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**1. Discovering drugs to treat coronavirus disease 2019 (COVID-19).**

**Authors** Dong, Liying; Hu, Shasha; Gao, Jianjun
**Source** Drug discoveries & therapeutics; 2020; vol. 14 (no. 1); p. 58-60
**Publication Date** 2020
**Publication Type(s)** Journal Article
**PubMedID** 32147628
**Database** Medline
Available at Drug discoveries & therapeutics from Unpaywall
**Abstract** The SARS-CoV-2 virus emerged in December 2019 and then spread rapidly worldwide, particularly to China, Japan, and South Korea. Scientists are endeavoring to find antivirals specific to the virus. Several drugs such as chloroquine, arbidol, remdesivir, and favipiravir are currently undergoing clinical studies to test their efficacy and safety in the treatment of coronavirus disease 2019 (COVID-19) in China; some promising results have been achieved thus far. This article summarizes agents with potential efficacy against SARS-CoV-2.

**2. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro.**

**Authors** Liu, Jia; Cao, Ruiyuan; Xu, Mingyue; Wang, Xi; Zhang, Huanyu; Hu, Hengrui; Li, Yufeng; Hu, Zhihong; Zhong, Wu; Wang, Manli
**Source** Cell discovery; 2020; vol. 6 ; p. 16
**Publication Date** 2020
**Publication Type(s)** Journal Article
**PubMedID** 32194981
**Database** Medline
Available at Cell discovery from Europe PubMed Central - Open Access
Available at Cell discovery from Nature (Open Access)
Available at Cell discovery from ProQuest (Health Research Premium) - NHS Version
Available at Cell discovery from Unpaywall

**3. Clinical considerations for patients with diabetes in times of COVID-19 epidemic**

**Authors** Gupta R.; Ghosh A.; Misra A.; Singh A.K.
**Source** Diabetes and Metabolic Syndrome: Clinical Research and Reviews; 2020; vol. 14 (no. 3); p. 211-212
**Publication Date** 2020
**Publication Type(s)** Review
**PubMedID** 32172175
**Database** EMBASE
Available at Diabetes & metabolic syndrome from ClinicalKey
Available at Diabetes & metabolic syndrome from Unpaywall

**4. The Trial of Chloroquine in the Treatment of Corona Virus Disease 2019 （COVID-19） and Its Research Progress in Forensic Toxicology.**

**Authors** Duan, Y J; Liu, Q; Zhao, S Q; Huang, F; Ren, L; Liu, L; Zhou, Y W
**Source** Fa yi xue za zhi; Mar 2020; vol. 36 (no. 2)
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article Review
**PubMedID** 32212513
**Database** Medline
**Abstract** AbstractChloroquine is a long-established prescription drug that is often used clinically to treat malaria and connective tissue diseases. Since December 2019, COVID-19 （corona virus disease 2019） outbreaks caused by SARS-CoV-2 （severe acute respiratory syndrome coronavirus 2） has occurred in China and many countries around the world. Due to the lack of drugs against COVID-19, the disease spreads rapidly and the mortality rate is relatively high. Therefore, specific drugs against SARS-CoV-2 need to be quickly screened. The antimalarial drug Chloroquine phosphate which has already been approved is confirmed to have an anti-SARS-CoV-2 effect and has been included in diagnostic and therapeutic guidelines. However, awareness of the risk of chloroquine phosphate causing acute poisoning or even death should be strengthened. The dosage used according to current clinical recommended dosage and course of treatment are larger than that of previous treatment of malaria. Many provinces have required close clinical monitoring of adverse reactions. This paper reviews the pharmacological effects, poisoning and toxicological mechanisms, in vivo metabolism and distribution, and forensic issues of chloroquine drugs, in order to provide help to forensic practice and clinical work.

**5. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Facts and myths.**

**Authors** Lai, Chih-Cheng; Liu, Yen Hung; Wang, Cheng-Yi; Wang, Ya-Hui; Hsueh, Shun-Chung; Yen, Muh-Yen; Ko, Wen-Chien; Hsueh, Po-Ren
**Source** Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article Review
**PubMedID** 32173241
**Database** Medline
Available at Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi from ClinicalKey
Available at Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi from Unpaywall
**Abstract** Since the emergence of coronavirus disease 2019 (COVID-19) (formerly known as the 2019 novel coronavirus [2019-nCoV]) in Wuhan, China in December 2019, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), more than 75,000 cases have been reported in 32 countries/regions, resulting in more than 2000 deaths worldwide. Despite the fact that most COVID-19 cases and mortalities were reported in China, the WHO has declared this outbreak as the sixth public health emergency of international concern. The COVID-19 can present as an asymptomatic carrier state, acute respiratory disease, and pneumonia. Adults represent the population with the highest infection rate; however, neonates, children, and elderly patients can also be infected by SARS-CoV-2. In addition, nosocomial infection of hospitalized patients and healthcare workers, and viral transmission from asymptomatic carriers are possible. The most common finding on chest imaging among patients with pneumonia was ground-glass opacity with bilateral involvement. Severe cases are more likely to be older patients with underlying comorbidities compared to mild cases. Indeed, age and disease severity may be correlated with the outcomes of COVID-19. To date, effective treatment is lacking; however, clinical trials investigating the efficacy of several agents, including remdesivir and chloroquine, are underway in China. Currently, effective infection control intervention is the only way to prevent the spread of SARS-CoV-2.

**6. New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?**

**Authors** Devaux, Christian A; Rolain, Jean-Marc; Colson, Philippe; Raoult, Didier
**Source** International journal of antimicrobial agents; Mar 2020 ; p. 105938
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32171740
**Database** Medline
Available at International journal of antimicrobial agents from ClinicalKey
Available at International journal of antimicrobial agents from Unpaywall
**Abstract** Recently, a novel coronavirus (2019-nCoV), officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in China. Despite drastic containment measures, the spread of this virus is ongoing. SARS-CoV-2 is the aetiological agent of coronavirus disease 2019 (COVID-19) characterised by pulmonary infection in humans. The efforts of international health authorities have since focused on rapid diagnosis and isolation of patients as well as the search for therapies able to counter the most severe effects of the disease. In the absence of a known efficient therapy and because of the situation of a public-health emergency, it made sense to investigate the possible effect of chloroquine/hydroxychloroquine against SARS-CoV-2 since this molecule was previously described as a potent inhibitor of most coronaviruses, including SARS-CoV-1. Preliminary trials of chloroquine repurposing in the treatment of COVID-19 in China have been encouraging, leading to several new trials. Here we discuss the possible mechanisms of chloroquine interference with the SARS-CoV-2 replication cycle.

**7. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).**

**Authors** Yao, Xueting; Ye, Fei; Zhang, Miao; Cui, Cheng; Huang, Baoying; Niu, Peihua; Liu, Xu; Zhao, Li; Dong, Erdan; Song, Chunli; Zhan, Siyan; Lu, Roujian; Li, Haiyan; Tan, Wenjie; Liu, Dongyang
**Source** Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32150618
**Database** Medline
Available at Clinical infectious diseases : an official publication of the Infectious Diseases Society of America from Unpaywall

**Abstract** BACKGROUNDThe Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) first broke out in Wuhan (China) and subsequently spread worldwide. Chloroquine has been sporadically used in treating SARS-CoV-2 infection. Hydroxychloroquine shares the same mechanism of action as chloroquine, but its more tolerable safety profile makes it the preferred drug to treat malaria and autoimmune conditions. We propose that the immunomodulatory effect of hydroxychloroquine also may be useful in controlling the cytokine storm that occurs late-phase in critically ill SARS-CoV-2 infected patients. Currently, there is no evidence to support the use of hydroxychloroquine in SARS-CoV-2 infection.METHODSThe pharmacological activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2 infected Vero cells. Physiologically-based pharmacokinetic models (PBPK) were implemented for both drugs separately by integrating their in vitro data. Using the PBPK models, hydroxychloroquine concentrations in lung fluid were simulated under 5 different dosing regimens to explore the most effective regimen whilst considering the drug's safety profile.RESULTSHydroxychloroquine (EC50=0.72 μM) was found to be more potent than chloroquine (EC50=5.47 μM) in vitro. Based on PBPK models results, a loading dose of 400 mg twice daily of hydroxychloroquine sulfate given orally, followed by a maintenance dose of 200 mg given twice daily for 4 days is recommended for SARS-CoV-2 infection, as it reached three times the potency of chloroquine phosphate when given 500 mg twice daily 5 days in advance.CONCLUSIONSHydroxychloroquine was found to be more potent than chloroquine to inhibit SARS-CoV-2 in vitro.

**8. Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy.**

**Authors** Dashraath, Pradip; Jing Lin Jeslyn, Wong; Mei Xian Karen, Lim; Li Min, Lim; Sarah, Li; Biswas, Arijit; Arjandas Choolani, Mahesh; Mattar, Citra; Lin, Su Lin
**Source** American journal of obstetrics and gynecology; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32217113
**Database** Medline
Available at American journal of obstetrics and gynecology from ClinicalKey
Available at American journal of obstetrics and gynecology from Queen Elizabeth the Queen Mother Hospital Library (lib327275) Local Print Collection [location] : QEQM.
Available at American journal of obstetrics and gynecology from Unpaywall

**Abstract** The current coronavirus disease 2019 (COVID-19) pneumonia pandemic, caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) virus, is spreading globally at an accelerated rate, with a basic reproduction number (R0) of 2 - 2.5, indicating that 2 - 3 persons will be infected from an index patient. A serious public health emergency, it is particularly deadly in vulnerable populations and communities in which healthcare providers are insufficiently prepared to manage the infection. As of March 16, 2020, there are more than 180,000 confirmed cases of COVID-19 worldwide, with over 7,000 related deaths. The SARS-CoV-2 virus has been isolated from asymptomatic individuals, and affected patients continue to be infectious two weeks after cessation of symptoms. The substantial morbidity and socioeconomic impact have necessitated drastic measures across all continents, including nationwide lockdowns and border closures. Pregnant women and their fetuses represent a high-risk population during infectious disease outbreaks. To date, the outcomes of 55 pregnant women infected with COVID-19 and 46 neonates have been reported in the literature, with no definite evidence of vertical transmission. Physiological and mechanical changes in pregnancy increase susceptibility to infections in general, particularly when the cardiorespiratory system is affected, and encourage rapid progression to respiratory failure in the gravida. Furthermore, the pregnancy bias towards T-helper 2 (Th2) system dominance which protects the fetus, leaves the mother vulnerable to viral infections, which are more effectively contained by the Th1 system. These unique challenges mandate an integrated approach to pregnancies affected by SARS-CoV-2. Here we present a review of COVID-19 in pregnancy, bringing together the various factors integral to the understanding of pathophysiology and susceptibility, diagnostic challenges with real-time reverse transcriptase polymerase chain reaction (RT-PCR) assays, therapeutic controversies, intrauterine transmission and maternal-fetal complications. We discuss the latest options in antiviral therapy and vaccine development, including the novel use of chloroquine in the management of COVID-19. Fetal surveillance, in view of the predisposition to growth restriction and special considerations during labor and delivery are addressed. Additionally, we focus on keeping frontline obstetric care providers safe while continuing to provide essential services. Our clinical service model is built around the principles of workplace segregation, responsible social distancing, containment of cross-infection to healthcare providers, judicious use of personal protective equipment and telemedicine. Our aim is to share a framework which can be adopted by tertiary maternity units managing pregnant women in the flux of a pandemic while maintaining the safety of the patient and healthcare provider at its core.

