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ABSTRACT & COMMENTARY

Managing Appendicitis Medically

By Joseph E. Scherger, MD, MPH

Core Faculty, Eisenhower Health Family Medicine, Residency Program, Eisenhower Health Center, La Quinta, CA; Clinical Professor, Keck School of Medicine, University of Southern California, Los Angeles

Dr. Scherger reports no financial relationships relevant to this field of study.

SYNOPSIS: A multicenter, randomized trial showed that 10 days of antibiotics results in comparable outcomes as surgery. Three in 10 patients treated with antibiotics required surgery within 90 days.

SOURCE: CODA Collaborative, Flum DR, Davidson GH, Monsell SE, et al. A randomized trial comparing antibiotics with appendectomy for appendicitis. *N Engl J Med* 2020;383:1907-1919.

Researchers randomized 1,552 adults from 25 centers in the United States to receive 10 days of antibiotics or surgery for acute appendicitis. In the group treated with antibiotics, 47% were not hospitalized.

The antibiotics varied and were selected from the Surgical Infection Society and the Infectious Diseases Society of America guidelines for intra-abdominal infections.[1,2] The first dose of antibiotics were given in the ED. These included cefoxitin, moxifloxacin, and ticarcillin-clavulanic acid. In some cases, the authors used dual antibiotics. Outpatient regimens included metronidazole with clindamycin.

In the antibiotics group, 41% of those with an appendicolith went to surgery within 90 days compared with 29% who did not exhibit this finding. There were more complications in the antibiotics group, but those were seen mostly in patients with an appendicolith.

■ COMMENTARY

The standard treatment for acute appendicitis has been surgery. Laparoscopy is the most common surgical technique for this condition today. However, like all medical procedures, risk exists.

Using antibiotics to treat appendicitis was first reported more than 60 years ago.[3] Since then, investigators have performed other randomized studies of treating appendicitis with antibiotics.[4,5] However, this work by the CODA Collaborative is the largest and the first to separate patients with an appendicolith. Although

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[INSIDE]

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this work is promising, the author of an accompanying editorial urged clinicians to take a cautious approach.[6] ■

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ABSTRACT & COMMENTARY

Healthcare Personnel COVID-19 Hospitalizations and Vaccine Prioritization

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University

Dr. Deresinski reports no financial relationships relevant to this field of study.

SYNOPSIS: During the period of study, 5.9% of individuals hospitalized for COVID-19-related reasons were healthcare providers (HCP), with approximately one-third involving HCP who were not expected to directly contact patients.

SOURCE: Kambhampati AK, O'Halloran AC, Whitaker M, et al. COVID-19-associated hospitalizations among health care personnel — COVID-NET, 13 states, March 1-May 31, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1576-1583.

Kambhampati et al used data collected by the COVID-NET population-based survey to evaluate the proportion and characteristics of healthcare personnel (HCP) who had been hospitalized for COVID-19 in 98 counties of 13 states between March 1 and May 31, 2020. HCP were broadly defined to include anyone in a healthcare occupation with potential exposure to patients or infectious materials. In-depth medical chart abstractions were performed on a subset, and 438 of the 6,760 for whom documentation was available were HCP.

The median age of the HCP hospitalized with COVID-19 was 49 years, and 71.9% were women. Approximately one-half were categorized as non-Hispanic Black, one-fourth as non-Hispanic white, and one-tenth as Hispanic or Latino. Just more than two-thirds (67.4%) worked jobs for which direct patient contact was expected to occur, with 36.3% of the total in nursing-related categories. Almost nine in 10 had an underlying condition: obesity (72.5%), hypertension (40.6%), or diabetes mellitus (30.9%). Among the women who were age 18-49 years, 9.6% were pregnant. ICU attention was required for 27.5%, 15.9% received mechanical ventilation, and 4.2% died.

