International Journal of Innovative Research and Advanced Studies (IJIRAS)
Volume 7 Issue 5, May 2020

ISSN: 2394-4404

Viability And Infectivity Of Coronavirus (2019-nCoV)

Samuel Mwesige

Department of Biochemistry, School of Health Sciences,
Soroti University, Uganda

Abstract: ***2019-nCoV is one of the seven human coronaviruses responsible for causing COVID-19. The disease started in Wuhan China and was declared a global pandemic by the World Health Organization because of high number of confirmed COVID-19 cases and deaths across the world. COVID-19 is a rapidly spreading novel disease and yet has no defined treatment plan. It is imperative for us to understand viability and infectivity of 2019-nCoV with the hope of finding interventional and treatment solutions. Based on behavioral similarity and biological relatedness between 2019-nCoV and SARS-CoV, a number of viability and infectivity factors that influence the spread of COVID-19 have been elucidated. The viability factors are viral genes, protein factors and metrological features (fomites, low temperatures low humidity). Factors responsible for 2019-nCoV infectivity are virion N and S proteins and the human biology aspects of gender, sex hormones, sex-linked genes and immune cells. The biological factors can be used as biomarkers to develop therapies and diagnostics for COVID-19. Public health interventional strategies such as social distancing, isolation, contact tracing and use of facemasks should be encouraged to break COVID-19 transmission chain.***

Keywords: 2019-nCoV, COVID-19, Viability, Infectivity

I. INTRODUCTION

Coronaviruses are a group of related viruses that cause diseases in mammals and birds. These viruses are zoonotic but have developed capability of attacking human host as well. There are at least seven known human coronaviruses namely; 2019-nCoV, SARS-CoV, MERS-CoV, HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1 (7). In humans, coronaviruses cause respiratory tract infections that range from mild to lethal. Mild illness include common cold while lethal varieties cause SARS, MERS and COVID-19. In other animals, symptoms vary from upper respiratory tract disease in chicken to diarrhea in cows and pigs. The 2019 novel corona virus (2019-nCoV) also known as SARs-CoV-2 (14) is the viral pathogen responsible for causing COVID-19, the latest pandemic that started in Wuhan, China.

On March. 11.2020, the World Health Organization (WHO) declared COVID-19 a global pandemic due to increasing numbers of confirmed cases boarder countries. As of April.18. 2020, there are 2,322,092 and 159,661 COVID-19 confirmed cases and COVID-19 deaths worldwide respectively (1). Among the affected countries, USA has the largest population of confirmed cases (734,631) and the highest death toll (38,773). In the meantime, Europe has also faced it rough with 191,726 and 175, 925 cases having been confirmed in Spain and Italy respectively (1). Being caused by a novel virus, little remains known about COVID-19 disease. This gap has diagnostic and therapeutic consequences with COVID-19 cases being treated on trial and error basis. Therefore, it is important to elucidate on viability and infectivity of 2019-nCoV with the aim of identifying diagnostic and treatment targets for COVID-19. Whereas it has been discovered that amino acid sequence of 2019-nCoV is similar to Manis coronavirus and bat coronavirus RaTG13 (14), it is still unclear of the factors that favor the rapid spread of this novel coronavirus from one human host to another.

II. CLASSIFICATION AND STRUCTURE OF CORONAVIRUS

Coronaviruses have been classified based on genomic arrangement, replication protocols, viral protein properties, virion structural characteristics, physicochemical and

pathogenic properties (20). Coronaviruses belong to the Nidovirales order, which includes Coronaviridae, Arteriviridae, Roniviridae and Mesoniviridae families (38). Coronaviridae is the largest family compared to the three (Arteriviridae, Roniviridae and Mesoniviridae) families, with genomic sizes ranging from 26-32 kb (15). Coronaviridae is subdivided into two subfamilies, coronavirinae and torovirinae (11). Based on amino acid sequence analysis (7) and clinical presentation (14), the 2019-nCov falls under Coronavirinae subfamily which is divided into four genera; Alpha coronavirus, Beta coronavirus, Gamma coronavirus and Delta coronavirus.

