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Functional State of the Liver and Pancreas in Covid-19

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A B S T R A C T

COVID-19 (coronavirus disease 2019) has established itself as the agent primarily affecting the respiratory system, however, recent studies have shown that an increasing number of patients have reported extrapulmonary manifestations, such as thrombotic complications, myocardial dysfunction and arrhythmias, acute coronary syndromes, acute kidney injury, gastrointestinal symptoms, hepatocellular damage, hyperglycemia and ketosis, neurological diseases, ocular symptoms and dermatological complications. An important aspect of the diagnostic search and differential diagnosis of the new coronavirus infection COVID-19 is the study of the functional state of the gastrointestinal tract, liver and pancreas in this formidable infection. The time of onset of symptoms from the gastrointestinal tract, hepatobiliary system and pancreas compared to the respiratory manifestations of COVID-19 is delayed. The review article presents data on the functional state of the liver and pancreas in a new coronavirus infection (COVID-19).

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Introduction

COVID-19 (coronavirusdisease2019) is known to develop significant lung damage, including pneumonia and acute respiratory distresssyndrome (ARDS). At the same time, researchers observe many extrapulmonary manifestations of this formidable infectious disease. The accumulated clinical experience and emerging data from scientific studies suggest that in addition to the respiratory system, hematological, cardiovascular, renal, gastrointestinal and hepatobiliary, endocrinological, neurological, ophthalmological and dermatological systems may be affected[2,18]. This pathology may reflect either extrapulmonary spread and replication of SARS-CoV-2, as was observed for other zoonotic coronaviruses [22], or widespread immunepathological consequences of the disease. To give an idea of these extrapulmonary manifestations, including in cases of liver and pancreatic damage, it is necessary to take into account the crucial role of systemic mechanisms for the development of multiple organ damage in COVID-19. Etiopathogenetic and epidemiological issues of the new coronavirus infection COVID-19 The new coronavirus infection COVID-19 very quickly became a global problem that affected all people without exception. The new human coronavirus disease COVIDCOVID-19 has become the fifth recorded pandemic afterthe 2019 flu pandemic. COVID-19 was first reported in Wuhan, China, and then spread around the world. Based on phylogenetic analysis, the coronavirus was officially named Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2 - Severe Acute Respiratory Syndrome coronavirus 2) by the International Committee on Virus Taxonomy. The World Health Organization (WHO) temporarily named the new virus 2019 Novel coronavirus (2019-nCoV) on January 12, 2020, and then officially named this infectious disease 2019 coronavirus (COVID-19 – Corona virus) on February 12, 2020.virus Disease-19). Since COVID-19 first emerged in China, the virus has evolved and spread rapidly to other countries around the world as a global threat. On 11 March 2020 the who has finally made the assessment

that COVID-19 can be characterized as a pandemic, after the Spanish flu of 1918 (H1N1), the Asian flu of 1957 (H2N2), the Hong Kong flu of 1968 (H3N2) and pandemic 2009 influenza (H1N1), which led to the death of about 50 million, 1.5 million, 1 million and 300,000 peopleavec respectively [25,26]. SARS-CoV-2 is a spherical particle with a diameter of approximately 120 nmontaining a single-stranded RNA genome. It is classified as a beta-coronavirus (β-CoV) [line B] and is the seventh coronavirusto infect people, after 2 α-CoV (HCoV-229E and HKU-NL63) and 4 βCoV (HCoV-OC43 [line A), HCoV- HKU1 [line A], severe acute respiratory syndrome SARS-CoV [line B] Among the structural proteins of SARS-CoV-2 isolated S-proteins or "protein spikes" (from the English. Spike - spike), a membrane protein, a protein shell and a nucleocapsid. The presence of spiked S-proteins in electron microscopic imaging shows a "halo" or" crown " around the virus, which gave the corresponding name to the virus. S-protein plays an important role in the attachment, fusion and penetration of the virus into cells, which allows it to be considered as a possible target for the production of antibodies and vaccines. It is believed that the angiotensinconverting enzyme 2 (ACE2) receptor is the main receptor for the spiked S-protein of the virus and determines иthe infectivity of the pathogen [17]. Protein receptor ACE2 in addition to the respiratory system (more than 80% of the alveolar cells