



Foreword

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Accelerated by global connectivity, the newly discovered Sars CoV 2 virus has spread like wildfire from what was initially a distant problem in Wuhan to now being responsible for several clusters of community transmission in Singapore. It seemed inconceivable just a month ago that risk acquisition of the disease called Covid-19 would implicate church going or sharing a 'lo hei' lunch. Thankfully the majority of persons affected have only mild illness and recover well. But we have to remain vigilant especially about elderly individuals and those with co-morbidities, as they may potentially have a more severe clinical course.

Much more needs to be learnt about this disease and there are many unanswered questions. We as clinicians have to keep up with the rapidly evolving science regarding this condition amidst a plethora of information which may not necessarily be credible. In this regard, the Chapter of Infectious Diseases will work to bring you up to date, high quality and impactful publications. A link to these will be made available soon.

COVID-19

COVID-19 ARTICLES

1 [2019 Novel Coronavirus—Important Information for Clinicians](#) [FULL ARTICLE ACCESS](#)

del Rio C, Malani PN

JAMA 2020 Feb 5; Epub ahead of print

PMID: 32022836

The Covid-19 virus was first identified in Wuhan, China in early December 2019. It has since spread globally, with more than 20000 cases diagnosed (98.9% of which are in China) and more than 400 reported deaths. Early estimates of the transmissibility of Covid-2019 is at 2.68 (95% CI, 2.47-2.86), making it more infectious than the closely related SARS-CoV and MERS-CoV. The fatality rate of Covid-19 appears to be lower than that of SARS-CoV and MERS-CoV. Genetic sequencing of Covid-19 reveals that it shares 79.5% sequence similarity with SARS-CoV, as well as the same cell entry receptor, ACE2. The average incubation period of this virus is 5.2 days (95% CI, 4.1-7.0). While there has been some indication of asymptomatic transmission, it is likely that the majority of infections are from symptomatic individuals. A variety of symptoms has been reported in patients infected by the Covid-19 virus with most of them experiencing fever, dry cough and shortness of breath. The median age of patients is between 49 and 56 years of age and patients with comorbidities are more likely to develop more advanced disease. With this information, the article recommends that patients presenting with fever, dry cough and/or shortness of breath and have travelled to china in the past 14 days be classified as a patient under investigation (PUI) for Covid-19. They also recommend testing for other respiratory pathogens



since it is flu season. The authors note that there is little value in wearing a face mask in the absence of symptoms or obvious patient contact. Various antiviral therapy are being trialled. While the authors note that international travel bans as well as various quarantine measures have been put in place, they are doubtful of the efficacy of these precautions as they were ineffective in prior outbreaks of H1N1 and the 2014 Ebola outbreak. They also note that good personal hygiene habits and respiratory etiquette are likely more useful in stemming the spread of Covid-19.

2 [Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.](#) [FULL ARTICLE ACCESS](#)

Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y et. al.

Lancet 2020 Jan 30 Epub ahead of print.

PMID: 32007143

The 2019 novel coronavirus (Covid-19) has become a growing cause of concern worldwide with the WHO declaring it a global health emergency. This retrospective, single-centre study describes the epidemiological and clinical features of 99 patients infected with the Covid-19. Of the cases studied, 49% had been exposed to the Huanan seafood market where the virus is thought to have originated. 50% of the patients had pre-existing chronic diseases and most of them presented with fever (83%) or cough (82%) or multiple symptoms (90%) on admission. Less common symptoms include muscle ache (11 [11%] patients), confusion (9 [9%] patients), headache (8 [8%] patients), sore throat (5 [5%] patients), rhinorrhoea (4 [4%] patients). Many patients also showed abnormal blood biochemistry and cell counts, as well as liver and kidney function damage. The patients were prescribed a variety of interventions including antiviral therapy (76%), antibiotics (70%) and mechanical ventilation (17%), to varying degrees of success. Clinical characteristics of the 11% of patients who eventually died were in line with the MuLBSTA score, which predicts mortality in viral pneumonia. The authors recognised that even though this was a fairly small study, they were able to conclude that the Covid-19 is of a clustering onset that is more likely to infect older men with comorbidities, and lead to severe respiratory conditions such as acute respiratory distress syndrome (ARDS).

3 [Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents](#) [FULL ARTICLE ACCESS](#)

Kampf G, Todt D, Pfaender S, Steinmann E et. al.