■ COMMENTARY

Kambhampati et al provide useful information regarding the burden of COVID-19 on HCP. However, they studied data from relatively early in the pandemic. Circumstances may be different today (e.g., possible better treatment options). During the time studied, some institutions may have owned limited supplies of personal protective equipment.

Although nursing occupations make up the largest single proportion of cases, no

denominator data were presented. Registered nurses are reported to account for one-third of all U.S. healthcare practitioners. The picture presented in this study provides some useful input into initial tactics for COVID-19 vaccination. Although national recommendations for vaccine prioritization have been published, these will have to be adapted to circumstances at the level of healthcare organizations, including hospitals, something which has been addressed, to an extent, by the Society for Healthcare Epidemiology of America.[1]

The difficulties of vaccination prioritization will be dictated by the extent of vaccine availability. Many recommendations suggest the first target should be individuals who provide direct care to COVID-19 patients regularly. However, Kambhampati et al found approximately one-third of the hospitalized HCP did not directly contact patients. Other data from serosurveys suggest direct caregivers are not the HCP at greatest risk for infection. A recent survey at our institution revealed low levels of seropositivity overall, and the highest rates were not in HCP but in environmental and food workers. Others have reported the seroprevalence was not significantly different among direct-care providers vs. others.[2,3] None of these data address the issue of where the infections occur. It is almost certain the most infections occur in the community rather than in the healthcare setting. Although different arguments can be made, the data indicate HCP, such as environmental and food workers, should be, at a minimum, at the same priority level as those providing direct care to COVID-19 patients. Also, the finding that three-fourths of HCP hospitalized for COVID-19-related reasons are obese suggests healthcare institutions should be directly addressing this problem among their employees. ■

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ABSTRACT & COMMENTARY

The Effect of Age on Cholesterol-Lowering Therapy

By Michael H. Crawford, MD

Professor of Medicine, Associate Chief for Education, Division of Cardiology, University of California, San Francisco

Dr. Crawford reports no financial relationships relevant to this field of study.

SYNOPSIS: Investigators analyzed data on the effect of age on cardiovascular (CV) outcomes and LDL cholesterol-lowering by alirocumab vs. placebo in recent acute coronary syndrome patients. They found alirocumab can lower the rate of CV events regardless of age — and produce more absolute benefit with age.

SOURCE: Sinnaeve PR, Schwartz GG, Wojdyla DM, et al. Effect of alirocumab on cardiovascular outcomes after acute coronary syndromes according to age: An ODYSSEY OUTCOMES trial analysis. *Eur Hear J* 2020;41:2248-2258.

The dearth of older patients in studies of LDL cholesterol-lowering has left uncertainty about the advisability of statin therapy in patients older than age 75 years. Recently, Sinnaeve et al conducted a prespecified analysis of the Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With alirocumab (ODYSSEY OUTCOMES) trial. They assessed the effect of age on cardiovascular outcomes and LDL cholesterol-lowering effects of alirocumab vs. placebo in patients with a recent (less than 12 months) acute coronary syndrome (ACS) and LDL levels above target (> 70 mg/dL) on maximally tolerated, high-intensity statin therapy.

The investigators were blinded to the treatment assignment and LDL levels. The primary endpoint was major adverse cardiovascular events (MACE), which was a composite of cardiac death, myocardial infarction, stroke, or unstable angina requiring hospitalization. The mean age of the 18,924 patients was 59 years (27% were > age 65 years and 5% > age 75 years). Because of the paucity of patients in the latter group, the data analysis was dichotomized at age 65 years. Older patients were more likely to be women and to be living with other cardiovascular disease. Adherence to the study drug and the degree of LDL lowering were similar in both age groups.