of the lung) is detected in the endothelium of small vessels and large arteries and veins in the basal layer of the squamous epithelium of the mucous membrane of the nose, mouth and throat, in the glandular cells, enterocytes, colonocyte, the smooth muscle cells of the stomach and intestines, podocytes, the cells of the proximal tubules of the kidney, and alsocevisama system and liver [19,20] and islet cells of the pancreas [32]. These data indicate that SARS-CoV-2 has a high tropicity to the gastrointestinal tract, liver and pancreas, where there are areas of active viral replication, direct or indirect damage to organs and tissues. The main natural reservoirs of alphacoronaviruses and beta-coronavirusesb are bats [1-6]. According to previous studies on metagenomic sequencing of Malay pangolin (Manisjavanica) samples inGuangxi andin Guangdong, China, it has been suggested that pangolins may be intermediate hosts between bats and humans due to the similarity of the coronavirus pangolin whisker to SARS-CoV-2 [28]. In addition to its zoonotic origin, the SARS-CoV2 spiky protein interacts perfectly with the human ACE2 receptor, facilitating human-to-human transmission. The SARS-CoV-2 virus genome from Wuhan, China, analyzed in late December 2019 was different from the viral genome collected from COVID-19 patients in North America. Building a phylogenetic network is crucial for studying virus adaptation in different human populations and environments. A recent study claimed that three genetic types of the virus were circulating around the world [16]. Three central variants differing in amino acid changes were named A, B, and C, with variant A being an extra-group coronavirus by hereditary type, it is similar to bat viruses. Variants of the virus A and C are found in significant proportions outside of East Asia, that is, in Europeans and Americans. In contrast, type B is the most common type in East Asia, and its inherited genome does not appear to have spread beyond East Asia without prior mutation to derived types B, which indicates the ecological stability of this type of pathogen outside of Asia [16]. A study of the geographical features of SARSCoV-2 variations will provide information on the development of vaccines for different populations. According to van Doremalen N. SARS-CoV-2 is a resistant microorganism and can remain viable for from 2 hours to 14 days, depending on the objects contaminated with viruses that are exposed to the risk of infection, as well as on weather conditions [2-1]. The transmission potential of an infection in a community is based on its base rate of reproduction, which is usually referred to as the disease transmission rate (R0). This coefficient represents the number of secondary cases that occurred in the susceptible population. According to Li Q. and co-authors (R0 - R zero) COVID-19 is 2.2 [11]. Direct cytopathic effects of SARS-CoV-2 or indirect systemic inflammatory and immune-mediated cellular responses leading toorgan and tissue damage [2, 2], as well as drug-induced effects determine the pulmonary and extrapulmonary symptoms of the COVID-19 clinical picture. The hepatobiliary component of the new coronavirus infection COVID-19 According to Fan Z. It has been noted that an increasing number of patients with COVID-19 experience liver injuries ranging from a spectrum of mild to severe injuries [14]. According to the American College of Gastroenterology (ACG), abnormal liver enzymes are seen in 20-30% of people with confirmed COVID-19 infection [11-5]. In a study that examined 148 confirmed patients infected with SARS-CoV-2 in China, Fan Z. The authors and co-authors found liver function disorders in 50.7% of patients upon admission to the hospital [14]. Additional scientific studies have shown similar results with hepatic hyperermentemia and an increase in total bilirubin [10,15,18,23]. Patients with elevated liver function tests were more likely to have moderate-to-high fever, and these increases in body temperature

were more common in men - 68.67% versus 38.36% in women. In addition, CD4 + and CD8 + T-cell counts were significantly lower in these patients compared to those without impaired liver function tests [14]. According to ACG data, a decrease in the number of white blood cells is observed in COVID-19 infection, and an increased level of white blood cells is considered a poor prognostic sign [5]. Research by Zhang C. The authors of the study and their colleagues have shown that most liver injuries are mild and transient, but serious liver damage can also occur [2, 2]. A higher degree of liver damage was observed in severe cases of COVID-19, when it may be necessary to prescribe hepatoprotective drugs [25]. The ultimate mechanism by which liver damage occurs in COVID-19 patients is unclear. ACE2 expression