J Hosp Infect. 2020 Feb 6; pii: S0195-6701(20)30046-3.

PMID: 32035997

With the advent of the 2019 novel coronavirus (Covid-19), this article reviews the persistence of various stains of coronaviruses, including SARS-coronavirus and MERS-coronavirus, and the efficacies of various biocidal agents against these viruses. Information gleaned from literature on coronaviruses revealed that human coronaviruses are able to survive on inanimate surfaces for up to 9 days. While there was no data on the frequency of hands becoming contaminated or the viral load on hands after contact with a contaminated surface or patient contact, it is recommended that hands should be decontaminated after such contact. As such, based on the data available for SARS-CoV and MERS-CoV, the authors suggest that alcohol based hand sanitisers as well as alcohol or bleach-based cleaning agents are superior to 0.05-0.2% benzalkonium chloride or 0.02% chlorhexidine digluconate for decontaminating surfaces. They conclude that the data available on SARS-CoV and MERS-CoV can be extended to Covid-19.



4 [Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China](#) FULL ARTICLE ACCESS

Wang DW, Hu B, Hu C et. al.

JAMA 2020 Feb 7; Epub ahead of print

PMID: 32031570

The Covid-19 outbreak that started in Wuhan, China has now spread to 24 other countries worldwide. This article describes the clinical characteristics of 138 patients infected with the Covid-19 virus in a single hospital in Wuhan, China. Similar to another descriptive study published on 30th Jan (see article 2 above), about half of the patients (64 [46.4%]) had pre-existing conditions such as hypertension (43 [31.2%]), cardiovascular disease (20 [14.5%]) and diabetes (14 [10.1%]). Patients commonly presented with fever (98.6%), dry cough (59.4%), muscle aches (34.8%) and shortness of breath (31.2%) on admission. Other less common symptoms included headache (9 [6.5%]), dizziness (13 [9.4%]), abdominal pain (3 [2.2%]), diarrhoea (14 [10.1%]), nausea (14 [10.1%]), and vomiting (5 [3.6%]). The authors noted that patients who required ICU care (36 patients) tend to be older at a median age of 66 years compared to 51 years ($p < 0.001$). These patients were also more likely to have comorbidities, and are more likely to report pharyngeal pain, dyspnea, dizziness, abdominal pain and anorexia. The median time from first symptoms to dyspnea, hospital admission and ARDS were 5 days (IQR, 1-10), 7 days (IQR, 4-8), and 8 days (IQR, 6-12), respectively, and that from onset of symptoms to admission into ICU was 10 days. All 138 patients showed bilateral involvement (patchy shadows and ground glass opacity) from chest CT scans. The patients were prescribed a variety of interventions including antiviral therapy (89.9%), antibiotics (moxifloxacin, 89 [64.4%]; ceftriaxone, 34 [24.6%]; azithromycin, 25 [18.1%]), glucocorticoid therapy (44.9%) and mechanical ventilation (23%), to varying degrees of success. As of 3rd Feb 2020, 34.1% were discharged, 6 died (4.3%), and 61.6% remain hospitalized.



5 [COVID-19 in Singapore-Current Experience: Critical Global Issues That Require Attention and Action](#) FULL ARTICLE ACCESS

Wong JEL, Leo YS, Tan CC

JAMA 2020 Feb 20; Epub ahead of print

PMID: 32077901

This article chronicles the Covid-19 outbreak in Singapore, describing the spread of the virus and the measures that have been taken so far to stem its spread. Singapore reported its first case of the virus in a tourist from Wuhan, China on the 23rd of January 2020 and has since confirmed 84 cases of Covid-19 infections, of which 23 cases were imported from China, 43 cases of local transmission from 5 clusters who further infected another 10 people, and 8 cases of yet to be known origin. A series of increasingly aggressive public health measures were taken with the spread of the virus. On top of extensive contact tracing and quarantine of close contacts of confirm cases, Singapore also placed entry restrictions on people who had travelled to China in the preceding 14 days, as well as imposed a compulsory 14-day leave of absence from work on Singapore residents who returned from China. The authors note the similarities that clinical progression of Covid-19 infection shares with SARS where patients develop pneumonia after about 1 week of illness. Additionally, like SARS, symptomatic infections in children is rare and mild. However, unlike SARS, the Covid-19 infection appear to have a broader spectrum of severity. Learning from the lessons of the SARS outbreak, Singapore had stepped up its capabilities to handle a virus outbreak by constructing a new purpose-built National Centre for Infectious Diseases and National Public Health Laboratory; significantly expanding the number of negative-pressure isolation beds throughout the public hospital system; stockpiling personal protective equipment (PPE) and masks; establishing formal platforms for multi-Ministry and cross-agency coordination; developing a strong capability to perform contact tracing quickly and at scale; training of health professionals including in the correct use of PPE; and building more biosafety level 3 laboratories. Even as Singapore is currently better equipped to handle the outbreak, the authors highlight 7 critical issues that need to be resolved – (1) better understanding of how the virus spreads, in particular asymptomatic transmission and infections in children; (2) development of a rapid, sensitive, affordable point-of-care screening test in the primary care setting; (3) identification of clinical biomarkers to establish prognosis; (4) identification of antiviral therapy; (5) establishment of effective communication channels between the medical/scientific community and the public to prevent panic; (6) addressing the physical and mental stress that healthcare workers experience in a crisis like this; and (7) development of a vaccine to Covid-19. The authors call for unity and better communication between global health authorities to get through the outbreak.