**9. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19).**

**Authors** Inciardi, Riccardo M; Lupi, Laura; Zaccone, Gregorio; Italia, Leonardo; Raffo, Michela; Tomasoni, Daniela; Cani, Dario S; Cerini, Manuel; Farina, Davide; Gavazzi, Emanuele; Maroldi, Roberto; Adamo, Marianna; Ammirati, Enrico; Sinagra, Gianfranco; Lombardi, Carlo M; Metra, Marco

**Source** JAMA cardiology; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32219357
**Database** Medline
**Abstract** ImportanceVirus infection has been widely described as one of the most common causes of myocarditis. However, less is known about the cardiac involvement as a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.ObjectiveTo describe the presentation of acute myocardial inflammation in a patient with coronavirus disease 2019 (COVID-19) who recovered from the influenzalike syndrome and developed fatigue and signs and symptoms of heart failure a week after upper respiratory tract symptoms.Design, Setting, and ParticipantThis case report describes an otherwise healthy 53-year-old woman who tested positive for COVID-19 and was admitted to the cardiac care unit in March 2020 for acute myopericarditis with systolic dysfunction, confirmed on cardiac magnetic resonance imaging, the week after onset of fever and dry cough due to COVID-19. The patient did not show any respiratory involvement during the clinical course.ExposureCardiac involvement with COVID-19.Main Outcomes and MeasuresDetection of cardiac involvement with an increase in levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) and high-sensitivity troponin T, echocardiography changes, and diffuse biventricular myocardial edema and late gadolinium enhancement on cardiac magnetic resonance imaging.ResultsAn otherwise healthy 53-year-old white woman presented to the emergency department with severe fatigue. She described fever and dry cough the week before. She was afebrile but hypotensive; electrocardiography showed diffuse ST elevation, and elevated high-sensitivity troponin T and NT-proBNP levels were detected. Findings on chest radiography were normal. There was no evidence of obstructive coronary disease on coronary angiography. Based on the COVID-19 outbreak, a nasopharyngeal swab was performed, with a positive result for SARS-CoV-2 on real-time reverse transcriptase-polymerase chain reaction assay. Cardiac magnetic resonance imaging showed increased wall thickness with diffuse biventricular hypokinesis, especially in the apical segments, and severe left ventricular dysfunction (left ventricular ejection fraction of 35%). Short tau inversion recovery and T2-mapping sequences showed marked biventricular myocardial interstitial edema, and there was also diffuse late gadolinium enhancement involving the entire biventricular wall. There was a circumferential pericardial effusion that was most notable around the right cardiac chambers. These findings were all consistent with acute myopericarditis. She was treated with dobutamine, antiviral drugs (lopinavir/ritonavir), steroids, chloroquine, and medical treatment for heart failure, with progressive clinical and instrumental stabilization.Conclusions and RelevanceThis case highlights cardiac involvement as a complication associated with COVID-19, even without symptoms and signs of interstitial pneumonia.

**10. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies.**

**Authors** Gao, Jianjun; Tian, Zhenxue; Yang, Xu
**Source** Bioscience trends; Mar 2020; vol. 14 (no. 1); p. 72-73
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32074550
**Database** Medline
Available at Bioscience trends from Unpaywall
**Abstract** The coronavirus disease 2019 (COVID-19) virus is spreading rapidly, and scientists are endeavoring to discover drugs for its efficacious treatment in China. Chloroquine phosphate, an old drug for treatment of malaria, is shown to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicenter clinical trials conducted in China. The drug is recommended to be included in the next version of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China for treatment of COVID-19 infection in larger populations in the future.

**11. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19.**

**Authors** Cortegiani, Andrea; Ingoglia, Giulia; Ippolito, Mariachiara; Giarratano, Antonino; Einav, Sharon
**Source** Journal of critical care; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32173110
**Database** Medline
Available at Journal of critical care from ClinicalKey
Available at Journal of critical care from Unpaywall

**Abstract** PURPOSECOVID-19 (coronavirus disease 2019) is a public health emergency of international concern. As of this time, there is no known effective pharmaceutical treatment, although it is much needed for patient contracting the severe form of the disease. The aim of this systematic review was to summarize the evidence regarding chloroquine for the treatment of COVID-19.METHODSPubMed, EMBASE, and three trial Registries were searched for studies on the use of chloroquine in patients with COVID-19.RESULTSWe included six articles (one narrative letter, one in-vitro study, one editorial, expert consensus paper, two national guideline documents) and 23 ongoing clinical trials in China. Chloroquine seems to be effective in limiting the replication of SARS-CoV-2 (virus causing COVID-19) in vitro.CONCLUSIONSThere is rationale, pre-clinical evidence of effectiveness and evidence of safety from long-time clinical use for other indications to justify clinical research on chloroquine in patients with COVID-19. However, clinical use should either adhere to the Monitored Emergency Use of Unregistered Interventions (MEURI) framework or be ethically approved as a trial as stated by the World Health Organization. Safety data and data from high-quality clinical trials are urgently needed.

**12. COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression.**

**Authors** Zhou, Dan; Dai, Sheng-Ming; Tong, Qiang
**Source** The Journal of antimicrobial chemotherapy; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32196083
**Database** Medline
Available at The Journal of antimicrobial chemotherapy from Unpaywall
**Abstract** A novel coronavirus disease (COVID-19), caused by infection with SARS-CoV-2, has swept across 31 provinces in China and over 40 countries worldwide. The transition from first symptoms to acute respiratory distress syndrome (ARDS) is highly likely to be due to uncontrolled cytokine release. There is an urgent need to identify safe and effective drugs for treatment. Chloroquine (CQ) exhibits a promising inhibitory effect. However, the clinical use of CQ can cause severe side effects. We propose that hydroxychloroquine (HCQ), which exhibits an antiviral effect highly similar to that of CQ, could serve as a better therapeutic approach. HCQ is likely to attenuate the severe progression of COVID-19, inhibiting the cytokine storm by suppressing T cell activation. It has a safer clinical profile and is suitable for those who are pregnant. It is cheaper and more readily available in China. We herein strongly urge that clinical trials are performed to assess the preventive effects of HCQ in both disease infection and progression.

**13. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial.**

**Authors** Gautret, Philippe; Lagier, Jean-Christophe; Parola, Philippe; Hoang, Van Thuan; Meddeb, Line; Mailhe, Morgane; Doudier, Barbara; Courjon, Johan; Giordanengo, Valérie; Vieira, Vera Esteves; Dupont, Hervé Tissot; Honoré, Stéphane; Colson, Philippe; Chabrière, Eric; La Scola, Bernard; Rolain, Jean-Marc; Brouqui, Philippe; Raoult, Didier
**Source** International journal of antimicrobial agents; Mar 2020 ; p. 105949
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32205204
**Database** Medline
Available at International journal of antimicrobial agents from ClinicalKey
Available at International journal of antimicrobial agents from Unpaywall
**Abstract** BACKGROUNDChloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2, and reported to be efficient in Chinese COV-19 patients. We evaluate the role of hydroxychloroquine on respiratory viral loads.PATIENTS AND METHODSFrench Confirmed COVID-19 patients were included in a single arm protocol from early March to March 16th, to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment. Untreated patients from another center and cases refusing the protocol were included as negative controls. Presence and absence of virus at Day6-post inclusion was considered the end point.RESULTSSix patients were asymptomatic, 22 had upper respiratory tract infection symptoms and eight had lower respiratory tract infection symptoms. Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls, and much lower average carrying duration than reported of untreated patients in the literature. Azithromycin added to hydroxychloroquine was significantly more efficient for virus elimination.CONCLUSIONDespite its small sample size our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.

**14. Of chloroquine and COVID-19.**

**Authors** Touret, Franck; de Lamballerie, Xavier
**Source** Antiviral research; Mar 2020; vol. 177 ; p. 104762
**Publication Date** Mar 2020

**Publication Type(s)** Journal Article Review
**PubMedID** 32147496
**Database** Medline
Available at Antiviral research from Unpaywall
**Abstract** Recent publications have brought attention to the possible benefit of chloroquine, a broadly used antimalarial drug, in the treatment of patients infected by the novel emerged coronavirus (SARS-CoV-2). The scientific community should consider this information in light of previous experiments with chloroquine in the field of antiviral research.

**15. Chloroquine for the 2019 novel coronavirus SARS-CoV-2.**

**Authors** Colson, Philippe; Rolain, Jean-Marc; Raoult, Didier
**Source** International journal of antimicrobial agents; Mar 2020; vol. 55 (no. 3); p. 105923
**Publication Date** Mar 2020
**Publication Type(s)** Editorial Comment
**PubMedID** 32070753
**Database** Medline
Available at International journal of antimicrobial agents from ClinicalKey
Available at International journal of antimicrobial agents from Unpaywall

**16. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia].**

**Authors** multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia
**Source** Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases; Mar 2020; vol. 43 (no. 3); p. 185-188
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32164085
**Database** Medline
**Abstract** At the end of December 2019, a novel coronavirus (COVID-19) caused an outbreak in Wuhan, and has quickly spread to all provinces in China and 26 other countries around the world, leading to a serious situation for epidemic prevention. So far, there is still no specific medicine. Previous studies have shown that chloroquine phosphate (chloroquine) had a wide range of antiviral effects, including anti-coronavirus. Here we found that treating the patients diagnosed as novel coronavirus pneumonia with chloroquine might improve the success rate of treatment, shorten hospital stay and improve patient outcome. In order to guide and regulate the use of chloroquine in patients with novel coronavirus pneumonia, the multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia developed this expert consensus after extensive discussion. It recommended chloroquine phosphate tablet, 500mg twice per day for 10 days for patients diagnosed as mild, moderate and severe cases of novel coronavirus pneumonia and without contraindications to chloroquine.

**17. Controversial treatments: an updated understanding of the Coronavirus Disease 2019.**

**Authors** Zhang, Cantong; Huang, Shaoying; Zheng, Fengping; Dai, Yong
**Source** Journal of medical virology; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article Review
**PubMedID** 32219882
**Database** Medline
**Abstract** An outbreak of severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) infection has posed significant threats to international health and the economy. In the absence of specific treatment for this virus, there is an urgent need to learn from the experience and lessons in China. To reduce the case-fatality rate among COVID-19 patients, we should not ignore the complications, such as RNAaemia, acute respiratory distress syndrome, and multiple organ dysfunction. To help understand the advantages and limitations of differential treatments, we provide a timely review and discuss the complications and corresponding major treatments, especially controversial ones such as antiviral therapy (remdesivir, ribavirin, chloroquine), glucocorticoid therapy, extracorporeal support including an artificial liver system (ALS) and extracorporeal membrane oxygenation (ECMO), based on available evidence. As a result, we suggest that antiviral therapy and organ function support are vital to reduce mortality for mild patients and critical patients, respectively. 