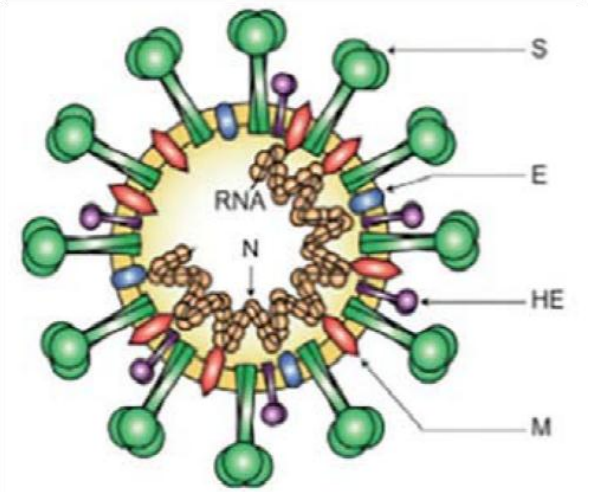

Figure 1: Structure of Coronavirus genome with structural proteins (Nucleocapsid-N protein- Spike-S protein, Membrane-M protein, Hemagglutinin-Esterase-HE and Envelope-E protein (18)

The structure of Coronavirus is composed of a central genome and proteins (S, H, E glycoproteins Nucleocapsids-N and Heamaglutinin Esterase-HE) which collectively form a virion (Figure 1). The genomic RNA is bound to N-proteins in the transcription region and plays important roles in the virion structure, replication and transcription of the coronaviruses (24). The genome consists of seven genes organized into the non-structural protein coding region and the structural and non-essential accessory protein coding region gene (22). The non-structural protein coding region is composed of the 5' replicase gene 1 which accounts for two thirds of the viral genome. Gene 1 encodes non-structural proteins which are converted into viral replication and transcription complexes called double membrane vesicles (16, 10). The structural and non-essential accessory protein coding region comprises of the 3' genes 2 to 7 which encode major viral structural proteins (Nucleocapsid-N protein- Spike-S protein, Membrane-M protein, Envelop-E proteins) and the accessory proteins, which aid viral binding to the host cell receptors (30). The complexity of COVID-19 disease can be traced from the structures and interaction of viral proteins, host immunity and environmental factors. Therefore, it is imperative to elucidate on the viability and infectivity of 2019-nCoV with hope of developing better treatment strategies.

III. VIABILITY OF 2019-nCoV

Viruses vary in their structures and genome make up which consequently affects virion viability and transmission. COVID-19 is a novel pandemic which has puzzled many Scientists with the hope of getting treatment being far from reach. The disease is caused by highly transmissible coronaviruses called 2019-nCov (14). Understanding viability of 2019-nCoV is an important step to the pandemic control with the historical disease triad (Figure 2) providing guiding insight. A number of factors are involved in the viability of viruses and they can be classified as virion-vector, environmental and host influencers.

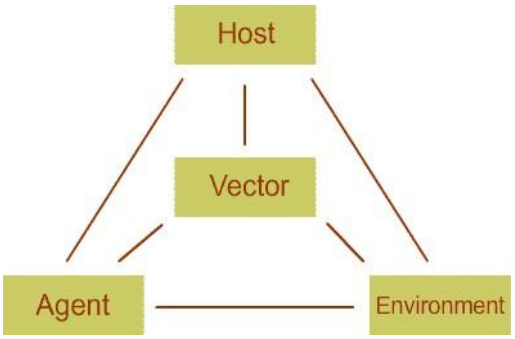

Figure 2: The historical disease triad

The rapid spread of COVID-19 is a function of 2019-nCoV viability which can primarily be traced in the virion genome and structure. Coronaviruses have a number of structure proteins (M, S, E, HE, accessory proteins) enclosing the N-protein bound genome (16, 10, 30). Being located in the transcription region of coronaviruses, the N-proteins play a vital role in virion structure, replication, transcription and viability (35, 30). However, more studies are needed to define the nucleoprotein specific roles, as one of the promising evidence points at interaction with accessory and nsp3-proteins (34).