TECHNOLOGY AND MEDICINE

ARTICLES

1 [Metagenomic next-generation sequencing aids the diagnosis of viral infections in febrile returning travellers](#) FULL ARTICLE ACCESS

Jerome H, Taylor C, Sreenu VB, Klymenko T, Filipe ADS, Jackson C, Davis C, Ashraf S, Wilson-Davies E, Jesudason N, Devine K, Harder L, Aitken C, Gunson R, Thomson EC.

J Infect. 2019 Oct;79(4):383-388.

PMID: 31398374

Travel-associated infections are a diagnostic challenge due to the spectrum of potential aetiologies. This proof-of-principle study explores the suitability of metagenomic next-generation sequencing (MNGS) as a diagnostic tool for identifying viral pathogens in clinical samples from returning travellers in a single centre. Plasma samples from 40 returning travellers presenting with fever $\geq 38^{\circ}\text{C}$ were sequenced using MNGS on the Illumina MiSeq platform and compared with standard-of-care diagnostic assays. 11 were diagnosed with viral infection. Standard of care diagnostics revealed 5 viral infections using plasma samples; dengue virus 1 (n = 2), hepatitis E (n = 1), Ebola virus (n = 1) and hepatitis A (n = 1)- all of which were detected by MNGS. 3 additional patients with Chikungunya virus (n = 2) and mumps virus were diagnosed by MNGS only. Respiratory infections detected by nasal/throat swabs only were not detected by MNGS of plasma. 1 patient had infection with malaria and mumps virus during the same admission. MNGS analysis of plasma samples improves diagnostic sensitivity of viral infections and has potential as an all-in-one diagnostic test for identifying infections not considered by the treating physician, are missed using standard methods, co-infections and new or emerging pathogens.



TABLE OF CONTENTS

COVID-19		View Summary	View Article
1	2019 Novel Coronavirus—Important Information for Clinicians <small>FULL ARTICLE ACCESS</small>		
2	Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. <small>FULL ARTICLE ACCESS</small>		
3	Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents <small>FULL ARTICLE ACCESS</small>		
4	Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China <small>FULL ARTICLE ACCESS</small>		
5	COVID-19 in Singapore—Current Experience Critical Global Issues That Require Attention and Action <small>FULL ARTICLE ACCESS</small>		

TECHNOLOGY AND MEDICINE		View Summary	View Article
1	Metagenomic next-generation sequencing aids the diagnosis of viral infections in febrile returning travellers <small>FULL ARTICLE ACCESS</small>		

INFECTIOUS DISEASES		View Summary	View Article
1	Epidemiology and Control of SARS in Singapore. <small>FULL ARTICLE ACCESS</small>		
2	Megatrends in Infectious Diseases: The Next 10 to 15 Years. <small>FULL ARTICLE ACCESS</small>		
3	Association of Duration and Type of Surgical Prophylaxis With Antimicrobial-Associated Adverse Events.		
4	Contact precautions in single-bed or multiple-bed rooms for patients with extended-spectrum β-lactamase-producing Enterobacteriaceae in Dutch hospitals: a cluster-randomised, crossover, non-inferiority study.		