**18. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro.**

**Authors** Wang, Manli; Cao, Ruiyuan; Zhang, Leike; Yang, Xinglou; Liu, Jia; Xu, Mingyue; Shi, Zhengli; Hu, Zhihong; Zhong, Wu; Xiao, Gengfu

**Source** Cell research; Mar 2020; vol. 30 (no. 3); p. 269-271
**Publication Date** Mar 2020
**Publication Type(s)** Research Support, Non-u.s. Gov't Letter
**PubMedID** 32020029
**Database** Medline
Available at Cell research from Unpaywall

**19. Aminoquinolines Against Coronavirus Disease 2019 (COVID-19): Chloroquine or Hydroxychloroquine.**

**Authors** Sahraei, Zahra; Shabani, Minoosh; Shokouhi, Shervin; Saffaei, Ali
**Source** International journal of antimicrobial agents; Mar 2020 ; p. 105945
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32194152
**Database** Medline
Available at International journal of antimicrobial agents from ClinicalKey
Available at International journal of antimicrobial agents from Unpaywall

**20. Could chloroquine /hydroxychloroquine be harmful in Coronavirus Disease 2019 (COVID-19) treatment?**

**Authors** Guastalegname, Maurizio; Vallone, Alfredo
**Source** Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32211771
**Database** Medline

**21. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19.**

**Authors** Colson, Philippe; Rolain, Jean-Marc; Lagier, Jean-Christophe; Brouqui, Philippe; Raoult, Didier
**Source** International journal of antimicrobial agents; Mar 2020 ; p. 105932
**Publication Date** Mar 2020
**Publication Type(s)** Editorial
**PubMedID** 32145363
**Database** Medline
Available at International journal of antimicrobial agents from ClinicalKey
Available at International journal of antimicrobial agents from Unpaywall

**22. Insights from nanomedicine into chloroquine efficacy against COVID-19.**

**Authors** Hu, Tony Y; Frieman, Matthew; Wolfram, Joy
**Source** Nature nanotechnology; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32203437
**Database** Medline

**23. Covid-19: six million doses of hydroxychloroquine donated to US despite lack of evidence.**

**Authors** Mahase, Elisabeth
**Source** BMJ (Clinical research ed.); Mar 2020; vol. 368 ; p. m1166
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32205321
**Database** Medline
Available at BMJ (Clinical research ed.) from BMJ Journals
Available at BMJ (Clinical research ed.) from Unpaywall

**24. Is Hydroxychloroquine a possible post-exposure prophylaxis drug to limit the transmission to health care workers exposed to COVID19?**

**Authors** Pagliano, Pasquale; Piazza, Ornella; De Caro, Francesco; Ascione, Tiziana; Filippelli, Amelia
**Source** Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Mar 2020
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article
**PubMedID** 32211764
**Database** Medline

**25. Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): A systematic review**

**Authors** Pang J.; Wang M.X.; Ang I.Y.H.; Tan S.H.X.; Lewis R.F.; Chen J.I.-P.; Gwee S.X.W.; Chua P.E.Y.; Yang Q.; Ng X.Y.; Yap R.K.S.; Tan H.Y.; Teo Y.Y.; Cook A.R.; Yap J.C.-H.; Hsu L.Y.; Gutierrez R.A.; Tan C.C.
**Source** Journal of Clinical Medicine; Mar 2020; vol. 9 (no. 3)
**Publication Date** Mar 2020
**Publication Type(s)** Review
**Database** EMBASE
Available at Journal of clinical medicine from Europe PubMed Central - Open Access
Available at Journal of clinical medicine from Unpaywall
**Abstract** Rapid diagnostics, vaccines and therapeutics are important interventions for the management of the 2019 novel coronavirus (2019-nCoV) outbreak. It is timely to systematically review the potential of these interventions, including those for Middle East respiratory syndrome-Coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS)-CoV, to guide policymakers globally on their prioritization of resources for research and development. A systematic search was carried out in three major electronic databases (PubMed, Embase and Cochrane Library) to identify published studies in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Supplementary strategies through Google Search and personal communications were used. A total of 27 studies fulfilled the criteria for review. Several laboratory protocols for confirmation of suspected 2019-nCoV cases using real-time reverse transcription polymerase chain reaction (RT-PCR) have been published. A commercial RT-PCR kit developed by the Beijing Genomic Institute is currently widely used in China and likely in Asia. However, serological assays as well as point-of-care testing kits have not been developed but are likely in the near future. Several vaccine candidates are in the pipeline. The likely earliest Phase 1 vaccine trial is a synthetic DNA-based candidate. A number of novel compounds as well as therapeutics licensed for other conditions appear to have in vitro efficacy against the 2019-nCoV. Some are being tested in clinical trials against MERS-CoV and SARS-CoV, while others have been listed for clinical trials against 2019-nCoV. However, there are currently no effective specific antivirals or drug combinations supported by high-level evidence.


**26. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges**

**Authors** Lai C.-C.; Shih T.-P.; Ko W.-C.; Tang H.-J.; Hsueh P.-R.
**Source** International Journal of Antimicrobial Agents; Mar 2020; vol. 55 (no. 3)
**Publication Date** Mar 2020
**Publication Type(s)** Review
**PubMedID** 32081636
**Database** EMBASE
Available at International journal of antimicrobial agents from ClinicalKey
Available at International journal of antimicrobial agents from Unpaywall
**Abstract** The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously provisionally named 2019 novel coronavirus or 2019-nCoV) disease (COVID-19) in China at the end of 2019 has caused a large global outbreak and is a major public health issue. As of 11 February 2020, data from the World Health Organization (WHO) have shown that more than 43 000 confirmed cases have been identified in 28 countries/regions, with >99% of cases being detected in China. On 30 January 2020, the WHO declared COVID-19 as the sixth public health emergency of international concern. SARS-CoV-2 is closely related to two bat-derived severe acute respiratory syndrome-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21. It is spread by human-to-human transmission via droplets or direct contact, and infection has been estimated to have mean incubation period of 6.4 days and a basic reproduction number of 2.24-3.58. Among patients with pneumonia caused by SARS-CoV-2 (novel coronavirus pneumonia or Wuhan pneumonia), fever was the most common symptom, followed by cough. Bilateral lung involvement with ground-glass opacity was the most common finding from computed tomography images of the chest. The one case of SARS-CoV-2 pneumonia in the USA is responding well to remdesivir, which is now undergoing a clinical trial in China. Currently, controlling infection to prevent the spread of SARS-CoV-2 is the primary intervention being used. However, public health authorities should keep monitoring the situation closely, as the more we can learn about this novel virus and its associated outbreak, the better we can respond.


**27. A Case of Novel Coronavirus Disease 19 in a Chronic Hemodialysis Patient Presenting with Gastroenteritis and Developing Severe Pulmonary Disease.**

**Authors** Ferrey AJ; Choi G; Hanna RM; Chang Y; Tantisattamo E; Ivaturi K; Park E; Nguyen L; Wang B; Tonthat S; Rhee CM; Reddy U; Lau WL; Huang SS; Gohil S; Amin AN; Hsieh L; Cheng TT; Lee RA; Kalantar-Zadeh K
**Source** American journal of nephrology; Mar 2020 ; p. 1-6
**Publication Date** Mar 2020
**Publication Type(s)** Journal Article

**PubMedID** 32222713
**Database** PubMed
**Abstract** Novel coronavirus disease 2019 (COVID-19) is a highly infectious, rapidly spreading viral disease with an alarming case fatality rate up to 5%. The risk factors for severe presentations are concentrated in patients with chronic kidney disease, particularly patients with end-stage renal disease (ESRD) who are dialysis dependent. We report the first US case of a 56-year-old nondiabetic male with ESRD secondary to IgA nephropathy undergoing thrice-weekly maintenance hemodialysis for 3 years, who developed COVID-19 infection. He has hypertension controlled with angiotensin receptor blocker losartan 100 mg/day and coronary artery disease status-post stent placement. During the first 5 days of his febrile disease, he presented to an urgent care, 3 emergency rooms, 1 cardiology clinic, and 2 dialysis centers in California and Utah. During this interval, he reported nausea, vomiting, diarrhea, and low-grade fevers but was not suspected of COVID-19 infection until he developed respiratory symptoms and was admitted to the hospital. Imaging studies upon admission were consistent with bilateral interstitial pneumonia. He was placed in droplet-eye precautions while awaiting COVID-19 test results. Within the first 24 h, he deteriorated quickly and developed acute respiratory distress syndrome (ARDS), requiring intubation and increasing respiratory support. Losartan was withheld due to hypotension and septic shock. COVID-19 was reported positive on hospital day 3. He remained in critical condition being treated with hydroxychloroquine and tocilizumab in addition to the standard medical management for septic shock and ARDS. Our case is unique in its atypical initial presentation and highlights the importance of early testing.

**28. Covid-19: what treatments are being investigated?**

**Authors** Mahase, Elisabeth
**Source** BMJ : British Medical Journal (Online); Mar 2020; vol. 368
**Publication Date** Mar 2020
**Publication Type(s)** News
**Database** BNI
Available at BMJ from BMJ Journals
**Abstract** The World Health Organization has now launched the SOLIDARITY trial to investigate four potential treatments: remdesivir, chloroquine/hydroxychloroquine; lopinavir and ritonavir; and lopinavir and ritonavir plus interferon-β.1 The trial will not be double blind, as WHO said it needed to find a balance between gold standard research practice and speed, but it will include thousands of patients from several countries. While it has previously been tested in vitro against a number of viruses, including SARS, and found to inhibit growth, no benefit has been seen in animal models.3 In a limited way, the drug has been tested against SARS-CoV-2—the cause of covid-19—and has reportedly been found "highly effective," although the evidence is still limited, with much of the data unpublished.45 Andrew Preston, reader in microbial pathogenesis at the University of Bath, said that while the early results are "promising" they have "yet to be fully scrutinised, and, of course, it is essential to conduct other, larger controlled trials to determine accurately the effectiveness of chloroquine as a treatment for covid-19. [...]chloroquine has subtle effects on a wide variety of immune cells. Ian Hall, professor of molecular medicine at the University of Nottingham, said, "The idea behind the trial is that by giving more of this molecule to the lung it could help reduce the severity of infection with covid-19, especially in those people who have reduced immune responses to the virus.

**29. [Expert consensus on chloroquine phosphate for the treatment of novel coronavirus pneumonia].**

**Authors** multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia
**Source** Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases; Feb 2020; vol. 43 (no. 0); p. E019
**Publication Date** Feb 2020
**Publication Type(s)** English Abstract Journal Article
**PubMedID** 32075365
**Database** Medline
**Abstract** At the end of December 2019, a novel coronavirus (COVID-19) caused an outbreak in Wuhan, and has quickly spread to all provinces in China and 26 other countries around the world, leading to a serious situation for epidemic prevention. So far, there is still no specific medicine. Previous studies have shown that chloroquine phosphate (chloroquine) had a wide range of antiviral effects, including anti-coronavirus. Here we found that treating the patients diagnosed as novel coronavirus pneumonia with chloroquine might improve the success rate of treatment, shorten hospital stay and improve patient outcome. In order to guide and regulate the use of chloroquine in patients with novel coronavirus pneumonia, the multicenter collaboration group of Department of Science and Technology of Guangdong Province and Health Commission of Guangdong Province for chloroquine in the treatment of novel coronavirus pneumonia developed this expert consensus after extensive discussion. It recommended chloroquine phosphate tablet, 500mg twice per day for 10 days for patients diagnosed as mild, moderate and severe cases of novel coronavirus pneumonia and without contraindications to chloroquine.

