review & editing. **Benoit Visseaux:** Conceptualization, Methodology, Validation, Supervision, Project administration, Funding acquisition, Writing – review & editing. **Diane Descamps:** Supervision, Project administration, Funding acquisition, Writing – review & editing. **Marc Vasse:** Validation, Investigation, Resources, Supervision, Project administration, Funding acquisition, Writing – review & editing. **Eric Farfour:** Conceptualization, Methodology, Validation, Investigation, Resources, Supervision, Project administration, Funding acquisition, Writing – review & editing.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.virusres.2022.198950.

References

Botosso, V.F., Zanotto, P.M., de, A., Ueda, M., Arruda, E., Gilio, A.E., Vieira, S.E., Stewien, K.E., Peret, T.C.T., Jamal, L.F., Pardini, M.I., de, M.C., Pinho, J.R.R., Massad, E., Sant'anna, O.A., Holmes, E.C., Durigon, E.L., VGDN Consortium, 2009. Positive selection results in frequent reversible amino acid replacements in the G protein gene of human respiratory syncytial virus. PLoS Pathog. 5, e1000254 https://doi.org/10.1371/journal.ppat.1000254.

Casalegno, J.-S., Ploin, D., Cantais, A., Masson, E., Bard, E., Valette, M., Fanget, R., Targe, S.C., Myar-Dury, A.-F., Doret-Dion, M., Massoud, M., Queromes, G., Vanhems, P., Claris, O., Butin, M., Pillet, S., Ader, F., Bin, S., Gaymard, A., Lina, B., Morfin, F., Javouhey, E., Gillet, Y., Ouziel, A., Tardy, J., Gaucherand, P., Panetta, L., Massardier, J., Polazzi, S., Duclos, A., Benchaib, M., Cartier, R., Jourdain, M., Ottmann, M., Kramer, R., Fiorini, S., Rivat, N., Mekki, Y., Fort-Jacquier, J., Barral, M.-C., Noelie, V., Haesebaert, J., Horvat, C., Vidoni, L., Reynes, J.-M., Eleouet, J.-F., Josset, L., Receveur, M., 2021. Characteristics of the delayed

respiratory syncytial virus epidemic, 2020/2021, Rhône Loire, France. Eurosurveillance 26, 2100630. https://doi.org/10.2807/1560-7917.ES.2021.26.29.2100630.

Corry, J., Johnson, S.M., Cornwell, J., Peeples, M.E., 2016. Preventing Cleavage of the Respiratory Syncytial Virus Attachment Protein in Vero Cells Rescues the Infectivity of Progeny Virus for Primary Human Airway Cultures. J. Virol. 90, 1311–1320. https://doi.org/10.1128/JVI.02351-15.

Danecek, P., Bonfield, J.K., Liddle, J., Marshall, J., Ohan, V., Pollard, M.O., Whitwham, A., Keane, T., McCarthy, S.A., Davies, R.M., Li, H., 2021. Twelve years of SAMtools and BCFtools. Gigascience 10. https://doi.org/10.1093/gigascience/giab008 giab008.

de Lima, C.R.A., Mirandolli, T.B., Carneiro, L.C., Tusset, C., Romer, C.M., Andreolla, H.F., Baethgen, L.F., Pasqualotto, A.C., 2014. Prolonged respiratory viral shedding in transplant patients. Transpl. Infect. Dis. Off. J. Transplant. Soc. 16, 165–169. https://doi.org/10.1111/tid.12167.

Domachowske, J.B., Anderson, E.J., Goldstein, M., 2021. The Future of Respiratory Syncytial Virus Disease Prevention and Treatment. Infect. Dis. Ther. 10, 47–60. https://doi.org/10.1007/s40121-020-00383-6.

Eshaghi, A., Duvvuri, V.R., Lai, R., Nadarajah, J.T., Li, A., Patel, S.N., Low, D.E., Gubbay, J.B., 2012. Genetic variability of human respiratory syncytial virus A strains circulating in Ontario: a novel genotype with a 72 nucleotide G gene duplication. PLoS ONE 7, e32807. https://doi.org/10.1371/journal.pone.0032807.