Mean LDL levels at three years were 63 mg/dL in those younger than age 65 years and 57 mg/dL in those older than age 65 years vs. 102 mg/dL and 97 mg/dL, respectively, in the placebo groups. Relative risk reductions were similar for both groups: age > 65 years HR, 0.78; 95% CI, 0.68-0.81 and age < 65 years HR, 0.89; 95% CI, 0.80-1.0; *P* for the interaction = 0.19. The HR for all-cause death was 0.77 (95% CI, 0.62-0.95) in the age > 65 years group and 0.94 (95% CI, 0.77-1.15) in the < 65 years group (*P* interaction = 0.46).

Dichotomizing the data at age 75 years produced similar results: HR for MACE in both groups was 0.85. Analyzing age as a continuous variable showed advancing age raised the risk of MACE and the absolute reduction in MACE with alirocumab. The number needed to treat to prevent one MACE at three years was 43 at age 45 years, 26 at age 75 years, and 12 at age 85 years. More patients experienced severe adverse events in the age > 65 years group, but there was no difference between alirocumab and placebo. The authors concluded that in patients with recent ACS, alirocumab reduces MACE, regardless of age — but with increasing absolute benefit (not harm) with advancing age. Thus, aggressive LDL lowering should not be withheld from older patients.

■ COMMENTARY

Elderly patients with cardiovascular disease often are undertreated, presumably over fear of adverse effects, polypharmacy, potential drug-drug interactions, or the concept that they have fewer years left to gain. In this prespecified analysis of the ODYSSEY OUTCOMES study, the authors noted those older than age 65 years were on less intense statin regimens at baseline and rarely were taking ezetimibe, despite their recent ACS event. Since the safety profile of alirocumab is similar to placebo, investigators believed this might be a good way to lower LDL cholesterol to target (< 70 mg/dL) in elderly patients. Hence, this analysis of the ODYSSEY OUTCOMES trial is of interest. Sinnaeve et al showed that not only did intensive lowering of LDL reduce MACE and all-cause death in post-ACS patients age older than 65 years, but it did so with increased absolute benefit compared to younger patients. Also, these results were obtained without any increase in adverse events over placebo. This resulted in a progressively smaller number needed to treat to prevent one MACE to an impressive 12 in those age 85 years. These data are similar to two other randomized, controlled trials published while ODYSSEY OUTCOMES was conducted. In the PROVE-IT TIMI 22 study of atorvastatin vs. pravastatin in post-ACS patients, at age > 70 years, the number needed to treat was 13 vs. 44 for those < age 70 years.[1] In the similar IMPROVE-IT study of adding ezetimibe to simvastatin therapy, those > age 75 years had a number needed to treat of 11.[2] Other researchers confirmed these results further in the Cholesterol Treatment Trialists meta-analysis 8.[3] In addition, reducing MACE in older patients should improve quality of life and lower medical care costs. Thus, a strong picture is emerging that older patients with coronary artery disease should be treated with LDL-lowering therapy as aggressively as younger patients.

There were a few limitations to the Sinnaeve et al analysis. The low end age cutoff for enrollment of 40 years and the dichotomization at age 65 years was by trial design. The number of very elderly patients was small, so estimates of effectiveness and safety in those > age 80 years is less precise. All the patients were on maximally tolerated, high-intensity statins at baseline, and few were on ezetimibe. Considering the entry criteria for the study, it is unlikely many were frail, so the results are less likely to apply to sicker elderly patients. Although the follow-up duration for this study was long (four years, median 2.8 years), it is difficult to estimate years gained beyond the trial duration. However, the consistency of the data with other studies supports the conclusion that aggressive lipid-lowering for secondary prevention in elderly patients is important. ■

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ABSTRACT & COMMENTARY

Antibiotics for Traveler's Diarrhea

By Philip R. Fischer, MD, DTM&H

Professor of Pediatrics, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN

Dr. Fischer reports no financial relationships relevant to this field of study.

SYNOPSIS: International travel carries a risk of colonization by antimicrobial-resistant intestinal flora. Using quinolone, but not a macrolide, during travel further increases the risk of acquisition of extended-spectrum, beta-lactamase-producing *Enterobacteriaceae*.