in cholangiocytes was shown to be much higher than in hepatocytesand comparable to the level of ACE2 expression in alveolocytes 2 types [19,20]. Among the possible factors of damage, the virus-induced effect due to ACE2-mediated direct viral infection of hepatocytes, systemic inflammation "cytokine storm", hypoxia, hypovolemia, hypotension in shock, drug-induced hepatotoxicity, etc. are considered [2-5]. Liver damage can also occur when ACE2 expression in liver tissue is increased, as a manifestation of compensatory proliferation of hepatocytesoriginatingfrombile duct epithelial cells [2-6]. While SARSCoV-2 can cause dysregulation of liver function by directly binding to ACE2 receptor cholangiocytes, histological examination of a liver biopsy obtained from a deceased patient with COVID-19 did not reveal viral inclusions in hepatocytes, manifestations of microvesicular steatosis and mild lobular activity were detected [25]. In addition, in critically ill patients with COVID-19, hepatocellular damage or even liver failure may be secondary to hypotension and immune-mediated inflammation, due to the "cytokine storm" or hypoxia associated with pneumonia [22]. Finally, drug-induced hepatotoxicity may play a role in increasing the activity of liver enzymes, including drugs such as remdesivir (an RNApolymerase inhibitorРНК) and hydroxychloroquine [7]. Patients with pre-existing liver disease are an important group of people who require additional attention [1]. According to Mao R. In a study of 1,099 patients with COVID-19, 23 had signs of hepatitis B virus infection, and these patients were 4 times more likely to have severe cases of COVID-19 compared to mild and moderate cases of novel coronavirus infection (2.4% vs. 0.6%) [33]. In addition, according to Zhang C. In COVID-19 patients with autoimmune hepatitis, the role of glucocorticoids in the treatment of diseases is currently unclear [52]. In the setting of primary biliary cholangitis, the presence of COVID19 can worsen cholestasis. Therefore, alkaline phosphatase and gamma-glutamyltransferase (GGT) levels should be carefully monitored in this category of Patients with weakened immune systems, cirrhosis of the liver, or cancer may be more susceptible to COVID19 [52]. In addition, the risk group includes patients who have undergone liver transplantation and are receiving immunesuppressants, patients with cirrhosis of the liver, the presence of acute liver failure on the background of chronic, hepatocellular carcinoma, and immunodeficiency [27,29,30]. Patients with non-alcoholic steatohepatitis (NASH) associated with comorbidities (diabetes, arterial hypertension, cardiovascular disorders) [3] are at high risk of SARSCoV infection and the development of a severe form of COVID-19 [24]. The fight against the global pandemic must include sharing and open access to scientific data and new technologies. Recently, the European Society for the Study of the Liver actively supported the COVID-Hep project, which was launched by the University of Oxford and is the creation of a registry to collect data on patients with liver diseases at any stage or liver transplantation with the presence of COVID-19 (information about the register can be found at: http://covid-hep.net). Pancreatic damage in COVID-19, the expression of ACE-2 in pancreatic tissue makes it a target for SARS-COV-2, with subsequent damage to both exocrine and endocrine functions. In a recent study by Wang F. in 52 patients with COVID-19 pneumonia, 17% of patients had signs of pancreatic damage, determined by an increase in the concentrationof amylase or blood lipase [1-4]. However, they did not have clinicalsymptoms of severe pancreatitis [2-4]. However, DeMadaria E. and co-authors, commenting on the data obtained by Wang F. The authors of the study, published in the Journal Neurology, state that increased amylase and lipase in patients with COVID19 may be associated with acidosis, renal failure, and gastroenteritis, especially if imaging showed a negative result for pancreatic damage [12]. Dioscoridi L. also agrees that hyperamylasemia and hyperlipazemia do not mean pancreatitis in the absence of symptoms and image correlation [13]. The ACE2 receptor is also highly expressed in pancreatic islet cells, so SARS-CoV-2 infection could theoretically cause islet damage leading to acute diabetes. According to Wang F. of the nine patients with pancreatic damage, six had elevatedblood glucose levels [1-4]. Mechanisms by which pancreatic damage can occur include direct cytopathic effects of SARS-CoV-2 or indirect systemic inflammatory and immune-mediated cellular