Falsey, A.R., Hennessey, P.A., Formica, M.A., Cox, C., Walsh, E.E., 2005. Respiratory syncytial virus infection in elderly and high-risk adults. N. Engl. J. Med. 352, 1749–1759. https://doi.org/10.1056/NEJMoa043951.

Fedechkin, S.O., George, N.L., Nuñez Castrejon, A.M., Dillen, J.R., Kauvar, L.M., DuBois, R.M., 2020. Conformational Flexibility in Respiratory Syncytial Virus G Neutralizing Epitopes. J. Virol. 94 https://doi.org/10.1128/JVI.01879-19 e01879-19.

Goya, S., Galiano, M., Nauwelaers, I., Trento, A., Openshaw, P.J., Mistchenko, A.S., Zambon, M., Viegas, M., 2020. Toward unified molecular surveillance of RSV: a proposal for genotype definition. Influenza Other Respir. Viruses 14, 274–285. https://doi.org/10.1111/irv.12715.

Hodjat, P., Christensen, P.A., Subedi, S., Bernard, D.W., Olsen, R.J., Long, S.W., 2021. The Reemergence of Seasonal Respiratory Viruses in Houston, Texas, after Relaxing COVID-19 Restrictions. Microbiol. Spectr. 9, e0043021 https://doi.org/10.1128/Spectrum.00430-21.

Kamau, E., Otieno, J.R., Lewa, C.S., Mwema, A., Murunga, N., Nokes, D.J., Agoti, C.N., 2020. Evolution of respiratory syncytial virus genotype BA in Kilifi, Kenya, 15 years on. Sci. Rep. 10, 21176. https://doi.org/10.1038/s41598-020-78234-0.

Levine, S., Klaiber-Franco, R., Paradiso, P.R., 1987. Demonstration that glycoprotein G is the attachment protein of respiratory syncytial virus. J. Gen. Virol. 68 (Pt 9), 2521–2524. https://doi.org/10.1099/0022-1317-68-9-2521.

Li, H., Durbin, R., 2009. Fast and accurate short read alignment with Burrows–Wheeler transform. Bioinformatics 25, 1754–1760. https://doi.org/10.1093/bioinformatics/btp324.

Lin, G.-L., Drysdale, S.B., Snape, M.D., O'Connor, D., Brown, A., MacIntyre-Cockett, G., Mellado-Gomez, E., de Cesare, M., Bonsall, D., Ansari, M.A., Öner, D., Aerssens, J., Butler, C., Bont, L., Openshaw, P., Martinón-Torres, F., Nair, H., Bowden, R., Golubchik, T., Pollard, A.J., 2021. Distinct patterns of within-host virus populations between two subgroups of human respiratory syncytial virus. Nat. Commun. 12, 5125. https://doi.org/10.1038/s41467-021-25265-4.

McLellan, J.S., Chen, M., Leung, S., Graepel, K.W., Du, X., Yang, Y., Zhou, T., Baxa, U., Yasuda, E., Beaumont, T., Kumar, A., Modjarrad, K., Zheng, Z., Zhao, M., Xia, N., Kwong, P.D., Graham, B.S., 2013. Structure of RSV fusion glycoprotein trimer bound to a prefusion-specific neutralizing antibody. Science 340, 1113–1117. https://doi.org/10.1126/science.1234914.

Mufson, M.A., Orvell, C., Rafnar, B., Norrby, E., 1985. Two distinct subtypes of human respiratory syncytial virus. J. Gen. Virol. 66 (Pt 10), 2111–2124. https://doi.org/10.1099/0022-1317-66-10-2111.

Obando-Pacheco, P., Justicia-Grande, A.J., Rivero-Calle, I., Rodríguez-Tenreiro, C., Sly, P., Ramilo, O., Mejías, A., Baraldi, E., Papadopoulos, N.G., Nair, H., Nunes, M.C., Kragten-Tabatabaie, L., Heikkinen, T., Greenough, A., Stein, R.T., Manzoni, P., Bont, L., Martinón-Torres, F., 2018. Respiratory Syncytial Virus Seasonality: a Global Overview. J. Infect. Dis. 217, 1356–1364. https://doi.org/10.1093/infdis/jiy056.