SOURCE: Wuerz TC, Kassim SS, Atkins KE. Acquisition of extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL-PE) carriage after exposure to systemic antimicrobials during travel: Systematic review and meta-analysis. *Travel Med Infect Dis* 2020;37:101823.

International travel prompts changes in the intestinal flora, and colonization by extended-spectrum, beta-lactamase producing-*Enterobacteriaceae* (ESBL-PE) is associated with travel alone. Using antibiotics during travel is thought to further raise the risk of becoming colonized by these resistant microbes. ESBL-PE-colonized individuals usually show no symptoms but are at some risk of developing symptomatic illness that carries financial costs as well as risks of morbidity and mortality.

Using standard systematic review techniques, Wuerz et al identified 15 prospective cohort studies published from 2010 to 2017 that evaluated ESBL-PE acquisition associated with international travel and noted whether the traveler had been exposed to antibiotics during the trip. A total of 5,283 travelers were included in the 15 studies. Asia was the most common destination continent, followed by Africa. Diarrhea was reported in 38% of travelers, and 10% received antibiotics. The antibiotics received were beta-lactams (30%), fluoroquinolones (25%), doxycycline (20%), and macrolides (8%). Overall, 31% of travelers acquired ESBL-PE during their travel.

As determined by meta-analysis, antibiotic use increased the risk of ESBL-PE acquisition 2.37-fold. Fluoroquinolones, as compared to no antibiotic use, increased ESBL-PE acquisition 4.68-fold. Tetracyclines (which are used for malaria prevention as well as for diarrhea treatment) increased ESBL-PE acquisition 1.68-fold. Beta-lactams and macrolides did not increase the risk of acquisition of these organisms.

■ COMMENTARY

We imagine, anticipate, and dream of the opportunity to travel internationally again. Eventually, we will confront the possibility of providing presumptive antibiotic therapy for travelers who might develop bothersome traveler's diarrhea. Even during the pandemic, science is advancing. The helpful systematic review by Wuerz et al shows using antibiotics for healthy travelers with mild diarrhea should be questioned and, likely, avoided.

Traveler's diarrhea is common, affecting one-third or more of short-term visitors to less-resourced countries in tropical regions. In fact, a recent study showed 46% of medical students on overseas rotations developed traveler's diarrhea.[1] Typically, the diarrhea is self-limited, resolving within a few days. Nonetheless, the illness can be uncomfortable, inconvenient, and, rarely, severe. Bacteria, often enterotoxigenic *Escherichia coli*, are the usual cause of diarrhea in travelers from more-resourced to less-resourced countries, and antibiotics such as azithromycin and quinolones significantly shorten the duration of illness.[2]

Thus, it has been common practice to provide travelers with a course of oral antibiotics to use in the event that they develop diarrhea. The cost and side effects (rare allergic reactions) seemed minimal compared to the benefit of salvaging a day or two of lost activity and altered travel plans. It was assumed the number of treated travelers would be small compared to the total population numbers and that a few days of antibiotic use would not contribute significantly to population-level alterations in antimicrobial resistance.

However, as previously proposed by an expert panel of the International Society of Travel Medicine,[2] there has been growing concern that antibiotic use can increase the acquisition of resistant germs significantly, with resultant spread of these germs in new regions following the return from travel. Now, there are enough data on specific risks related to ESBL-PE to warrant the systematic review.

The review by Wuerz et al is extremely useful. Clearly, ESBL-PE acquisition is common with international travel, with about one-third of travelers from North America and Europe to Asia or Africa becoming colonized; antibiotics increase the risk. However, as this meta-analysis clearly shows, it is not just any antibiotic that increases the risk; fluoroquinolones are problematic, and macrolides are not.