**30. A Systematic Review of therapeutic agents for the treatment of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

**Authors** Momattin H.; Al-Ali A.Y.; Al-Tawfiq J.A.
**Source** Travel Medicine and Infectious Disease; 2019; vol. 30 ; p. 9-18
**Publication Date** 2019
**Publication Type(s)** Article
**PubMedID** 31252170
**Database** EMBASE
Available at Travel medicine and infectious disease from ClinicalKey
Available at Travel medicine and infectious disease from Unpaywall
**Abstract** Background: The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first described in 2012 and attracted a great international attention due to multiple healthcare associated outbreaks. The disease carries a high case fatality rate of 34.5%, and there is no internationally or nationally recommended therapy.
Method(s): We searched MEDLINE, Science Direct, Embase and Scopus databases for relevant papers published till March 2019 describing in vitro, in vivo or human therapy of MERS.
Result(s): Initial search identified 62 articles: 52 articles were from Medline, 6 from Embase, and 4 from Science Direct. Based on the inclusions and exclusions criteria, 30 articles were included in the final review and comprised: 22 in vitro studies, 8 studies utilizing animal models, 13 studies in humans, and one study included both in vitro and animal model. There are a few promising therapeutic agents on the horizon. The combination of lopinavir/ritonavir and interferon-beta- 1b showed excellent results in common marmosets and currently is in a randomized control trial. Ribavirin and interferon were the most widely used combination and experience comes from a number of observational studies. Although, the data are heterogenous, this combination might be of potential benefit and deserve further investigation. There were no randomized clinical trials to recommend specific therapy for the treatment of MERS-CoV infection. Only one such study is planned for randomization and is pending completion. The study is based on a combination of lopinavir/ritonavir and interferon-beta- 1b. A fully human polyclonal IgG antibody (SAB-301) was safe and well tolerated in healthy individuals and this agent may deserve further testing for efficacy.
Conclusion(s): Despite multiple studies in humans there is no consensus on the optimal therapy for MERS-CoV. Randomized clinical trials are needed and potential therapies should be evaluated only in such clinical trials. In order to further enhance the therapeutic aroma for MERS-CoV infection, repurposing old drugs against MERS-CoV is an interesting strategy and deserves further consideration and use in clinical settings.


**31. High-throughput screening and identification of potent broad-spectrum inhibitors of coronaviruses**

**Authors** Shen L.; Niu J.; Huang B.; Wang W.; Zhu N.; Deng Y.; Wang H.; Ye F.; Tan W.; Wang C.; Cen S.
**Source** Journal of Virology; 2019; vol. 93 (no. 12)
**Publication Date** 2019
**Publication Type(s)** Article
**PubMedID** 30918074
**Database** EMBASE
Available at Journal of virology from Europe PubMed Central - Open Access
Available at Journal of virology from HighWire - Free Full Text
Available at Journal of virology from Unpaywall

**Abstract** Coronaviruses (CoVs) act as cross-species viruses and have the potential to spread rapidly into new host species and cause epidemic diseases. Despite the severe public health threat of severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome CoV (MERS-CoV), there are currently no drugs available for their treatment; therefore, broad-spectrum inhibitors of emerging and endemic CoVs are urgently needed. To search for effective inhibitory agents, we performed high-throughput screening (HTS) of a 2,000-compound library of approved drugs and pharmacologically active compounds using the established genetically engineered human CoV OC43 (HCoV-OC43) strain expressing Renilla luciferase (rOC43-ns2Del-Rluc) and validated the inhibitors using multiple genetically distinct CoVs in vitro. We screened 56 hits from the HTS data and validated 36 compounds in vitro using wild-type HCoV-OC43. Furthermore, we identified seven compounds (lycorine, emetine, monensin sodium, mycophenolate mofetil, mycophenolic acid, phenazopyridine, and pyrvinium pamoate) as broad-spectrum inhibitors according to their strong inhibition of replication by four CoVs in vitro at low-micromolar concentrations. Additionally, we found that emetine blocked MERS-CoV entry according to pseudovirus entry assays and that lycorine protected BALB/c mice against HCoV-OC43-induced lethality by decreasing viral load in the central nervous system. This represents the first demonstration of in vivo real-time bioluminescence imaging to monitor the effect of lycorine on the spread and distribution of HCoV-OC43 in a mouse model. These results offer critical information supporting the development of an effective therapeutic strategy against CoV infection. IMPORTANCE Currently, there is no approved therapy to treat coronavirus infection; therefore, broad-spectrum inhibitors of emerging and endemic CoVs are needed. Based on our high-throughput screening assay using a compound library, we identified seven compounds with broad-spectrum efficacy against the replication of four CoVs in vitro. Additionally, one compound (lycorine) was found to protect BALB/c mice against HCoV-OC43-induced lethality by decreasing viral load in the central nervous system. This inhibitor might offer promising therapeutic possibilities for combatting novel CoV infections in the future.


**32. MERS-CoV pathogenesis and antiviral efficacy of licensed drugs in human monocyte-derived antigen-presenting cells.**

**Authors** Cong, Yu; Hart, Brit J; Gross, Robin; Zhou, Huanying; Frieman, Matthew; Bollinger, Laura; Wada, Jiro; Hensley, Lisa E; Jahrling, Peter B; Dyall, Julie; Holbrook, Michael R
**Source** PloS one; 2018; vol. 13 (no. 3); p. e0194868
**Publication Date** 2018
**Publication Type(s)** Research Support, Non-u.s. Gov't Research Support, N.i.h., Extramural Journal Article
**PubMedID** 29566060
**Database** Medline
Available at PloS one from Europe PubMed Central - Open Access
Available at PloS one from Public Library of Science (PLoS)
Available at PloS one from ProQuest (Health Research Premium) - NHS Version
Available at PloS one from Unpaywall
**Abstract** Middle East respiratory syndrome coronavirus (MERS-CoV) presents an emerging threat to public health worldwide by causing severe respiratory disease in humans with high virulence and case fatality rate (about 35%) since 2012. Little is known about the pathogenesis and innate antiviral response in primary human monocyte-derived macrophages (MDMs) and dendritic cells (MDDCs) upon MERS-CoV infection. In this study, we assessed MERS-CoV replication as well as induction of inflammatory cytokines and chemokines in MDMs and immature and mature MDDCs. Immature MDDCs and MDMs were permissive for MERS-CoV infection, while mature MDDCs were not, with stimulation of proinflammatory cytokine and chemokine upregulation in MDMs, but not in MDDCs. To further evaluate the antiviral activity of well-defined drugs in primary antigen presenting cells (APCs), three compounds (chloroquine, chlorpromazine and toremifine), each with broad-spectrum antiviral activity in immortalized cell lines, were evaluated in MDMs and MDDCs to determine their antiviral effect on MERS-CoV infection. While chloroquine was not active in these primary cells, chlorpromazine showed strong anti-MERS-CoV activity, but it was associated with high cytotoxicity narrowing the potential window for drug utilization. Unlike in established cells, toremifene had marginal activity when tested in antigen presenting cells, with high apparent cytotoxicity, also limiting its potential as a therapeutic option. These results demonstrate the value of testing drugs in primary cells, in addition to established cell lines, before initiating preclinical or clinical studies for MERS treatment and the importance of carefully assessing cytotoxicity in drug screen assays. Furthermore, these studies also highlight the role of APCs in stimulating a robust protective immune response to MERS-CoV infection.

**33. Update on therapeutic options for Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

**Authors** Al-Tawfiq J.A.; Memish Z.A.
**Source** Expert Review of Anti-Infective Therapy; Mar 2017; vol. 15 (no. 3); p. 269-275
**Publication Date** Mar 2017
**Publication Type(s)** Review
**PubMedID** 27937060
**Database** EMBASE

Available at Expert review of anti-infective therapy from Unpaywall

**Abstract** Introduction: The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is an important emerging respiratory pathogen. MERS-CoV resulted in multiple hospital outbreaks within and outside the Arabian Peninsula. The disease has a high case fatality rate, with the need for a therapeutic option. Areas covered: In this review, we provide an overview of the progress in the development of therapeutic strategies for MERS. We searched PubMed, Embase, Cochrane, Scopus, and Google Scholar, using the following terms: 'MERS', 'MERS-CoV', 'Middle East respiratory syndrome' in combination with 'treatment' or 'therapy'. Expert commentary: There are multiple agents tried in vitro and in vivo. None of these agents were used in large clinical studies. Available clinical studies are limited to the use of the combination of interferon and other agents. These clinical studies are based solely on case reports and case series. There are no prospective or randomized trials. There is a need to have prospective and randomized clinical trials for the therapy of MERS-CoV. However, this strategy might be hampered by the sporadic cases outside the large hospital outbreaks.


**34. Targeting endosomal acidification by chloroquine analogs as a promising strategy for the treatment of emerging viral diseases.**

**Authors** Al-Bari, Md Abdul Alim
**Source** Pharmacology research & perspectives; Feb 2017; vol. 5 (no. 1); p. e00293
**Publication Date** Feb 2017
**Publication Type(s)** Journal Article Review
**PubMedID** 28596841
**Database** Medline
Available at Pharmacology research & perspectives from Europe PubMed Central - Open Access
Available at Pharmacology research & perspectives from ProQuest (Health Research Premium) - NHS Version
Available at Pharmacology research & perspectives from Unpaywall

**Abstract** Emerging viruses such as HIV, dengue, influenza A, SARS coronavirus, Ebola, and other viruses pose a significant threat to human health. Majority of these viruses are responsible for the outbreaks of pathogenic lethal infections. To date, there are no effective therapeutic strategies available for the prophylaxis and treatment of these infections. Chloroquine analogs have been used for decades as the primary and most successful drugs against malaria. Concomitant with the emergence of chloroquine-resistant Plasmodium strains and a subsequent decrease in the use as antimalarial drugs, other applications of the analogs have been investigated. Since the analogs have interesting biochemical properties, these drugs are found to be effective against a wide variety of viral infections. As antiviral action, the analogs have been shown to inhibit acidification of endosome during the events of replication and infection. Moreover, immunomodulatory effects of analogs have been beneficial to patients with severe inflammatory complications of several viral diseases. Interestingly, one of the successful targeting strategies is the inhibition of HIV replication by the analogs in vitro which are being tested in several clinical trials. This review focuses on the potentialities of chloroquine analogs for the treatment of endosomal low pH dependent emerging viral diseases.