responses leading to organ damage or a second daryincrease in enzymes [22]. Antipyretic medications, which most patients in this study took prior to admission, may also cause drug-related pancreatic damage [13]. Further research is needed to definitively determine the effect of SARS-CoV-2 on pancreatic function and regulation. When examining one hundred and twenty-one COVID-19-positive patients, Liu F. et al. found high levels of amylase and lipase depending on the severity of the disease; however, no signs of pancreatic necrosis were observed during imaging [29]. In addition, the authors pointed to drug-induced damage to the pancreas due to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and or glucocorticoidsas a possible damaging factor. It was also emphasized that long-term exposure to the pancreas may worsen the course of systemic inflammation and ARDS in the presence of chronic pancreatitis [3]. Dioscoridi L. agrees with Liu F.'s opinion. and co-authors that, on the one hand, damage to the pancreas can contribute to a "cytokine storm" during pregnancy. COVID-19 is caused by activation of the complement system (as in acute pancreatitis) and subsequent deterioration of ARDS; on the other hand, chronic pancreatic damage may develop the same fibrosis mechanisms as in the lungs [13]. Mukherjee R. and co-authors concluded that the existing pancreatic dysfunction associated with COVID-19 may be the cause of an atypical "pancreatitis-like" clinical picture of the disease [30]. Hadi A. and co-authors, while excluding other possible causes, described acute pancreatitis associated with COVID19 in two out of three family members, first-line relatives [21]. Patel KP. et al. reported that gastrointestinal symptoms, including abdominal pain in 2.2% of patients, occur later than respiratory symptoms, without a clear physiopathological mechanism [31]. The American National Pancreatic Foundation on its website assessed that, on the one hand, acute pancreatitis may impair the immune response to COVID-19, and, on the other hand, chronic pancreatitis-related diabetes is a poor prognostic factor in COVID-19. Unfortunately, there is little data in the scientific literature on the development of acute pancreatitis against the background of a new coronavirus infection, which requires further research on the functional state of the pancreas in this disease. Therefore, the Aloysius MM message is very valuableAloysius. and co-authors on a case of COVID-19, with a clinical picture of acute pancreatitis (OP) without any other risk factors [6]. Aloysius MM et al. describe the medical history of a 36-year-old obese Spanish-speaking woman (body mass index = 35 kg / m2) who was admitted to the hospital with fever, dry cough, progressive shortness of breath, nausea, vomiting, and diarrhea for 8 days [6]. The patient also complained of severe stabbing pains in the epigastric region, radiating to the back for two days. Her only home remedy was an anxiolytic – , alprazolam. From the medical history, the patient denied taking alcohol, smoking. Physical examination showed tachycardia (110 / min), fever (38.8°C) with hypoxia (SaO2: 85% in indoor air) and scattered wheezing. Examination of the abdominal cavity revealed pronounced epigastric soreness. Laboratory studies were characterized by a more than three-fold increase in lipase (ULN = 82 u/L) and amylase (ULN = 103 u/L), as well as a minimal increase in AST and ALT levels. Triglyceride levels were within the normal range. Computed tomography of the chest and abdominal organs revealed signs of multifocal bilateral opacities in the form of" frosted glass " in the lungs, normal gallbladder, biliary tract, and unchanged pancreas, respectively . Later, a nasal swab for SARSCoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) gave a positive result. The patient was diagnosed with COVID-19associated severe acute pancreatitis and she was placed in the intensive care unit. That is, the patient's diagnosis was verified using not only laboratory, but also instrumental visualization of COVID-19 lung damage with an unchanged pancreas. As a result of medical treatment and oxygen therapy, the patient's condition improved, the need for oxygen decreased over the next two weeks, with a gradual resolution of gastrointestinal and pulmonary symptoms [6]. Conclusion. Thus, given that ACE2, the input receptor for the causative agent of the SARS-CoV-2 coronavirus, is expressed in many extrapulmonary tissues, direct damage to organs and tissues, including the liver and pancreas, is one of the likely mechanisms of their damage. In addition, endothelial damage and thromboinflammation, as well as dysregulation of immune responses, may contribute to the extrapulmonary manifestations of COVID19 [4]. Although COVID-19 is best known for causing significant respiratory pathology, it can also lead to varying degrees of functional changes in the liver and pancreas, which requires appropriate correction of diagnostic search and therapy.