Of course, the data from Wuerz et al are not new, even if the systematic review and meta-analysis are new uses of previously published data. The prescribing patterns of experts at 20 United States travel clinics were followed from 2009-2018 as they provided care to more than 100,000 travelers before trip departure.[3] As updated data and expert guidelines and governmental concerns about antimicrobial use were published, antibiotic use dropped significantly, and quinolones, in particular, became used much less frequently.[2,3]

Overuse of antibiotics likely also relates to the changing resistance patterns of more serious infections, such as typhoid fever. A recent report of international travelers who acquired typhoid during their trips showed quinolone resistance in 78% of South Asian *S. typhi* isolates and in 60% of isolates from sub-Saharan Africa.[4]

In terms of avoiding increases in both general antimicrobial resistance and ESBL-PE acquisition, antibiotics should not be used to treat uncomplicated traveler's diarrhea in most healthy patients.[2] Rather, oral hydration and, perhaps, an anti-motility agent, such as loperamide (except in young children), can be effective in facilitating recovery and reducing poor outcomes. For immunocompromised patients, travelers with bloody diarrhea, and, possibly, those with very tight

travel itineraries, an antibiotic could be considered, with preference for a macrolide over a quinolone. ■

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ABSTRACT & COMMENTARY

Multiple Sclerosis and Vascular Disease

By Ulrike W. Kaunzner, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Kaunzner reports no financial relationships relevant to this field of study.

SYNOPSIS: Researchers evaluated the presence and pathological significance of extracranial systemic and cerebral small vessel disease in patients with multiple sclerosis (MS) compared to healthy controls. MS patients exhibited less systemic vascular disease and more small vessel disease in the brain vs. controls.

SOURCE: Geraldes R, Esiri MM, Perera R, et al. Vascular disease and multiple sclerosis: A post-mortem study exploring their relationships. *Brain* 2020;143:2998-3012.

Multiple sclerosis (MS) is an immune-mediated disease leading to demyelination, axonal loss, and progressive clinical disability. The etiology of MS remains elusive; however, different environmental and genetic factors are considered to contribute to disease onset. The disease course of each individual MS patient also varies significantly, and influences of vascular risk factors and vascular disease on the overall outcome have been discussed.

Geraldes et al examined a unique postmortem cohort with access to brain and whole-body pathology data of MS patients and healthy controls. They enrolled 85 MS cases (median age at death, 62.0 years) and 68 age-matched controls (median age at death, 58.0 years) and assessed the systemic vascular disease score based on autopsy records. They evaluated a subset of this original cohort, and examined the postmortem brain tissue of 42 MS cases and 39 healthy controls for cerebral small vessel disease and cerebral inflammation. The authors took the effect of age on vascular disease into consideration and dichotomized their cohorts into younger and older age groups, below and above the median age of 60 years, respectively. The authors created a reliable method to assess the systemic vascular disease score based on autopsy reports, using the extent of atheroma and end-organ damage, and found that MS patients, particularly in the younger age group, had a lower systemic cardiovascular disease burden vs. controls, but this increased with age. Conversely, cerebral small vessel disease was more severe in younger MS patients compared to controls. In addition, the investigators commented on pathophysiological findings that were specific for the MS cohort, noting periarteriolar space dilatation, hemosiderin deposits, and inflammation were found, and were distinctly different from the classic demyelinating MS plaque.

■ COMMENTARY

The authors accessed data from body and brain autopsies of untreated MS patients, evaluating the presence of systemic vascular disease and cerebral small vessel disease. These data from an MS cohort in the pre-treatment era improve our understanding of the natural course of the disease and the potential existence of vascular comorbidities. The presence of more cerebral small vessel disease in younger patients, with concomitantly less peripheral vascular disease, is intriguing. The authors asked, "Is an overall proinflammatory state contributing to a decrease in systemic vascular disease in these younger MS patients?" The mean and median ages for the evaluated cohorts were high (MS patients: median age at death 62.0 years, range 39-84 years; healthy control: median age at death 58.0 years, range 40-85 years), which is a result of the nature of a postmortem study. Since cerebral microvascular changes already are evident in the younger group of MS patients, it would be interesting to know the extent of cerebral small vessel disease in an even younger cohort of MS patients.