There is also a possibility that COVID-19 related viruses such as SARS-CoV, Bat coronavirus RatG13 or Manis coronaviruses could have undergone mutation to give rise to mutant 2019-nCoV. Mutant strains can replicate and express viable factors that are responsible for virion adaptability and survival under various environmental conditions. The stability of 2019-nCoV can be used to explain the pandemic nature of COVID-19. However, the probability of laboratory genetic manipulation of 2019-nCoV has been refuted based on virus backbone data (2) and lack of proof for associated reverse genetic systems like beta coronaviruses (9). Since complexity of coronaviruses is due to their protein network, it is therefore important to focus research on viral proteins of 2019-nCoV whose structures and interactions provide leeway for vaccine and drug development.

Viral pathogens do not replicate outside living cells but the infectious virions can persist in the environment for hours or even weeks as may be influenced by metrological and inanimate factors. Fomites (contaminated surfaces) are significant vectors in the viability and transmission of viruses in hospital premises and the community. Survival of respiratory viruses such as; influenza viruses, paramyxoviruses, poxviruses and retroviruses has been studied (28). Coronaviruses have also been studied and found to have

ISSN: 2394-4404

varying surface viabilities in different forms. The human coronavirus associated with common cold has been found to have dry surface and liquid suspension viability of 3 hours and several days respectively (29). SARS-CoV has shown higher stability compared to other human coronaviruses with a viability of at least two weeks at a dry state environment and three weeks in a liquid environment (4). The close relationship between SARS-CoV and 2019-nCoV gives an assumption that the two coronaviruses have similar surface viability characteristics. This calls for contact precautions and hand washing by the health care workers and the population, an approach that disruptions stability and transmission of 2019-nCov.

Biological vectors and animal hosts are important reservoirs for viruses, so they too could play a significant in long term viability of 2019-nCoV. The early cases of COVID-19 were linked to the Huanan market in Wuhan (39), it is possible that animal sources were present at the location. Given the similarity of 2019-nCoV to Bat coronavirus RaTG13 and Manis coronavirus (7), it is likely that Bats and Malayan pangolins serve as COVID-19 reservoirs. In the early 2000, there was an outbreak of SARS-CoV in 5 continents involving 30 countries (26). Following a viability study, the corona virions were found to be more stable at low temperature (< 38˚C) and low humidity (< 95%) compared to the higher temperature and high humidity environments (4). The stability characteristics of SARS-CoV played a vital role in the differential transmission of SARS disease in the tropical and sub-tropical areas. In the same way, more COVID-19 cases and deaths have been reported in countries (like US, China, Italy) in spring and air conditioned environments than tropical regions (1). Therefore, high temperature and high humidity environments can negatively influence viability of 2019-nCoV hence an important interventional blueprint.

IV. INFECTIVITY OF 2019-nCoV

Infectivity is a phenomenon where by a pathogen can establish an infection (31). Infectivity has been correlated to virulence whose definition varies with biological systems. In gene systems, frequently in plants, virulence states viral capability to cause infection to a resistant host (33). Other contexts particularly animal systems define virulence as the degree of damage caused by a virus to its host (27). Virulence can describe either disease severity and/or viral infectivity (8), hence a determinant to pathogenicity of a virion (23). On population level, viral infectivity can be described as transmissibility which is the virion capacity to pass from one infected host to another (3). In this study, we review pathogenicity (host infectivity) and transmissibility (population infectivity) of 2019-nCoV to elucidate on the possible control and treatment approaches for COVID-19.

V. PATHOGENICITY OF 2019-nCoV

Infection with COVID-19 occurs when a person comes into contact with fomites (indirect transmission) or through direct inhalation of virion-containing droplets (17). There is also a possibility of babies getting infected from their mothers during vaginal births given the fact that the pregnant women are more prone to respiratory infections and pneumonia (17). There are unjustified reports that SARS-CoV infections can be acquired through faecal contamination especially in areas of poor sanitation and waste disposal systems (4). SARS-CoV is one of the seven human coronaviruses whose genetic sequence is ≥70 % similar to 2019-nCoV. SARS-CoV initiates human infection by attaching the S-proteins to angiotensin-converting enzyme 2 (ACE2) receptors on the alveolar epithelial cells (19). The genetic similarity between the two coronaviruses shows that 2019-nCoV is capable of using the same ACE2 receptors in order to infect humans. It is therefore important to understand the structure and binding properties of 2019-nCoV S-proteins for possible drug targeting. ACE2 proteins play a protective role during acute lung injury, and whose function is down regulated by 2019-nCoV binding. Virions are able to replicate rapidly, trigger immune response with subsequent cytokine storm syndromes and respiratory tissue damage. The cytokine storm syndrome are a group of disorders involving excessive manufacture of cytokines which cause acute respiratory distress syndrome and multiple organ failure (36,5). Additionally, T cells are qualitatively and quantitatively affected in COVID-19 diseased patients resulting into a condition called immune suppression.