List of literature

1. Aitbaev KA, Murkamilov IT, Fomin BB. Liver diseases: the pathogenetic role of the intestinal microbiome and the potential of therapy for its modulation // Therapeutic Archive, 2017, vol. 89, no. 8, pp. 120128.
2. Murkamilov IT, Aitbaev KA, Fomin BB. New coronavirus infection (COVID-19) and the nephrocerebral system / / The Scientific Heritage. 2020. № 46(3):43-49.
3. Sabirov I. S. Prakticheskieaspektyprimeneniya ezetimibe prinealkogol'noizhirovoiboleznipechei [Practical aspects of ezetimibe use in non-alcoholic fatty liver disease]. The Scientific Heritage. 2020, No. 47-2 (47), pp. 50-57.
4. Sabirov IP, Murkamilov IT, Fomin BB. The hepatobiliary system and the new coronavirus infection
5. Харибова Е. А., Тешаев Ш. Ж. Морфофункциональные особенности тканевой организации энтероэндокринных клеток в возрастном аспекте //Проблемы биологии и медицины. – 2020. – №. 2. – С. 168-173.
6. Харибова Е. А. Особенности морфологии нейрональных ансамблей в тройничном узле человека //Морфология. – 2011. – Т. 140. – №. 5. – С. 123-124.
7. Khodzhaeva D. I. Changes in the Vertebral Column and Thoracic Spinecells after Postponement of Mastoectomy //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 4. – С. 109-113.
8. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //БарқарорликваЕтакчиТадқиқотларонлайнилмийжурнали. – 2021. – Т. 1. – №. 1. – С. 85-89.
9. Ilkhomovna K. D. Morphological Features of Tumor in Different Treatment Options for Patients with Locally Advanced Breast Cancer //International Journal of Innovative Analyses and Emerging Technology. – 2021. – Т. 1. – №. 2. – С. 4-5.
10. Khodjayeva D. I. MORPHOLOGY OF IDIOPATHIC SCOLIOSIS BASED ON SEGMENT BY SEGMENT ASSESSMENT OF SPINAL COLUMN DEFORMITY //Scientific progress. – 2022. – Т. 3. – №. 1. – С. 208-215.
11. Ходжаева Д. И. СОВРЕМЕННЫЕ ВОЗМОЖНОСТИ УЛЬТРАЗВУКОВОЙ ДИАГНОСТИКИ ПРИ РАКЕ КОЖИ ЛИЦА //Жизнеобеспечение при критических состояниях. – 2019. – С. 111-112.
12. Aslonov S. G. et al. Modern Approaches to Oropharyngeal Cancer Therapy //International Journal of Discoveries and Innovations in Applied Sciences. – 2021. – Т. 1. – №. 3. – С. 38-39.
13. Khodjaeva D. I. MAGNETIC-RESONANCE IMAGING IN THE DIAGNOSIS OF BREAST CANCER AND ITS METASTASIS TO THE SPINAL COLUMN //Scientific progress. – 2021. – Т. 2. – №. 6. – С. 540-547.
14. Sadulloeva I. K., Ashurova N. G. CLINICAL AND IMMUNOLOGICAL FEATURES OF CONGENITAL HEART DEFECTS IN ADOLESCENT GIRLS //Europe's Journal of Psychology. – 2021. – Т. 17. – №. 3. – С. 172-177.
15. Kurbanovna S. I. THYMOGENIC IMMUNOCORRECTION OF CHILDREN WITH CONGENITAL HEART DEFECTS //ResearchJet Journal of Analysis and Inventions. – 2022. – Т. 3. – №. 1. – С. 34-43.
16. Kurbanovna S. I. Functioning of the Immune System in Children, After Surgical Correction of Congenital Heart Defects //European Journal of Life Safety and Stability (2660-9630). – 2021. – Т. 12. – С. 439-446.