**35. Antiviral treatment guidelines for middle east respiratory syndrome**

**Authors** Chong Y.P.; Song J.Y.; Seo Y.B.; Choi J.-P.; Shin H.-S.; Yoon H.J.; Choi J.Y.; Kim T.H.; Choi Y.H.; Kim H.B.; Yoon J.H.; Lee J.; Eom J.S.; Lee S.-O.; Oh W.S.; Cheong H.J.; Song Y.G.; Choi J.H.; Kim W.J.
**Source** Infection and Chemotherapy; 2015; vol. 47 (no. 3); p. 212-222
**Publication Date** 2015
**Publication Type(s)** Article
**Database** EMBASE
Available at Infection & Chemotherapy from Europe PubMed Central - Open Access
Available at Infection & Chemotherapy from Unpaywall

**Abstract** Middle East respiratory syndrome (MERS) is an acute infectious disease of the respiratory system caused by the new betacoronavirus (MERS coronavirus, MERS-CoV), which shows high mortality rates. The typical symptoms of MERS are fever, cough, and shortness of breath, and it is often accompanied by pneumonia. The MERS-CoV was introduced to Republic of Korea in May 2015 by a patient returning from Saudi Arabia. The disease spread mostly through hospital infections, and by the time the epidemic ended in August, the total number of confirmed diagnoses was 186, among which 36 patients died. Reflecting the latest evidence for antiviral drugs in the treatment of MERS-CoV infection and the experiences of treating MERS patients in Republic of Korea, these guidelines focus on antiviral drugs to achieve effective treatment of MERS-CoV infections.


**36. Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture.**

**Authors** de Wilde, Adriaan H; Jochmans, Dirk; Posthuma, Clara C; Zevenhoven-Dobbe, Jessika C; van Nieuwkoop, Stefan; Bestebroer, Theo M; van den Hoogen, Bernadette G; Neyts, Johan; Snijder, Eric J

**Source** Antimicrobial agents and chemotherapy; Aug 2014; vol. 58 (no. 8); p. 4875-4884
**Publication Date** Aug 2014
**Publication Type(s)** Research Support, Non-u.s. Gov't Journal Article
**PubMedID** 24841269
**Database** Medline
Available at Antimicrobial agents and chemotherapy from Europe PubMed Central - Open Access
Available at Antimicrobial agents and chemotherapy from HighWire - Free Full Text
Available at Antimicrobial agents and chemotherapy from Unpaywall

**Abstract** Coronaviruses can cause respiratory and enteric disease in a wide variety of human and animal hosts. The 2003 outbreak of severe acute respiratory syndrome (SARS) first demonstrated the potentially lethal consequences of zoonotic coronavirus infections in humans. In 2012, a similar previously unknown coronavirus emerged, Middle East respiratory syndrome coronavirus (MERS-CoV), thus far causing over 650 laboratory-confirmed infections, with an unexplained steep rise in the number of cases being recorded over recent months. The human MERS fatality rate of ~ 30% is alarmingly high, even though many deaths were associated with underlying medical conditions. Registered therapeutics for the treatment of coronavirus infections are not available. Moreover, the pace of drug development and registration for human use is generally incompatible with strategies to combat emerging infectious diseases. Therefore, we have screened a library of 348 FDA-approved drugs for anti-MERS-CoV activity in cell culture. If such compounds proved sufficiently potent, their efficacy might be directly assessed in MERS patients. We identified four compounds (chloroquine, chlorpromazine, loperamide, and lopinavir) inhibiting MERS-CoV replication in the low-micromolar range (50% effective concentrations [EC(50)s], 3 to 8 μM). Moreover, these compounds also inhibit the replication of SARS coronavirus and human coronavirus 229E. Although their protective activity (alone or in combination) remains to be assessed in animal models, our findings may offer a starting point for treatment of patients infected with zoonotic coronaviruses like MERS-CoV. Although they may not necessarily reduce viral replication to very low levels, a moderate viral load reduction may create a window during which to mount a protective immune response.

### 37. Repurposing of clinically developed drugs for treatment of Middle East respiratory syndrome coronavirus infection

**Authors** Dyall J.; Hart B.J.; Holbrook M.R.; Kindrachuk J.; Olinger Jr. G.G.; Jahrling P.B.; Hensley L.E.; Coleman C.M.; Venkataraman T.; Frieman M.B.; Johnson R.F.; Laidlaw M.; Johansen L.M.; Lear-Rooney C.M.; Glass P.J.
**Source** Antimicrobial Agents and Chemotherapy; Aug 2014; vol. 58 (no. 8); p. 4885-4893
**Publication Date** Aug 2014
**Publication Type(s)** Article
**PubMedID** 24841273
**Database** EMBASE
Available at Antimicrobial agents and chemotherapy from Europe PubMed Central - Open Access
Available at Antimicrobial agents and chemotherapy from HighWire - Free Full Text
Available at Antimicrobial agents and chemotherapy from Unpaywall

**Abstract** Outbreaks of emerging infections present health professionals with the unique challenge of trying to select appropriate pharmacologic treatments in the clinic with little time available for drug testing and development. Typically, clinicians are left with general supportive care and often untested convalescent-phase plasma as available treatment options. Repurposing of approved pharmaceutical drugs for new indications presents an attractive alternative to clinicians, researchers, public health agencies, drug developers, and funding agencies. Given the development times and manufacturing requirements for new products, repurposing of existing drugs is likely the only solution for outbreaks due to emerging viruses. In the studies described here, a library of 290 compounds was screened for antiviral activity against Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV). Selection of compounds for inclusion in the library was dependent on current or previous FDA approval or advanced clinical development. Some drugs that had a well-defined cellular pathway as target were included. In total, 27 compounds with activity against both MERS-CoV and SARS-CoV were identified. The compounds belong to 13 different classes of pharmaceuticals, including inhibitors of estrogen receptors used for cancer treatment and inhibitors of dopamine receptor used as antipsychotics. The drugs identified in these screens provide new targets for in vivo studies as well as incorporation into ongoing clinical studies. Copyright © 2014, American Society for Microbiology. All Rights Reserved.

### 38. Use of chloroquine in viral diseases

**Authors** Savarino A.
**Source** The Lancet Infectious Diseases; Sep 2011; vol. 11 (no. 9); p. 653-654
**Publication Date** Sep 2011
**Publication Type(s)** Letter
**PubMedID** 21550312
**Database** EMBASE
Available at The Lancet. Infectious diseases from ClinicalKey

Available at The Lancet. Infectious diseases from ProQuest (Health Research Premium) - NHS Version

**39. SARS coronavirus anti-infectives**

**Authors** Tong T.R.
**Publication Date** 2010
**Publication Type(s)** Article
**Database** EMBASE
**Abstract** Severe acute respiratory syndrome (SARS) emerged in late 2002 and was controlled in July 2003 by public health measures. Its causative agent, SARS coronavirus (SARS-CoV) jumped from an animal reservoir to humans and has the potential to re-emerge. Since then, the world has seen another virus that emerged in 2009, the pandemic influenza A (H1N1)v virus. Following the sequencing of the genetic code of SARS-CoV and the deciphering of some of the functions of its proteins, including the cellular receptors and host proteins that participate in the life cycle of the virus, promising lead drugs and new uses of old drugs have been discovered. Engineered monoclonal antibodies have surmounted the hurdle of provoking antibody enhancement as well as providing broad coverage against various SARS-CoV strains and mutants to prevent viral escape. Protease inhibitors are favored small molecule inhibitors because of possible broad spectrum coverage as well as the ability to be formulated for oral use. RNAi-based therapeutics produced impressive in vitro data and is rapid to develop. Interferon and chloroquine are likely to be effective as nonspecific antivirals with a good safety profile. The development of SARS-CoV anti-infectives is ongoing and will undoubtedly strengthen the infrastructure and know-how in the field of antiviral drug discovery. © 2010 Bentham Science Publishers.

**40. Drug targets in severe acute respiratory syndrome (SARS) virus and other coronavirus infections**

**Authors** Tong T.R.
**Source** Infectious Disorders - Drug Targets; 2009; vol. 9 (no. 2); p. 223-245
**Publication Date** 2009
**Publication Type(s)** Review
**PubMedID** 19275708
**Database** EMBASE
**Abstract** Coronaviruses are important human and animal pathogens of the order Nidovirales. Several new members were discovered following the emergence of SARS-CoV in human populations, including two human coronaviruses and several animal coronaviruses. They cause respiratory and gastrointestinal illnesses and have been found in the brains of patients with multiple sclerosis. The high mortality of SARS, the identification of a natural reservoir, and the well-founded fear of provoking antibody-enhanced disease as a result of vaccination fueled the ongoing efforts in anti-coronavirus drug discovery. This review presents the results of current research. © 2009 Bentham Science Publishers Ltd.

**41. Antiviral activity of chloroquine against human coronavirus OC43 infection in newborn mice.**

**Authors** Keyaerts, Els; Li, Sandra; Vijgen, Leen; Rysman, Evelien; Verbeeck, Jannick; Van Ranst, Marc; Maes, Piet
**Source** Antimicrobial agents and chemotherapy; Aug 2009; vol. 53 (no. 8); p. 3416-3421
**Publication Date** Aug 2009
**Publication Type(s)** Research Support, Non-u.s. Gov't Journal Article
**PubMedID** 19506054
**Database** Medline
Available at Antimicrobial agents and chemotherapy from Europe PubMed Central - Open Access
Available at Antimicrobial agents and chemotherapy from HighWire - Free Full Text
Available at Antimicrobial agents and chemotherapy from Unpaywall
**Abstract** Until recently, human coronaviruses (HCoVs), such as HCoV strain OC43 (HCoV-OC43), were mainly known to cause 15 to 30% of mild upper respiratory tract infections. In recent years, the identification of new HCoVs, including severe acute respiratory syndrome coronavirus, revealed that HCoVs can be highly pathogenic and can cause more severe upper and lower respiratory tract infections, including bronchiolitis and pneumonia. To date, no specific antiviral drugs to prevent or treat HCoV infections are available. We demonstrate that chloroquine, a widely used drug with well-known antimalarial effects, inhibits HCoV-OC43 replication in HRT-18 cells, with a 50% effective concentration (+/- standard deviation) of 0.306 +/- 0.0091 microM and a 50% cytotoxic concentration (+/- standard deviation) of 419 +/- 192.5 microM, resulting in a selectivity index of 1,369. Further, we investigated whether chloroquine could prevent HCoV-OC43-induced death in newborn mice. Our results show that a lethal HCoV-OC43 infection in newborn C57BL/6 mice can be treated with chloroquine acquired transplacentally or via maternal milk. The highest survival rate (98.6%) of the pups was found when mother mice were treated daily with a concentration of 15 mg of chloroquine per kg of body weight. Survival rates declined in a dose-dependent manner, with 88% survival when treated with 5 mg/kg chloroquine and 13% survival when treated with 1 mg/kg chloroquine. Our results show that chloroquine can be highly effective against HCoV-OC43 infection in newborn mice and may be considered as a future drug against HCoVs.