5	Long-term changes of gut microbiota, antibiotic resistance, and metabolic parameters after <i>Helicobacter pylori</i> eradication: a multicentre, open-label, randomised trial		
6	Safety and efficacy of inactivated varicella zoster virus vaccine in immunocompromised patients with malignancies: a two-arm, randomised, double-blind, phase 3 trial.		
7	HLA-B*5701 Genotyping for Abacavir Prescription: Re-Examination of its Cost-Effectiveness in Singapore. <small>FULL ARTICLE ACCESS</small>		
8	Frailty is an independent risk factor for mortality, cardiovascular disease, bone disease and diabetes among aging adults with HIV.		
9	Oral vs Intravenous Antibiotics for Patients With <i>Klebsiella pneumoniae</i> Liver Abscess: A Randomized, Controlled Noninferiority Study.		

INFECTIOUS DISEASES

ARTICLES

1	<p>Epidemiology and Control of SARS in Singapore. <small>FULL ARTICLE ACCESS</small></p> <p><i>Goh KT, Cutter J, Heng BH, Ma S, Koh BK, Kwok C, Toh CM, Chew SK et. al.</i> Ann Acad Med Singapore. 2006 May;35(5):301-16. <i>PMID: 16829997</i></p> <p>Severe Acquired Respiratory Syndrome (SARS) was an outbreak caused by the SARS-coronavirus (SARS-CoV) in 2003. The authors describe the epidemiology of the outbreak as well as the measures that were and have since been put in place to respond to emerging infectious diseases. SARS was first identified in Singapore in a local resident who had returned from Hong Kong in late February of 2003. The disease eventually spread to 4 healthcare institutions and a wholesale vegetable market, leading to a total of 238 probable cases and 33 deaths. 90% of the cases were transmitted within the healthcare or household setting and Singapore was removed from the WHO's list of areas with local transmission about 3 months after initial detection of the disease. The late identification and subsequent isolation of the first patient with SARS led to the scale and speed at which the disease spread. In view of this, various measures were put into place to quickly stem the spread the disease including enhanced surveillance for suspected cases and improved personal protection equipment (PPE) in healthcare institutions. Operational readiness for future emerging infectious diseases was also increased. A contact tracing centre, streamlined quarantine operations, additional isolation facilities and improved legislative framework for biosafety are among the steps taken to better prepare Singapore any future outbreaks.</p>
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- 2 [Megatrends in Infectious Diseases: The Next 10 to 15 Years.](#) FULL ARTICLE ACCESS
- Wong SY, Tan BH.
Ann Acad Med Singapore. 2019 Jun;48(6):188-194.
 PMID: 31377763
- Despite remarkable progress in reducing related mortality, infections still account for 13-15 million deaths annually and this estimate is expected to remain unchanged until 2050. The authors have identified 4 megatrends in infectious diseases- namely, “emerging and re-emerging infections”, “antimicrobial resistance”, “demographic changes” and “technological advances”. Understanding these trends and challenges should allow opportunities for the medical community to reshape the future while further inroads will require broad approaches involving surveillance, public health and translating scientific discoveries into disease control efforts.
- 3 [Association of Duration and Type of Surgical Prophylaxis With Antimicrobial-Associated Adverse Events.](#)
- Branch-Elliman W, O'Brien W, Strymish J, Itani K, Wyatt C, Gupta K.
JAMA Surg. 2019 Jul 1;154(7):590-598.
 PMID: 31017647
- Antibiotic prophylaxis prior to incision clearly decreases surgical site infections (SSI) incidence but what are the relative risks and benefits of continuing it? This US national retrospective study analysed the incidence of SSI, acute kidney injury (AKI), and *Clostridioides difficile* infection (CDI) in relation to prophylaxis type and duration in 79,058 patients who underwent cardiac, colorectal, vascular, and total joint-replacement surgery within the Veterans Affairs Healthcare system from 2008-2013. Incidence of AKI increased with use of vancomycin for prophylaxis in all types of surgery while that of CDI increased with use of clindamycin or fluoroquinolones. Extending antibiotic prophylaxis duration >24 hours did not reduce SSI incidence for any type of surgery but progressively increased AKI and CDI relative incidence with each additional day of use. Specifically, the adjusted odds ratio (aOR) of AKI post a cardiac procedure and subjected to prophylaxis for 24h to <48h, 48h to <72h, 72h or more is 1.03 (95% CI, 0.95-1.12), 1.22 (95% CI, 1.08-1.39) and 1.82 (95% CI, 1.54-2.16) respectively. aOR of AKI after a noncardiac procedure and subjected to prophylaxis for 24h to <48h, 48h to <72h, 72h or more is 1.31 (95% CI, 1.21-1.42), 1.72 (95% CI, 1.47-2.01) and 1.79 (95% CI, 1.27-2.53) respectively. A similar trend is observed with postoperative CDI where the aOR of CDI after prophylaxis for 24h to <48h, 48h to <72h, 72h or more is 1.08 (95% CI, 0.89-1.31), 2.43 (95% CI, 1.80-3.27) and 3.65 (95% CI, 2.40-5.53) respectively. The unadjusted numbers needed to harm (NNH) for AKI after 24h to <48h, 48h to <72h, 72h or more of postoperative prophylaxis were 9, 6, and 4 respectively, and that for CDI were 2000, 90, and 50 respectively. Sub-analysis of cardiac patients showed use of vancomycin plus a beta-lactam compared with use of either agent alone was associated with significant increase in AKI incidence at all stages. Results show no benefit in increasing antibiotic prophylaxis duration >24 hours post-surgery and even a small but measurable level of harm. Institutions need to assess use of surgical antibiotic prophylaxis regimens beyond 24 hours in relation to SSI risk and antibiotic-associated adverse effects.
- 4 [Contact precautions in single-bed or multiple-bed rooms for patients with extended-spectrum \$\beta\$ -lactamase-producing Enterobacteriaceae in Dutch hospitals: a cluster-randomised, crossover, non-inferiority study.](#)
- Kluytmans-van den Bergh MFQ, Buijning-Verhagen PCJ, Vandenbroucke-Grauls CMJE, de Brauwier EIGB, Buiting AGM et al