Pathogenicity of 2019-nCoV can be influenced by a number of host factors. Gender differences may indirectly or directly influence the male to female ratio of COVID-19. Females exhibit more robust immune responses to antigenic challenges, such as infections than males (12). This is mediated to a large extent by sex hormones that have adverse effects on the immune cell types such as B cells, T cells, neutrophils, dendritic cells, macrophages and natural killer cells (12). Another important factor is the difference in X-linked genes between males and females. The X-chromosomes contains about 1100 genes, with majority being immunomodulatory. The Y-chromosome has only 100 genes (12), a phenomenon that makes males more prone to COVID-19 compared to females. In a Hong Kong SARS-CoV outbreak in 2002 to 2003, an association between the disease and ABO blood group was reported (6). Blood group-O individuals were more resistant to the infection than blood groups-A, B and AB. ABO blood group antigens are found on a number of cells, tissues and secretions in the human body (13). Like SARS-CoV, 2019-nCoV is an enveloped virus that has important S and E structural proteins. Given the fact that 2019-nCoV attaches on the human respiratory epithelium, there is a possibility of virions expressing ABH antigens on the S and E proteins. Virons whose S and E proteins express a particular antigen can be blocked by a corresponding monoclonal and human antibody. Therefore pathogenic determinants of 2019-nCoV infection such as viral structural proteins, genes, immune cells, sex hormones and antigens provide a stepping stone for vaccine and drug development to combat COVID-19 pandemic.

VI. TRANSMISSIBILITY OF 2019-nCov

The risk of disease transmissibility in a population can be assessed by the basic reproduction number usually denoted as R-nought (Ro). The Ro is the average number of secondary infections that result from an infectious person. If Ro is > 1, then the number of infected cases are expected to increase exponentially and result into an epidemic or pandemic. The Ro of SARS-CoV ranges from 2 to 5 but that of 2019-nCoV has been reviewed and found to be higher, ranging 1.4 to 6.49 (21). Transmissibility of COVID-19 is majorly a function of behavior. Differences in social obligations, risk behaviors and life activities influence exposure and transmission of COVID-19. Males travel frequently, have more social contacts and spend more time in settings that may be favorable to 2019-nCoV transmission such as markets. Males also engage in highly perilous ventures such as transport which is associated with a higher risk of COVID-19. Other predisposing factors include smoking, drinking, pregnancy, age, cancer and HIV/TB infection, which are linked to immune-suppression. Therefore, behavioral and biological factors (genes, sex hormones, immunity) front the male gender as a more susceptible sub population to 2019-nCoV which plays a big role in the transmissibility of COVID.

VII. CONCLUSION

COVID-19 is a global public health problem which has affected over 70 countries. The recent discovery of relatedness of 2019-nCoV with human SARS-CoV, Manis coronavirus and Bat RatG13 coronavirus was a milestone in understanding the novel pandemic. Based on behavioral similarity and biological relatedness between 2019-nCoV and SARS-CoV, a number of viability and infectivity factors that influence the spread of COVID-19 have been elucidated. The viability factors are viral genes, protein factors and metrological features (fomites, low temperatures low humidity). Factors responsible for 2019-nCoV infectivity are virion N and S proteins, human biology aspects of gender, sex hormones, sex-linked genes and immune cells. The biological factors can be used as biomarkers to develop therapies and diagnostics for COVID-19. Public health interventional strategies such as social distancing, isolation, contact tracing and use of facemasks should be encouraged to break COVID-19 transmission chain.