**42. The management of coronavirus infections with particular reference to SARS**

**Authors** Wong S.S.Y.; Yuen K.-Y.
**Source** Journal of Antimicrobial Chemotherapy; 2008; vol. 62 (no. 3); p. 437-441
**Publication Date** 2008
**Publication Type(s)** Article
**PubMedID** 18565970
**Database** EMBASE
Available at The Journal of antimicrobial chemotherapy from HighWire - Free Full Text
Available at The Journal of antimicrobial chemotherapy from Unpaywall
**Abstract** The human coronaviruses (HCoV) OC43 and 229E are common causes of upper respiratory tract infections. Severe diseases were rare, however, until the emergence of the severe acute respiratory syndrome (SARS)-CoV in 2003. Since then, other novel CoV (NL63 and HKU1) have been described, and they have caused respiratory infections worldwide. Potentially exposed laboratory workers or animal handlers with rapidly progressive pneumonia not responding to standard antibacterial coverage must be isolated with contact and droplet, and for specific situations, airborne precautions, till rapid tests of respiratory and faecal samples are negative for SARS-CoV. Generally, the viral loads collected at different anatomical sites correlate with the severity of symptoms and mortality. Shedding of SARS-CoV peaks at day 10 after the onset of symptoms, which theoretically allows ample time for antiviral treatment. The disease is characterized by uncontrolled replication of the virus and a prominent pro-inflammatory response. No randomized controlled trials with a specific anti-coronavirus agent have been conducted with respect to therapy or prophylaxis. Reports using historical matched controls have suggested that treatment with interferon alfacon-1 (a synthetic interferon) combined with steroid, protease inhibitors together with ribavirin, or convalescent plasma containing neutralizing antibody, could be useful. Prophylaxis with interferon or hyperimmune globulin may be considered for unprotected exposure. The role of immunomodulators to decrease excessive inflammation remains elusive. Other non-SARS-CoV infections are generally milder in immunocompetent hosts, and scientific data on antiviral treatment of these viruses are scarce. © The Author 2008. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved.

**43. Inhibition of human coronavirus 229E infection in human epithelial lung cells (L132) by chloroquine: involvement of p38 MAPK and ERK.**

**Authors** Kono, Masakazu; Tatsumi, Koichiro; Imai, Alberto M; Saito, Kengo; Kuriyama, Takayuki; Shirasawa, Hiroshi
**Source** Antiviral research; Feb 2008; vol. 77 (no. 2); p. 150-152
**Publication Date** Feb 2008
**Publication Type(s)** Journal Article
**PubMedID** 18055026
**Database** Medline
Available at Antiviral research from Unpaywall
**Abstract** The antiviral effects of chloroquine (CQ) on human coronavirus 229E (HCoV-229E) infection of human fetal lung cell line, L132 are reported. CQ significantly decreased the viral replication at concentrations lower than in clinical usage. We demonstrated that CQ affects the activation of p38 mitogen-activated protein kinase (MAPK) and extracellular signal-regulated kinase (ERK). Furthermore, p38 MAPK inhibitor, SB203580, inhibits CPE induced by HCoV-229E infection and viral replication. Our findings suggest that CQ affects the activation of MAPKs, involved in the replication of HCoV-229E.

**44. Pathobiology of virus glycosylation: Implications to disease and prospects for treatment**

**Authors** Vigerust D.J.
**Source** Future Virology; Nov 2007; vol. 2 (no. 6); p. 615-623
**Publication Date** Nov 2007
**Publication Type(s)** Review
**Database** EMBASE
Available at Future Virology from ProQuest (Health Research Premium) - NHS Version
**Abstract** Change to the overall glycosylation profile of viral glycoproteins have been shown to be advantageous to virus survival and virulence. Many human viral pathogens rely on specific oligosaccharides to evade detection by the host immune system. Viruses such as HIV, Hendra, SARS-CoV, influenza, respiratory syncytial virus, hepatitis and West Nile virus rely on N-linked and O-Linked glycosylation for critical functions such as entry into host cells, proteolytic processing and protein trafficking. Recent findings demonstrate the importance of glycosylation to viral virulence, infectivity and immune evasion in several virus families impacting on human health. This review considers the role of glycosylation in viral infection and will detail several potential therapies for these important human pathogens and emerging infections. © 2007 Future Medicine Ltd.

**45. Severe acute respiratory syndrome coronavirus as an agent of emerging and reemerging infection**

**Authors** Cheng V.C.C.; Lau S.K.P.; Woo P.C.Y.; Kwok Y.Y.
**Source** Clinical Microbiology Reviews; Oct 2007; vol. 20 (no. 4); p. 660-694

**Publication Date** Oct 2007
**Publication Type(s)** Review
**PubMedID** 17934078
**Database** EMBASE
Available at Clinical Microbiology Reviews from Europe PubMed Central - Open Access
Available at Clinical Microbiology Reviews from HighWire - Free Full Text
Available at Clinical Microbiology Reviews from Unpaywall

**Abstract** Before the emergence of severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV) in 2003, only 12 other animal or human coronaviruses were known. The discovery of this virus was soon followed by the discovery of the civet and bat SARS-CoV and the human coronaviruses NL63 and HKU1. Surveillance of coronaviruses in many animal species has increased the number on the list of coronaviruses to at least 36. The explosive nature of the first SARS epidemic, the high mortality, its transient reemergence a year later, and economic disruptions led to a rush on research of the epidemiological, clinical, pathological, immunological, virological, and other basic scientific aspects of the virus and the disease. This research resulted in over 4,000 publications, only some of the most representative works of which could be reviewed in this article. The marked increase in the understanding of the virus and the disease within such a short time has allowed the development of diagnostic tests, animal models, antivirals, vaccines, and epidemiological and infection control measures, which could prove to be useful in randomized control trials if SARS should return. The findings that horseshoe bats are the natural reservoir for SARS-CoV-like virus and that civets are the amplification host highlight the importance of wildlife and biosecurity in farms and wet markets, which can serve as the source and amplification centers for emerging infections. Copyright © 2007, American Society for Microbiology. All Rights Reserved.

**46. Recycling of chloroquine and its hydroxyl analogue to face bacterial, fungal and viral infections in the 21st century**

**Authors** Rolain J.-M.; Colson P.; Raoult D.
**Source** International Journal of Antimicrobial Agents; Oct 2007; vol. 30 (no. 4); p. 297-308
**Publication Date** Oct 2007
**Publication Type(s)** Short Survey
**PubMedID** 17629679
**Database** EMBASE
Available at International journal of antimicrobial agents from ClinicalKey

**Abstract** Chloroquine (CQ) and its hydroxyl analogue hydroxychloroquine (HCQ) are weak bases with a half-century long use as antimalarial agents. Apart from this antimalarial activity, CQ and HCQ have gained interest in the field of other infectious diseases. One of the most interesting mechanisms of action is that CQ leads to alkalinisation of acid vesicles that inhibit the growth of several intracellular bacteria and fungi. The proof of concept of this effect was first used to restore intracellular pH allowing antibiotic efficacy for Coxiella burnetii, the agent of Q fever, and doxycycline plus HCQ is now the reference treatment for chronic Q fever. There is also strong evidence of a similar effect in vitro against Tropheryma whipplei, the agent of Whipple's disease, and a clinical trial is in progress. Other bacteria and fungi multiply in an acidic environment and encouraging in vitro data suggest that this concept may be generalised for all intracellular organisms that multiply in an acidic environment. For viruses, CQ led to inhibition of uncoating and/or alteration of post-translational modifications of newly synthesised proteins, especially inhibition of glycosylation. These effects have been well described in vitro for many viruses, with human immunodeficiency virus (HIV) being the most studied. Preliminary in vivo clinical trials suggest that CQ alone or in combination with antiretroviral drugs might represent an interesting way to treat HIV infection. In conclusion, our review re-emphasises the paradigm that activities mediated by lysosomotropic agents may offer an interesting weapon to face present and future infectious diseases worldwide. © 2007 Elsevier B.V. and the International Society of Chemotherapy.

**47. Antiviral strategies against human coronaviruses**

**Authors** Pyrc K.; Berkhout B.; van der Hoek L.
**Source** Infectious Disorders - Drug Targets; Mar 2007; vol. 7 (no. 1); p. 59-66
**Publication Date** Mar 2007
**Publication Type(s)** Review
**PubMedID** 17346212
**Database** EMBASE

**Abstract** Since the mid 60's the human coronaviruses (HCoV), represented by HCoV-OC43 and HCoV-229E, were generally considered relatively harmless viruses. This status changed dramatically with the emergence of SARS-CoV in 2002/2003. The SARS-CoV pandemic took 774 lives around the globe and infected more than 8000 people in 29 countries. SARS-CoV is believed to be of zoonotic origin, transmitted from its natural reservoir in bats through several animal species (e.g., civet cats, raccoon dogs sold for human consumption in markets in southern China). The epidemic was halted in 2003 by a highly effective global public health response, and SARS-CoV is currently not circulating in humans. The outbreak of SARS-CoV and the danger of its re-introduction into the human population, as well as the danger of the emergence of other zoonotic coronaviral infections triggered an intense survey for an efficient treatment that resulted in the evaluation of several anticoronaviral compounds. HCoV-NL63 and HCoV-HKU1 were identified shortly after the SARS-CoV outbreak. The 4 human coronaviruses HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1 cause mild respiratory illnesses when compared to SARS, but these infections are involved in 10 - 20 % of hospitalizations of young children and immunocompromised adults with respiratory tract illness. Therefore, there is an urgent need for a successful therapy to prevent disease induction or a vaccine to prevent new infections. This review summarizes the current status of anticoronaviral strategies. © 2007 Bentham Science Publishers Ltd.

**48. Evaluation of immunomodulators, interferons and known in vitro SARS-coV inhibitors for inhibition of SARS-coV replication in BALB/c mice.**

**Authors** Barnard, Dale L; Day, Craig W; Bailey, Kevin; Heiner, Matthew; Montgomery, Robert; Lauridsen, Larry; Chan, Paul K S; Sidwell, Robert W
**Source** Antiviral chemistry & chemotherapy; 2006; vol. 17 (no. 5); p. 275-284
**Publication Date** 2006
**Publication Type(s)** Research Support, N.i.h., Extramural Comparative Study Journal Article
**PubMedID** 17176632
**Database** Medline
Available at Antiviral chemistry & chemotherapy from ProQuest (Health Research Premium) - NHS Version
Available at Antiviral chemistry & chemotherapy from Unpaywall

**Abstract** Compounds approved for therapeutic use and in vitro inhibitors of severe acute respiratory syndrome coronavirus (SARS-CoV) were evaluated for inhibition in the mouse SARS-CoV replication model. A hybrid interferon, interferon alpha (IFN-alpha) B/D, and a mismatched double-stranded (ds) RNA interferon (IFN) inducer, Ampligen (poly I:poly C124), were the only compounds that potently inhibited virus titres in the lungs of infected mice as assessed by CPE titration assays. When mice were dosed intraperitoneally (i.p.) with IFN-alpha B/D once daily for 3 days beginning 4 h after virus exposure, SARS-CoV replication in the lungs of infected mice was reduced by 1 log10 at 10,000 and 32,000 IU; at the highest dose of 100,000 IU, virus lung titres were below detectable limits. Ampligen used i.p. at 10 mg/kg 4 h prior to virus exposure also reduced virus lung titres to below detectable limits. Nelfinavir, beta-D-N4-hydroxycytidine, calpain inhibitor VI, 3-deazaneplanocin A and Alferon (human leukocyte IFN-alpha-n3) did not significantly reduce lung virus titres in mice. Anti-inflammatory agents, chloroquine, amodiaquin and pentoxifylline, were also inactive in vivo, suggesting that although they may be useful in ameliorating the hyperinflammatory response induced by the virus infection, they will not significantly reduce the replication of the virus, the inducer of inflammatory response. Thus, anti-inflammatory agents may only be useful in treating virus lung infections if used in combination with agents that inhibit virus replication. In summary, the data suggest that induction of IFN by mismatched dsRNA or actual treatment with exogenous IFN-alpha can inhibit SARS-CoV replication in the lungs of mice.