Lancet Infect Dis. 2019 Aug 23. pii: S1473-3099(19)30262-2.

PMID: 31451419

Use of single-bed rooms for control of extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae is under debate and the value of applying contact precautions unproven. This cluster-randomised, crossover, non-inferiority study of medical and surgical wards in 16 hospitals assessed whether an isolation strategy of contact precautions in a multiple-bed room was non-inferior to that in a single-bed room for preventing transmission of ESBL-producing Enterobacteriaceae. Primary outcome was transmission to wardmates, defined as rectal carriage of the bacterial isolate clonally related to that of the index patient's in ≥ 1 wardmate. It was found that for patients with ESBL-producing Enterobacteriaceae cultured from routine sampling, an isolation strategy of contact precautions in a multiple-bed room was non-inferior (10% non-inferiority margin) to that in a single-bed room.

5 [Long-term changes of gut microbiota, antibiotic resistance, and metabolic parameters after *Helicobacter pylori* eradication: a multicentre, open-label, randomised trial](#)

Jyh-Ming Liou, Chieh-Chang Chen, Chih-Min Chang, Yu-Jen Fang, Ming-Jong Bair, Po-Yueh Chen et al.

Lancet Infect Dis. 2019 Oct;19(10):1109-1120.

PMID: 31559966

First-line options for *H.pylori* eradication include 14-day triple therapy (T14), 10-day concomitant therapy (C10) and 10-day bismuth quadruple therapy (BQ10). This multicentre, open-label, randomised trial of 1620 participants from 9 medical centres assessed short and long-term effects of these therapies on gut microbiota, antibiotic resistance and metabolic parameters. Patients were randomised to receive T14, C10 or BQ10 and assessed for the above as well as reinfection frequency. Faecal samples were collected before, at 2 weeks, 2 months and ≥ 1 year after eradication therapy. Compared to baseline, gut microbiota diversity was significantly altered at 2 weeks in all groups. α and β diversities were restored at 2 months and 1 year respectively for T14, but neither fully recovered after 1 year for C10 and BQ10. A transient increase in resistance rates of *E.Coli* to several antibiotics occurred at 2 weeks but returned to baseline at 2 months and after 1 year. A slight increase in body-mass index (BMI) was noted, but alongside improvements in other metabolic parameters. There was no significant change in prevalence of metabolic syndrome at 2 months and 1 year after T14, C10, and BQ10.

6 [Safety and efficacy of inactivated varicella zoster virus vaccine in immunocompromised patients with malignancies: a two-arm, randomised, double-blind, phase 3 trial.](#)

Mullane KM, Morrison VA, Camacho LH, Arvin A, McNeil SA, Durrand J, Campbell B, Su SC, Chan ISF, Parrino J et. al

Lancet Infect Dis. 2019 Sep;19(9):1001-1012.