REFERENCES

[1] 2019 Novel Coronavirus (2019-nCoV) in the United States, Centers for Disease Control and Prevention (CDC)
[2] Almazán, F. et al. (2014). Virus Res. 189, 262–270
[3] Bush, A.O. et al. (2001). Parasitism: the diversity and ecology of animal parasites. Cambridge University Press. Pp 391-399.
[4] Chan K. H, Malik Peiris J. S, Lam S. Y, Poon L. L .M, Yuen K. Y, and Seto W. H. (2011). The effects of temperature and relative humidity on the viability of the SARS coronavirus. Advances in virology volume. Hindawi Publishing Corporation. Article ID 734690, 7 pages doi:10.1155/2011/734690
[5] Channappanavar R, Perlman S. (2017). Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathol-ogy. Semin Immunopathol doi:10.10 07/s0 0281-017- 0629-x .
[6] Chen Y, Chen G, Chui CH, Lau FY, Chan PKS, Ng MHL, Sung JJY, Wong RSM. (2005). ABO blood group and susceptibility to severe acute respiratory syndrome. JAMA 293:1450–1451. http://dx.doi.org/10.1001 /jama.293.12.1450-c.
[7] Chengxin Zhang, Wei Zheng, Xiaoqiang Huang, Eric W. Bell, Xiaogen Zhou, and Yang Zhang. (2020). Protein structure and sequence reanalysis of 2019-nCoV genome refutes snakes as its intermediate host and the unique similarity between its spike protein insertions and HIV‑1. Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan
[8] Compact Oxford English Dictionary
[9] Cui, J., Li, F. & Shi, Z.-L. (2019). Nat. Rev. Microbiol. 17, 181–192
[10] Cynthia SG, Kathleen MT, Thomas GK, Pierre ER, James AC, et al. (2004). Ultra Structural characterization of SARS coronavirus. Emerg Infect Dis. 10: 320-326. https://goo.gl/CHVMg5
[11] De Groot RJ, Baker SC, Baric R, Enjuanes L, Gorbalenya AE, Holmes KV, et al. Family Coronaviridae. In Virus Taxonomy; Ninth Report of the International Committee on Taxonomy of Viruses. pp. 806–828. Edited by King AMQ, Adams MJ, Carstens EB, Lefkowitz EJ, editors. Oxford: Elsevier Academic Press
[12] Fish EN. The X-files in immunity: (2008). Sex-based differences predispose immune responses. Nat Rev Immunol; 8:737–44.
[13] Green C. (1989). The ABO, Lewis and related blood group antigens; a review of structure and biosynthesis. FEMS Microbiol Immunol.1:321–330. DOI: 10.1111/j. 1574- 6968.1989. Tb02417.x [PubMed: 2698728]
[14] Gorbalenya A. E.; Baker, S. C.; Baric, R.S.; de Groot, R. J.; Drosten, C.; Gulyaeva, A. A.; Haagmans, B. L.; Lauber, C.; Leontovich, A. M.; Neuman, B. W.; Penzar, D.; Perlman, S. Poon, L. L. M.; Samborskiy, D.; Sidorov, I. A.; Sola, I.; Ziebuhr, J (2020). The species severe acute respiratory syndrome-related coronavirus: Classifying 2019-nCoV and naming it SARS-CoV-2. Nat. Microbiol. 2020, 5, 536−544.
[15] Gorbalenya A. E, Enjuanes L, Ziebuhr J, Snijder E. J. (2006). Nidovirales: evolving the largest RNA virus genome. Virus Research. 117: 17-37. https://goo.gl/A2FJCP
[16] Gosert R, Kanjanahaluethai A, Egger D, Bienz K, Baker SC. (2002). RNA replication of mouse hepatitis virus takes place at double-membrane vesicles. J Virol. 76: 3697-708. https://goo.gl/GhSd.
[17] Hussin A. Rothan, Siddappa N. Byrareddy. (2020). The epidemiology & pathogenesis of coronavirus disease (COVID-19) outbreak. Department of Biology, College of Arts and Sciences, Georgia State University, Atlanta, GA, USA, Department of Pharmacology and Experimental

Neuroscience, University of Nebraska Medical Centre, Omaha, NE, USA, Department of Genetics, Cell Biology and Anatomy, Omaha, NE, USA, Department of Biochemistry and Molecular Biology, University of Nebraska Medical Centre, Omaha, NE, USA.