**49. Potential therapies for coronaviruses**

**Authors** Savarino A.; Norelli S.; Cassone A.; Bounavoglia C.; Di Trani L.
**Source** Expert Opinion on Therapeutic Patents; Sep 2006; vol. 16 (no. 9); p. 1269-1288
**Publication Date** Sep 2006
**Publication Type(s)** Review
**Database** EMBASE
Available at Expert Opinion on Therapeutic Patents from Unpaywall

**Abstract** Coronavirus replication offers several attractive targets for chemotherapy. These include: viral entry (inhibited by chloroquine and peptides); viral RNA (targeted by antisense approaches/RNAi); the main protease 3CLpro (inhibited by peptidic molecules such as HIV-1 protease inhibitors and miscellaneous compounds); the accessory protease(s) PLpro(s) (inhibited by zinc ions); RNA-dependent RNA polymerase (inhibited by aurintricarboxylic acid and antisense approaches); and helicase (inhibited by bananins). Chloroquine and HIV-1 protease inhibitors (with well-known toxicity profiles) should be considered for clinical tests if severe acute respiratory syndrome (SARS) re-emerges; however, there are other attractive compounds. Lessons should be learnt from AIDS research for choosing the best strategies. © 2006 Informa UK Ltd.

**50. Coronaviruses and their therapy**

**Authors** Haagmans B.L.; Osterhaus A.D.M.E.
**Source** Antiviral Research; Sep 2006; vol. 71 (no. 2); p. 397-403

**Publication Date** Sep 2006
**Publication Type(s)** Short Survey
**PubMedID** 16837072
**Database** EMBASE
Available at Antiviral Research from Unpaywall
**Abstract** Coronaviruses may cause respiratory, enteric and central nervous system diseases in many species, including humans. Until recently, the relatively low burden of disease in humans caused by few of these viruses hampered development of coronavirus specific therapeutics. However, the emergence of severe acute respiratory syndrome coronavirus (SARS-CoV) has prompted the discovery of such drugs. Subsequent studies in animal models demonstrated the efficacy of SARS-CoV specific monoclonal antibodies, pegylated-interferon-alpha and siRNAs against SARS-CoV. Furthermore, several antivirals shown to be effective against other viruses were tested in vitro. Because of availability and shown efficacy, the use of interferons may be considered should SARS-CoV or a related coronavirus (re)-emerge. The more recent design of wide-spectrum inhibitors targeting the coronavirus main proteases may lead to the discovery of new antivirals against multiple coronavirus induced diseases. 

**51. Antiviral drug discovery against SARS-CoV**

**Authors** Wu Y.-S.; Lin W.-H.; Hsu J.T.-A.; Hsieh H.-P.
**Source** Current Medicinal Chemistry; Jul 2006; vol. 13 (no. 17); p. 2003-2020
**Publication Date** Jul 2006
**Publication Type(s)** Review
**PubMedID** 16842194
**Database** EMBASE
Available at Current medicinal chemistry from ProQuest (Health Research Premium) - NHS Version
**Abstract** Severe Acute Respiratory Syndrome (SARS) is a life-threatening infectious disease caused by SARS-CoV. In the 2003 outbreak, it infected more than 8,000 people worldwide and claimed the lives of more than 900 victims. The high mortality rate resulted, at least in part, from the absence of definitive treatment protocols or therapeutic agents. Although the virus spreading has been contained, due preparedness and planning, including the successful development of antiviral drugs against SARS-CoV, is necessary for possible reappearance of SARS. In this review, we have discussed currently available strategies for antiviral drug discovery and how these technologies have been utilized to identify potential antiviral agents for the inhibition of SARS-CoV replication. Moreover, progress in the drug development based on different molecular targets is also summarized, including 1) Compounds that block the S protein-ACE2-mediated viral entry; 2) Compounds targeting SARS-CoV $M^{pro}$; 3) Compounds targeting papain-like protease 2 (PLP2); 4) Compounds targeting SARS-CoV RdRp; 5) Compounds targeting SARS-CoV helicase; 6) Active compounds with unspecified targets; and 7) Research on siRNA. This review aims to provide a comprehensive account of drug discovery on SARS. The experiences with the SARS outbreak and drug discovery would certainly be an important lesson for the drug development for any new viral outbreaks that may emerge in the future. 

**52. Design and synthesis of hydroxyferroquine derivatives with antimalarial and antiviral activities.**

**Authors** Biot, Christophe; Daher, Wassim; Chavain, Natascha; Fandeur, Thierry; Khalife, Jamal; Dive, Daniel; De Clercq, Erik
**Source** Journal of medicinal chemistry; May 2006; vol. 49 (no. 9); p. 2845-2849
**Publication Date** May 2006
**Publication Type(s)** Research Support, Non-u.s. Gov't Journal Article
**PubMedID** 16640347
**Database** Medline
Available at Journal of medicinal chemistry from Unpaywall
**Abstract** Three ferroquine (FQ) derivatives, closely mimicking the antimalarial drug hydroxychloroquine (HCQ), have been prepared. Whereas these organometallic compounds provide the expected reduced cytotoxic effects compared to FQ, they inhibit in vitro growth of Plasmodium falciparum far better than chloroquine (CQ). Moreover, this new class of bioorganometallic compounds exert antiviral effects with some selectivity toward SARS-CoV infection. These new drugs may offer an interesting alternative for Asia where SARS originated and malaria has remained endemic.

**53. Potential antivirals and antiviral strategies against SARS coronavirus infections.**

**Authors** De Clercq, Erik
**Source** Expert review of anti-infective therapy; Apr 2006; vol. 4 (no. 2); p. 291-302
**Publication Date** Apr 2006
**Publication Type(s)** Journal Article Review
**PubMedID** 16597209
**Database** Medline
Available at Expert review of anti-infective therapy from ProQuest (Health Research Premium) - NHS Version

Available at Expert review of anti-infective therapy from Unpaywall

**Abstract** There are a number of antivirals as well as antiviral strategies that could be envisaged to prevent or treat severe acute respiratory syndrome (SARS) (or similar) coronavirus (CoV) infections. Targets for the prophylactic or therapeutic interventions include interaction of the spike (S) glycoprotein (S1 domain) with the host cell receptor, fusion of the S2 domain with the host cell membrane, processing of the replicase polyproteins by the virus-encoded proteases (3C-like cysteine protease [3CLpro] and papain-like cysteine protease) and other virus-encoded enzymes such as the NTPase/helicase and RNA-dependent RNA polymerase. Human monoclonal antibody blocking S1 may play an important role in the immunoprophylaxis of SARS. Fusion inhibitors reminiscent of enfuvirtide in the case of HIV may also be developed for SARS-CoV. Various peptidomimetic and nonpeptidic inhibitors of 3CLpro have been described, the best ones inhibiting SARS-CoV replication with a selectivity index greater than 1000. Human interferons, in particular alpha- and beta-interferon, as well as short interfering RNAs could further be pursued for the control of SARS. Various other compounds, often with an ill-defined mode of action but selectivity indexes up to 100, have been reported to exhibit in vitro activity against SARS-CoV: valinomycin, glycopeptide antibiotics, plant lectins, hesperetin, glycyrrhizin, aurintricarboxylic acid, chloroquine, niclosamide, nelfinavir and calpain inhibitors.

**54. New insights into the antiviral effects of chloroquine.**

**Authors** Savarino, Andrea; Di Trani, Livia; Donatelli, Isabella; Cauda, Roberto; Cassone, Antonio
**Source** The Lancet. Infectious diseases; Feb 2006; vol. 6 (no. 2); p. 67-69
**Publication Date** Feb 2006
**Publication Type(s)** Letter
**PubMedID** 16439323
**Database** Medline
Available at The Lancet. Infectious diseases from ProQuest (Health Research Premium) - NHS Version

**55. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread.**

**Authors** Vincent, Martin J; Bergeron, Eric; Benjannet, Suzanne; Erickson, Bobbie R; Rollin, Pierre E; Ksiazek, Thomas G; Seidah, Nabil G; Nichol, Stuart T
**Source** Virology journal; Aug 2005; vol. 2 ; p. 69
**Publication Date** Aug 2005
**Publication Type(s)** Research Support, Non-u.s. Gov't Journal Article
**PubMedID** 16115318
**Database** Medline
Available at Virology journal from BioMed Central
Available at Virology journal from Europe PubMed Central - Open Access
Available at Virology journal from PubMed
Available at Virology journal from virologyj.com
Available at Virology journal from PubMed Central
Available at Virology journal from doi.org
Available at Virology journal from Unpaywall

**Abstract** BACKGROUNDSevere acute respiratory syndrome (SARS) is caused by a newly discovered coronavirus (SARS-CoV). No effective prophylactic or post-exposure therapy is currently available.RESULTSWe report, however, that chloroquine has strong antiviral effects on SARS-CoV infection of primate cells. These inhibitory effects are observed when the cells are treated with the drug either before or after exposure to the virus, suggesting both prophylactic and therapeutic advantage. In addition to the well-known functions of chloroquine such as elevations of endosomal pH, the drug appears to interfere with terminal glycosylation of the cellular receptor, angiotensin-converting enzyme 2. This may negatively influence the virus-receptor binding and abrogate the infection, with further ramifications by the elevation of vesicular pH, resulting in the inhibition of infection and spread of SARS CoV at clinically admissible concentrations.CONCLUSIONChloroquine is effective in preventing the spread of SARS CoV in cell culture. Favorable inhibition of virus spread was observed when the cells were either treated with chloroquine prior to or after SARS CoV infection. In addition, the indirect immunofluorescence assay described herein represents a simple and rapid method for screening SARS-CoV antiviral compounds.

**56. Development of antiviral therapy for severe acute respiratory syndrome**

**Authors** Cinatl Jr. J.; Michaelis M.; Hoever G.; Preiser W.; Doerr H.W.
**Source** Antiviral Research; Jun 2005; vol. 66 (no. 2); p. 81-97
**Publication Date** Jun 2005
**Publication Type(s)** Review
**PubMedID** 15878786
**Database** EMBASE
Available at Antiviral research from Unpaywall

**Abstract** A new disease, the severe acute respiratory distress syndrome (SARS), caused by the SARS coronavirus (SARS-CoV), emerged at the beginning of 2003 and rapidly spread throughout the world. Although the disease had disappeared in June 2003 its re-emergence cannot be excluded. The development of vaccines against SARS-CoV may take years. Therefore, the availability of effective antiviral drugs against SARS-CoV may be crucial for the control of future SARS outbreaks. In this review, experimental and clinical data about potential anti-SARS drugs is summarised and discussed. Animal model studies will be needed to help to determine which interventions warrant controlled clinical testing. 