The authors described perivascular space dilatation, hemosiderin deposits, and microbleeds, independent from classic MS lesions. Are these vascular changes part of the inflammatory process, or do they represent an independent pathophysiology? Are these observed vascular

changes the contributing factors and potential missing link to an increased disability score and more progressive outcome in a subset of MS patients? The potential presence of hypoxia in MS has been considered as an inducer of proinflammatory pathways and a potential contributor to MS pathogenesis. The direct or indirect effect of hypoxic changes on continued inflammation and progression of the disease will be crucial for the evaluation of MS patients, particularly those susceptible to vascular changes. More studies, and ideally in vivo studies, are warranted to assess the effect of systemic and cerebral vascular disease on the course and disability levels of MS patients of all age groups. Thorough evaluation of vascular risk factors and vascular disease will be warranted, and imaging techniques differentiating the burden of central nervous system inflammation and vascular disease might be important in the future. A better understanding of the extent and contribution of vascular disease might offer a different target to modify the disease course of MS patients. ■

PHARMACOLOGY UPDATE

Casirivimab + Imdevimab Injection

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Assistant Clinical Professor of Medicine, University of California, San Francisco.
Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

Drs. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has issued an emergency use authorization (EUA) to Regeneron Pharmaceuticals, Inc. for its monoclonal antibody cocktail for the treatment of mild to moderate COVID-19.[1] Casirivimab and imdevimab are recombinant human IgG1 monoclonal antibodies that target the receptor-binding domain of the spike protein of SARS-CoV-2.[2] Binding the viral spike protein reduces the attachment and entry of the virus into human cells. This combination gained early publicity when it was administered to President Trump after he tested positive for COVID-19 in October. The U.S. Department of Health and Human Services will make allocations to the states and territories, while AmerisourceBergen will distribute for the U.S. government.[2]

INDICATIONS

Casirivimab/imdevimab should be used to treat mild to moderate COVID-19 in adults and patients ≥ 12 years of age weighing at least 40 kg who have tested positive for SARS-CoV-2. These patients also would be considered high risk for developing severe COVID-19 or winding up in the hospital.[2]

DOSAGE

The authorized dose is 1,200 mg of casirivimab and 1,200 mg of imdevimab, administered together as one intravenous infusion over at least one hour.[2] Administer this combination as soon as possible after a positive viral test for SARS-CoV-2 (molecular or antigen) and within 10 days of the onset of symptoms. Casirivimab injection and imdevimab injection are available in separate 300 mg/2.5 mL increments.

POTENTIAL ADVANTAGES

The two monoclonal antibody combination approach may offer an advantage over the single monoclonal antibody (i.e., bamlanivimab). SARS-CoV-2 may mutate to viral variants with reduced susceptibility to either casirivimab or imdevimab because of different spike protein amino acid substitutions. These mutations have resulted in reduced susceptibility to one monoclonal antibody, but retained susceptibility to the other. This has led to maintained combination effectiveness.[2]

POTENTIAL DISADVANTAGES

Casirivimab/imdevimab should not be used for patients who are hospitalized or require oxygen because of COVID-19.[2] The combination also should not be used for those who are on chronic oxygen therapy and require a higher baseline oxygen flow rate because of COVID-19.[2] Hypersensitivity, including anaphylaxis and infusion-related reactions (e.g., fever, chills, bronchospasm, hypotension, urticaria, and pruritus), may occur.[2]

COMMENTS

Data supporting the EUA were drawn from a randomized, double-blind, placebo-controlled Phase I/II trial that included 799 nonhospitalized adults with mild to moderate COVID-19 symptoms.[2] Subjects were randomized to 1,200 mg of casirivimab and 1,200 mg of imdevimab (n = 266), 4,000 mg of casirivimab and 4,000 mg of imdevimab (n = 267), or placebo (n = 266), initiated within three days of a positive test. The prespecified primary endpoint was average change in viral load from baseline. The secondary endpoint was medically attended visits related to COVID-19 (hospitalization, ED visit, urgent care visits, office/telemedicine visits) within 28 days after treatment.