[18] Weiss S. R & Leibowitz J. L. (2011). Coronavirus pathogenesis. Adv Virus Res. 81:85-164. Doi: 10. 1016/B978-0-12-385885-6.00009-2

[19] Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, et al. (2005). A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung in- jury. Nat Med; 11:875– 9. doi: 10.1038/nm1267 .

[20] Lai MM, Cavanagh D. (1997). The molecular biology of coronaviruses. Adv Virus Res.48: 1-100. https://goo.gl/AUaxWf

[21] Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. (2020). The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med; 27 pii: taaa021. doi: 10.1093/jtm/taaa021 .

[22] Masters PS. (2006). The molecular biology of coronaviruses. Adv Virus Res.66:193-292. https://goo.gl/ x66XSJ

[23] MeSH. (2010). Medical subject headings, Karolinska Institute.

[24] Narayanan K, Makino S. (2001). Characterization of nucleocapsid-M protein interaction in murine coronavirus. Adv Exp Med Biol. 494:577-582. https://goo.gl/MkAA2B

[25] Novel Coronavirus (2019-nCoV) situation reports- World Health Organization (WHO)

[26] Peiris J. S. M, Lai S. T, Poon L. L. M et al. (2003). "Coronavirus as a possible cause of Severe acute respiratory syndrome," The Lancet, vol. 361, no. 9366, pp. 1319–1325,

[27] Pirofski LA, Casadevall A (2012). "Q and A: What is a pathogen? A question that begs the point". BMC Biology. 10: 6. Doi:10.1186/1741-7007-10 6. PMC 3269390. PMID 22293325

[28] Pirtle E. C and Beran G. W. (1991). "Virus survival in the environment," OIE revue scientifique et technique, vol. 10, no. 3, pp.733–748,

[29] Sizun J, Yu M. W. N, and Talbot. P.J, (2000). "Survival of human coronaviruses 229E and OC43 in suspension and after drying on surfaces: a possible source of hospital-acquired infections," Journal of Hospital Infection, vol. 46, no. 1, pp. 55–60,

[30] Stertz S, Reichelt M, Spiegel M, Kuri T, Martinez Sobrido L, Garcia Sastre A, et al. (2007). The intracellular sites of early replication and budding of SARS coronavirus. Virology 361: 304-15 https://goo.gl/LfTwph

[31] Stewart, AD, Logsdon, JM, Kelley, SE (April 2005). "An empirical study of the evolution of virulence under both horizontal and vertical transmission". Evolution. 59 (4): 730 739. doi:10.1554/03-330. PMID 15926685.

[32] Susan RW, Julian LL. (2011). Coronavirus Pathogenesis. Adv Virus Res. 81: 85-164. https://goo.gl/r0Nydb

[33] Thrall, Peter H., Burdon, Jeremy J. (2003)."Evolution of Virulence in a Plant Host-Pathogen Metapopulation". Science. 299(5613): 17351737. Doi:10.1126/science. 1080070. ISSN 0036-8075. PMID 12637745.

[34] Tok TT, Tatar G. (2017). Structures and functions of coronavirus proteins: Molecular modeling of viral nucleoprotein. Int J Virol Infect Dis. 2017; 2(1): 001-001.

[35] Vennema H, Godeke GJ, Rossen JW, Voorhout WF, Horzinek MC, Opstelten DJ, et al. Nucleo capsid-independent assembly of coronavirus-like particles by co-expression of viral envelope protein genes. EMBO J. 1996; 15: 2020-2028. https://goo.gl/tFRLYY

[36] Villar J, Zhang H, Slutsky AS. (2019). Lung repair and regeneration in ARDS: role of PECAM1 and Wnt signaling. Chest; 155:587–94. doi: 10.1016/j.chest.2018. 10.022

[37] Wu, F. et al. (2020). Nature https://doi.org/10.1038/ s41586-020-2008-3

[38] Zirkel F, Kurth A, Quan PL, Briese T, Ellerbrok H, Pauli G, et al. (2011). An insect Nidovirus emerging from a primary tropical rainforest. M Bio. 2: e00077-11. https://goo.gl/bpBvNn

[39] Zhou, P. et al. (2020). Nature https://doi.org/10.1038/ s41586-020-2012-7