**57. Overview of antiviral and anti-inflammatory treatment for severe acute respiratory syndrome**

**Authors** Chihrin S.; Loutfy M.R.
**Source** Expert Review of Anti-Infective Therapy; Apr 2005; vol. 3 (no. 2); p. 251-262
**Publication Date** Apr 2005
**Publication Type(s)** Review
**PubMedID** 15918782
**Database** EMBASE
Available at Expert review of anti-infective therapy from ProQuest (Health Research Premium) - NHS Version
Available at Expert review of anti-infective therapy from Unpaywall
**Abstract** In 2003, an outbreak of a novel respiratory virus exploded from mainland China Into an international issue, catching the world by surprise. The ensuing challenges to hospital and public health workers rose to a level never before seen in healthcare, in part due to the unknown nature of the disease, the fear of the human-to-human transmission and the significant media involvement. A new coronavirus was identified as the causative agent and named the severe acute respiratory syndrome-associated virus. A number of antiviral and anti-inflammatory treatment strategies were explored during the epidemic, with varying success. Following the epidemic, in vitro antiviral analyses of numerous compounds have been conducted. This review summarizes treatment agents assessed during and after the 2003 severe acute respiratory syndrome outbreak, with the aim of guiding future decision makers should the virus return. 

**58. In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine.**

**Authors** Keyaerts, Els; Vijgen, Leen; Maes, Piet; Neyts, Johan; Van Ranst, Marc
**Source** Biochemical and biophysical research communications; Oct 2004; vol. 323 (no. 1); p. 264-268
**Publication Date** Oct 2004
**Publication Type(s)** Research Support, Non-u.s. Gov't Journal Article
**PubMedID** 15351731
**Database** Medline
Available at Biochemical and biophysical research communications from PubMed
Available at Biochemical and biophysical research communications from PubMed Central
Available at Biochemical and biophysical research communications from doi.org
**Abstract** We report on chloroquine, a 4-amino-quinoline, as an effective inhibitor of the replication of the severe acute respiratory syndrome coronavirus (SARS-CoV) in vitro. Chloroquine is a clinically approved drug effective against malaria. We tested chloroquine phosphate for its antiviral potential against SARS-CoV-induced cytopathicity in Vero E6 cell culture. Results indicate that the IC50 of chloroquine for antiviral activity (8.8 +/- 1.2 microM) was significantly lower than its cytostatic activity; CC50 (261.3 +/- 14.5 microM), yielding a selectivity index of 30. The IC50 of chloroquine for inhibition of SARS-CoV in vitro approximates the plasma concentrations of chloroquine reached during treatment of acute malaria. Addition of chloroquine to infected cultures could be delayed for up to 5h postinfection, without an important drop in antiviral activity. Chloroquine, an old antimalarial drug, may be considered for immediate use in the prevention and treatment of SARS-CoV infections.

**59. Malaria drug a possible treatment for SARS**

**Authors** anonymous
**Source** Expert Review of Anti-Infective Therapy; Oct 2004; vol. 2 (no. 5); p. 667-669
**Publication Date** Oct 2004
**Publication Type(s)** Note
**Database** EMBASE
Available at Expert Review of Anti-Infective Therapy from ProQuest (Health Research Premium) - NHS Version

**60. Malaria drug is effective against SARS.**

**Source** Nursing Times; Sep 2004; vol. 100 (no. 37); p. 7-7
**Publication Date** Sep 2004
**Publication Type(s)** Periodical
**Database** CINAHL
Available at Nursing Times from Kent and Canterbury Hospital Library (lib327265) Local Print Collection [location] : Kent and Canterbury Hospital Library.

**61. Effects of chloroquine on viral infections: an old drug against today's diseases?**

| | |
|---|---|
| **Authors** | Savarino, Andrea; Boelaert, Johan R; Cassone, Antonio; Majori, Giancarlo; Cauda, Roberto |
| **Source** | The Lancet. Infectious diseases; Nov 2003; vol. 3 (no. 11); p. 722-727 |
| **Publication Date** | Nov 2003 |
| **Publication Type(s)** | Research Support, Non-u.s. Gov't Journal Article Review |
| **PubMedID** | 14592603 |
| **Database** | Medline |
| | Available at The Lancet. Infectious diseases from ProQuest (Health Research Premium) - NHS Version |
| **Abstract** | Chloroquine is a 9-aminoquinoline known since 1934. Apart from its well-known antimalarial effects, the drug has interesting biochemical properties that might be applied against some viral infections. Chloroquine exerts direct antiviral effects, inhibiting pH-dependent steps of the replication of several viruses including members of the flaviviruses, retroviruses, and coronaviruses. Its best-studied effects are those against HIV replication, which are being tested in clinical trials. Moreover, chloroquine has immunomodulatory effects, suppressing the production/release of tumour necrosis factor alpha and interleukin 6, which mediate the inflammatory complications of several viral diseases. We review the available information on the effects of chloroquine on viral infections, raising the question of whether this old drug may experience a revival in the clinical management of viral diseases such as AIDS and severe acute respiratory syndrome, which afflict mankind in the era of globalisation. |

## **Strategy** 832389

| # | Database | Search term | Results |
|---|---|---|---|
| 1 | Medline | (coronavirus OR corona-virus OR "corona virus").ti,ab | 10835 |
| 2 | Medline | (covid-19 OR covid19 OR "covid 19").ti,ab | 1292 |
| 3 | Medline | (sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab | 402 |
| 4 | Medline | exp CORONAVIRUS/ OR exp CORONAVIRIDAE/ | 12686 |
| 5 | Medline | exp "CORONAVIRIDAE INFECTIONS"/ OR exp "CORONAVIRUS INFECTIONS"/ OR exp "SEVERE ACUTE RESPIRATORY SYNDROME"/ | 10743 |
| 6 | Medline | (1 OR 2 OR 3 OR 4 OR 5) | 19974 |
| 7 | Medline | (chloroquine*).ti,ab | 17025 |
| 8 | Medline | (hydroxychloroquine*).ti,ab | 3826 |
| 9 | Medline | exp HYDROXYCHLOROQUINE/ OR exp CHLOROQUINE/ | 16643 |
| 10 | Medline | (7 OR 8 OR 9) | 25422 |
| 11 | Medline | (6 AND 10) | 55 |
| 12 | EMBASE | (coronavirus OR corona-virus OR "corona virus").ti,ab | 11678 |
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| 14 | EMBASE | (sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab | 318 |
| 15 | EMBASE | exp CORONAVIRINAE/ OR exp CORONAVIRIDAE/ OR exp CORONAVIRUS/ OR exp "CORONAVIRUS 229E, HUMAN"/ OR exp "CORONAVIRUS INFECTION"/ OR exp "CORONAVIRUS INFECTIONS"/ OR exp "CORONAVIRUS NL63, HUMAN"/ OR exp "CORONAVIRUS OC43, HUMAN"/ | 19120 |
| 16 | EMBASE | exp "CORONAVIRUS INFECTION"/ OR exp "CORONAVIRIDAE INFECTION"/ OR exp "SEVERE ACUTE RESPIRATORY SYNDROME"/ OR exp "CORONAVIRUS INFECTIONS"/ | 11489 |
| 17 | EMBASE | (12 OR 13 OR 14 OR 15 OR 16) | 23512 |
| 18 | EMBASE | (chloroquine* OR hydroxychloroquine*).ti,ab | 26983 |
| 19 | EMBASE | exp CHLOROQUINE/ | 34868 |
| 20 | EMBASE | HYDROXYCHLOROQUINE/ | 23394 |

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|---|---|---|---|
| 21 | EMBASE | (18 OR 19 OR 20) | 58857 |
| 22 | EMBASE | (17 AND 21) | 101 |
| 23 | PubMed | (coronavirus OR corona-virus OR "corona virus").ti,ab | 16315 |
| 24 | PubMed | (covid-19 OR covid19 OR "covid 19").ti,ab | 1934 |
| 25 | PubMed | (sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab | 733 |
| 26 | PubMed | (23 OR 24 OR 25) | 17004 |
| 27 | PubMed | (chloroquine* OR hydroxychloroquine*).ti,ab | 25690 |
| 28 | PubMed | (26 AND 27) | 54 |
| 29 | CINAHL | (coronavirus OR corona-virus OR "corona virus").ti,ab | 1279 |
| 30 | CINAHL | (covid-19 OR covid19 OR "covid 19").ti,ab | 189 |
| 31 | CINAHL | (sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab | 35 |
| 32 | CINAHL | exp CORONAVIRIDAE/ OR exp CORONAVIRUS/ | 762 |
| 33 | CINAHL | exp "CORONAVIRUS INFECTIONS"/ OR exp "CORONAVIRIDAE INFECTIONS"/ | 2940 |
| 34 | CINAHL | (29 OR 30 OR 31 OR 32 OR 33) | 3574 |
| 35 | CINAHL | (chloroquine* OR hydroxychloroquine*).ti,ab | 1854 |
| 36 | CINAHL | exp CHLOROQUINE/ OR exp HYDROXYCHLOROQUINE/ | 1429 |
| 37 | CINAHL | (35 OR 36) | 2414 |
| 38 | CINAHL | (34 AND 37) | 2 |
| 39 | BNI | (coronavirus OR corona-virus OR "corona virus").ti,ab | 226 |
| 40 | BNI | (covid-19 OR covid19 OR "covid 19").ti,ab | 151 |
| 41 | BNI | (sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab | 5 |
| 42 | BNI | (39 OR 40 OR 41) | 345 |
| 43 | BNI | (chloroquine* OR hydroxychloroquine*).ti,ab | 224 |
| 44 | BNI | (42 AND 43) | 4 |
| 45 | EMCARE | (coronavirus OR corona-virus OR "corona virus").ti,ab | 1180 |

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| 46 | EMCARE | (covid-19 OR covid19 OR "covid 19").ti,ab | 56 |
| 47 | EMCARE | (sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab | 15 |
| 48 | EMCARE | exp CORONAVIRIDAE/ OR exp CORONAVIRINAE/ OR exp CORONAVIRUS/ OR exp "CORONAVIRUS 229E, HUMAN"/ OR exp "CORONAVIRUS INFECTION"/ OR exp "CORONAVIRUS INFECTIONS"/ OR exp "CORONAVIRUS NL63, HUMAN"/ OR exp "CORONAVIRUS OC43, HUMAN"/ | 4185 |
| 49 | EMCARE | exp "CORONAVIRUS INFECTION"/ OR exp "CORONAVIRIDAE INFECTION"/ OR exp "CORONAVIRUS INFECTIONS"/ OR exp "CORONAVIRUS NL63, HUMAN"/ OR exp "CORONAVIRUS OC43, HUMAN"/ OR exp "CORONAVIRUS, HUMAN"/ | 4196 |
| 50 | EMCARE | (45 OR 46 OR 47 OR 48 OR 49) | 4399 |
| 51 | EMCARE | (chloroquine* OR hydroxychloroquine*).ti,ab | 2572 |
| 52 | EMCARE | exp CHLOROQUINE/ | 4163 |
| 53 | EMCARE | exp HYDROXYCHLOROQUINE/ | 5109 |
| 54 | EMCARE | (51 OR 52 OR 53) | 8872 |
| 55 | EMCARE | (50 AND 54) | 15 |