Casirivimab/imdevimab (pooled doses) produced a significant reduction in viral load from day 1 through

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Amy M. Johnson, MSN, RN, CPN

day 7, with the largest reduction occurring in subjects with high viral load or who were seronegative at baseline.[2] No difference was observed between the two active doses. No difference in median time to symptom improvement was observed (five days for antibodies vs. six days for placebo). The most significant observation was with the secondary endpoint (hospitalization/ED visits in subjects at higher risk of hospitalization). The frequency was 3% for casirivimab/imdevimab (n = 151) and 9% for placebo (n = 78), a 67% reduction. In the overall study population, including those not at high risk for hospitalization (n = 665), the outcomes were not significantly different (2% for casirivimab/imdevimab vs. 4% for placebo).

CLINICAL IMPLICATIONS

Casirivimab/imdevimab provides a second treatment option under an EUA for nonhospitalized COVID-19 patients with mild to moderate disease, after bamlanivimab. Both received an EUA based on their ability to reduce the risk of hospitalization/ED visits in patients at higher risk for hospitalization (based on age, BMI, and comorbidities). Bamlanivimab showed a similar reduction (70%) in a related study population.[3] There may be a theoretical advantage with a polyclonal vs. a monoclonal antibody in terms of development of antiviral resistance. *(For more information about bamlanivimab, please read the Pharmacology Update section of the December 15 issue of* Internal Medicine Alert*: https://bit.ly/37Ol9q2.)* ■

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1. U.S. Food & Drug Administration. Coronavirus (COVID-19) update: FDA authorizes monoclonal antibodies for treatment of COVID-19. Nov. 21, 2020. https://bit.ly/3m21pVH
2. U.S. Food & Drug Administration. Frequently asked questions on the emergency use authorization of casirivimab + imdevimab. Nov. 21, 2020. https://bit.ly/33NLdA3
3. U.S. Food & Drug Administration. Coronavirus (COVID-19) update: FDA authorizes monoclonal antibody for treatment of COVID-19. Nov. 9, 2020. https://bit.ly/2V3dWMt

CME QUESTIONS

1. In the CODA Collaborative, what percentage of patients receiving antibiotics for appendicitis eventually needed surgery within 90 days?
a. 10%
b. 20%
c. 30%
d. 50%

2. Which is correct regarding COVID-19-associated hospitalizations in healthcare personnel (HCP)?
a. In contrast to the general population, it occurs mostly in HCP with no underlying conditions.
b. HCP involved in nursing-related activities account for the largest proportion.
c. Phlebotomists/technicians make up the lowest proportion.
d. Housekeeping/maintenance personnel constitute the second-lowest proportion.

3. A recent study of aggressive LDL cholesterol-lowering in age > 65 years post-acute coronary syndrome patients with alirocumab therapy vs. those age < 65 years showed:
a. higher LDL levels.
b. higher relative risk reductions.
c. lower all-cause death rates.
d. smaller number needed to treat.

4. Which is true regarding colonization by extended-spectrum beta-lactamase-producing *Enterobacteriaceae*?
a. It is unrelated to international travel.
b. It is increased by using azithromycin.
c. It is prevented by treating traveler's diarrhea with doxycycline.
d. It is related to fluoroquinolone use as treatment of traveler's diarrhea.

5. In investigating the extent of vascular disease in patients with multiple sclerosis (MS), which statement is true?
a. Vascular disease does not affect the course or severity of MS.
b. MS patients have more systemic cardiovascular disease than age-matched controls.
c. MS patients have more cerebral small vessel disease than age-matched controls.
d. Vascular disease causes MS.

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