Quinlan, A.R., Hall, I.M., 2010. BEDTools: a flexible suite of utilities for comparing genomic features. Bioinforma. Oxf. Engl. 26, 841–842. https://doi.org/10.1093/bioinformatics/btq033.

Richardson, L., Brite, J., Del Castillo, M., Childers, T., Sheahan, A., Huang, Y.-.T., Dougherty, E., Babady, N.E., Sepkowitz, K., Kamboj, M., 2016. Comparison of respiratory virus shedding by conventional and molecular testing methods in patients with haematological malignancy. Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis. 22 https://doi.org/10.1016/j.cmi.2015.12.012, 380.e1-380.e7.

Shi, T., McAllister, D.A., O'Brien, K.L., Simoes, E.A.F., Madhi, S.A., Gessner, B.D., Polack, F.P., Balsells, E., Acacio, S., Aguayo, C., Alassani, I., Ali, A., Antonio, M., Awasthi, S., Awori, J.O., Azziz-Baumgartner, E., Baggett, H.C., Baillie, V.L., Balmaseda, A., Barahona, A., Basnet, S., Bassat, Q., Basualdo, W., Bigogo, G., Bont, L., Breiman, R.F., Brooks, W.A., Broor, S., Bruce, N., Bruden, D., Buchy, P., Campbell, S., Carosone-Link, P., Chadha, M., Chipeta, J., Chou, M., Clara, W., Cohen, C., de Cuellar, E., Dang, D.-.A., Dash-Yandag, B., Deloria-Knoll, M., Dherani, M., Eap, T., Ebruke, B.E., Echavarria, M., de Freitas Lázaro Emediato, C.C., Fasce, R.A., Feikin, D.R., Feng, L., Gentile, A., Gordon, A., Goswami, D., Goyet, S., Groome, M., Halasa, N., Hirve, S., Homaira, N., Howie, S.R.C., Jara, J., Jroundi, I., Kartasasmita, C.B., Khuri-Bulos, N., Kotloff, K.L., Krishnan, A., Libster, R., Lopez, O., Lucero, M.G., Lucion, F., Lupisan, S.P., Marcone, D.N., McCracken, J.P., Mejia, M., Moisi, J.C., Montgomery, J.M., Moore, D.P., Moraleda, C., Moyes, J., Munywoki, P., Mutyara, K., Nicol, M.P., Nokes, D.J., Nymadawa, P., da Costa Oliveira, M.T., Oshitani, H., Pandey, N., Paranhos-Baccalà, G., Phillips, L.N., Picot, V.S., Rahman, M., Rakoto-Andrianarivelo, M., Rasmussen, Z.A., Rath, B.A., Robinson, A., Romero, C., Russomando, G., Salimi, V., Sawatwong, P., Scheltema, N., Schweiger, B., Scott, J.A.G., Seidenberg, P., Shen, K., Singleton, R., Sotomayor, V., Strand, T.A., Sutanto, A., Sylla, M., Tapia, M.D., Thamthitiwat, S., Thomas, E.D., Tokarz, R., Turner, C., Venter, M., Waicharoen, S., Wang, J., Watthanaworawit, W., Yoshida, L.-.M., Yu, H., Zar, H.J., Campbell, H., Nair, H., RSV Global Epidemiology Network, 2017. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet Lond. Engl. 390, 946–958. https://doi.org/10.1016/S0140-6736(17)30938-8.

Trento, A., Galiano, M., Videla, C., Carballal, G., García-Barreno, B., Melero, J.A., Palomo, C., 2003. Major changes in the G protein of human respiratory syncytial virus isolates introduced by a duplication of 60 nucleotides. J. Gen. Virol. 84, 3115–3120. https://doi.org/10.1099/vir.0.19357-0.

Yin, H.-.S., Wen, X., Paterson, R.G., Lamb, R.A., Jardetzky, T.S., 2006. Structure of the parainfluenza virus 5 F protein in its metastable, prefusion conformation. Nature 439, 38–44. https://doi.org/10.1038/nature04322.