PMID: 31399378

Patients immunocompromised due to malignancy have increased risk of herpes zoster and related complications. This phase 3, randomised, double-blind, placebo-controlled trial involving 40 countries, aimed to investigate the efficacy and safety of an inactivated varicella zoster virus (VZV) vaccine for herpes zoster prevention in patients with a solid tumour malignancy and receiving chemotherapy, or a haematological malignancy (whether receiving chemotherapy or not). Patients were randomised to receiving 4 doses of VZV or placebo approximately 30 days apart. Results showed the inactivated VZV vaccine was well tolerated (<1% risk of vaccine-related serious events) and efficacious for herpes zoster prevention in patients with solid tumour malignancies receiving chemotherapy, but not in haematological malignancies where the study arm was terminated early due to evidence of futility.



7 [HLA-B*5701 Genotyping for Abacavir Prescription: Re-Examination of its Cost-Effectiveness in Singapore.](#) [FULL ARTICLE ACCESS](#)

Goh KS, Kapoor R, Lee CC, Ng CY, Leong KP.

Ann Acad Med Singapore. 2019 Apr;48(4):133-138.

PMID: 31131386

Abacavir is used to control HIV disease progression but has a potential side effect of hypersensitivity reaction (HSR) which can result in multi-organ system failure and is more common in patients with HLA-B*5701 polymorphism. Studies have demonstrated the efficacy of HLA-B*5701 screening prior to abacavir prescription for preventing HSR in those carrying the polymorphism, but a prior local study found that HLA-B*5701 genotyping was not cost-effective in Singapore except for a subgroup of newly diagnosed Indian patients with early-stage HIV contraindicated to tenofovir. This study assessed if new information on the cost-effectiveness of HLA-B*5701 genotyping in Singapore would change the conclusions of the earlier study. From the findings, the authors recommend genotyping late-stage Malay and Indian patients irrespective of whether they contraindicated to tenofovir.

8 [Frailty is an independent risk factor for mortality, cardiovascular disease, bone disease and diabetes among aging adults with HIV.](#)

Kelly SG, Wu K, Tassiopoulos K, Erlandson KM, Koletar SL, Palella FJ; ACTG A5322 Study Team.

Clin Infect Dis. 2019 Oct 69(8).

PMID: 30590451

A study of >1000 patients characterising associations between frailty and incidence of cardiovascular disease (CVD), diabetes mellitus (DM), bone disease and mortality within a cohort of aging persons with HIV (PWH). Patients with ≥ 3 criteria using Fried's frailty assessment (performed at baseline and annually) were defined as frail. Outcomes of mortality, incident CVD events, DM and bone disease events were recorded throughout the study period. Baseline frailty (6%) was associated with increased risk of incident CVD, DM and bone disease, with slow gait speed being associated with the former 2. Increased frailty scores from baseline to 48 weeks (6%) was associated with mortality but not other clinical outcomes.

9 [Oral vs Intravenous Antibiotics for Patients With Klebsiella pneumoniae Liver Abscess: A Randomized, Controlled Noninferiority Study.](#)

Molton JS, Chan M, Kalimuddin S, Oon J, Young BE, Low JG, Salada BMA, Lee TH, Wijaya L, Fisher DA, Izharuddin E et al.

Clin Infect Dis. 2019 Oct 23. pii: ciz881.

PMID: 31641767

Klebsiella pneumoniae liver abscess is emerging worldwide. Treatment includes drainage and prolonged intravenous (IV) antibiotics. This non-inferiority, parallel group, randomised clinical trial reviewed if oral antibiotics were noninferior to IV antibiotics. Hospitalised adults with liver abscess and *K. pneumoniae* isolated from blood or abscess fluid were recruited and randomised to oral ciprofloxacin or IV ceftriaxone for 28 days. 152 patients (mean age 58.7 years; 25.7% women) were recruited following a median 5 days of effective IV antibiotics. 69.7% underwent abscess drainage. 95.9% randomised to oral antibiotics met 1^o endpoint of clinical cure compared to 92.3% randomised to IV antibiotics (risk difference, 3.6%, 2-sided 95% confidence interval, -4.9% to 12.8%). Nonfatal serious adverse events occurred in 16.7% of the oral group and 16.9% of the IV group. The authors conclude oral antibiotics were noninferior to IV antibiotics for early treatment of *Klebsiella* liver abscess.



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