17. Хамраева Д. Р. ЧАСТОТА РАСПРОСТРАНЕНИЯ ФУНКЦИОНАЛЬНЫХ ЗАПОРОВ У ДЕТЕЙ В БУХАРСКОЙ ОБЛАСТИ //Опыт и перспективы развития экспортного потенциала образовательных услуг в высшем образовании. – 2021. – С. 227-232.

18. Хамраева Д. Р. Частота распространения и особенности течения функциональных заболеваний билиарного тракта при синдроме Жильбера //Интернаука. Молодой исследователь: вызовы и перспективы.-2020.06. – 2020. – Т. 23. – №. 170. – С. 35-38.
19. AtoyevaM. A.,Jumamuratova B. S. Psychoemotional factors related to COVID-19 quarantine //апрель-июнь. – 2021. – С. 98.
20. Atayeva M. A. Cardiomyopathy as a Manifestation of Complications of Chronic Viral Hepatitis //American Journal of Medicine and Medical Sciences. – 2020. – Т. 10. – №. 4. – С. 258-261.
21. ATOEVA M. A., BARATOVA M. S., JUMAMURATOVA B. S. PREVALENCE OF VIRAL HEPATITIS" B" AND" C" AMONG MEDICAL WORKERS //Journal of natural remedies. – 2021. – Т. 22. – №. 1 (2). – С. 54-59.
22. Баратова М. С. и др. Эффективность тиотриазолина при аритмиях //Вестник Совета молодых учёных и специалистов Челябинской области. – 2016. – Т. 1. – №. 2 (13).
23. Baratova M. S. et al. Periodontal diseases in military age persons and arterial hypertension //Asian Journal of Multidimensional Research (AJMR). – 2020. – Т. 9. – №. 4. – С. 111-113.
24. Баратова М. С., Атаева М. А., Худойдодова С. Г. Допплерграфия в диагностики нарушений функции миокарда левого желудочка после перенесенных инфекционных состояний //Tibbiyotdayangikun. – 2017. – №. 4. – С. 84-87.
25. Баратова М. С., Атаева М. А. РОЛЬ ОРВИ И ГРИППА В ФОРМИРОВАНИИ ОСЛОЖНЕНИЙ СЕРДЕЧНО-СОСУДИСТЫХ ЗАБОЛЕВАНИЙ //Редакционная коллегия. – 2018. – С. 35.
26. Жумамуратова Б. С. ИЗУЧЕНИЕ ПРИЧИНЫ СМЕРТНОСТИ ОТ COVID-19 И КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКАЯ ОЦЕНКА //БарқарорликваЕтакчиТадқиқотлар онлайн илмийжурнали. – 2022. – Т. 2. – №. 1. – С. 390-395.
27. Ёмгурова О. Р. Клинико-Иммунологического Обследованияу Детей С Дерматитом И Бранхиальной Астмой //БарқарорликваЕтакчиТадқиқотлар онлайн илмийжурнали. – 2021. – Т. 1. – №. 6. – С. 460-468.
28. Yomgurova O. R. CLINICAL, IMMUNOLOGICAL AND MEDICO-SOCIAL ASPECTS OF ALLERGIC DISEASES IN CHILDREN //湖南大学学报 (自然科学版). – 2021. – Т. 48. – №. 7.
29. Yomgurova O. R. ALLERGIC DISEASES IN INDUSTRIAL ZONES, IN THE POPULATION AROUND THE AFFECTED AREAS //Central Asian Journal of Medicine. – 2021. – Т. 2021. – №. 2. – С. 102-109.
30. Bakhadurovna H. D., Akmalovna I. G. THE ROLE OF MULTIGENIC THROMBOPHILIA IN WOMEN WITH UNFAVORABLE OUTCOMES AFTER EXTRACORPOREAL FERTILIZATION //ResearchJet Journal of Analysis and Inventions. – 2022. – Т. 3. – №. 1. – С. 44-50.
31. Rajabturdievna Y. O. CHILDREN WITH ALLERGIC BRONCHIAL ASTHMA AND ATOPIC DERMATITIS IgA, IgM, IgG LEVELS //EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE. – 2021. – Т. 1. – №. 1. – С. 61-66.