Currently the Centers for Disease Control and Prevention (CDC) recommend that everyone 6 months of age and older receive a flu vaccine every season. Because the influenza virus replicates and mutates frequently, the vaccine often does not contain all the strains that people are infected with.

In long-term care facilities, an influenza outbreak is declared when two cases of laboratory-confirmed influenza are identified within 72 hours of each other in residents on the same unit. Outbreak control measures should be implemented as soon as possible. If one or more residents have acute respiratory illness and suspected influenza, control measures can be considered as soon as possible, even if the laboratory results are not yet available.

The 2018–2019 flu season is coming to an end, but an influenza outbreak can occur outside the normal flu season, although it is not commonly seen. Because of this, testing for influenza viruses and other respiratory illness pathogens should be performed during months outside the influenza season as well. If an outbreak occurs, health care professionals and facility staff need to ensure that standard and droplet precautions are followed for all residents with suspected or confirmed disease according to the CDC’s guidance (“Prevention Strategies for Seasonal Influenza in Health-care Settings,” Oct. 20, 2018; http://bit.ly/2D73BXp).

The 2018–2019 flu season, there are four antiviral drugs approved by the U.S. Food and Drug Administration and recommended by the CDC to treat influenza:

- Baloxavir marboxil (trade name Xofluza, approved 2018)
- Peramivir (trade name Rapivab, approved 2014)
- Osel tamivir phosphate (trade name Tamiflu, approved 1999), generic available
- Zanamivir (trade name Relenza, approved 1999)

**Baloxavir marboxil (Xofluza)**
Baloxavir marboxil is the newest agent approved for the treatment of acute uncomplicated influenza in patients 12 years of age and older. It is a polymerase acidic endonuclease inhibitor given as a single oral dose within 48 hours of the onset of symptoms with or without food, and it is dosed according to body weight. Baloxavir is available as 20 mg and 40 mg tablets. Coadministration of dairy products, calcium-fortified beverages, polyvalent cation-containing laxatives, antacids, or oral supplements such as calcium, iron, magnesium, selenium, or zinc is not recommended.

<table>
<thead>
<tr>
<th>Patient Body Weight (kg)</th>
<th>Recommended Oral Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 kg to &lt;80 kg</td>
<td>Single dose of 40 mg</td>
</tr>
<tr>
<td>At least 80 kg</td>
<td>Single dose of 80 mg</td>
</tr>
</tbody>
</table>

The most common adverse reactions to baloxavir include diarrhea, anaphylaxis, serious skin/hypersensitivity reactions (i.e., Stevens-Johnson syndrome and erythema multiforme), and neuropsychiatric events. Peramivir is administered as an intravenous infusion and is only indicated for the treatment of influenza, so this medication is not recommended for prophylaxis of influenza in long-term care facilities.

**Oseltamivir (Tamiflu)**
Oseltamivir is a NAI indicated for the treatment of acute, uncomplicated influenza types A and B in patients 2 weeks old and older who have been symptomatic for no more than 2 days. It is given as a single infusion over 15 to 30 minutes, and it is available as a single-use vial containing 20 mg in 20 mL (10 mg/mL), which can be diluted with 0.9% or 0.45% sodium chloride, 5% dextrose, or lactated Ringer’s solution to a maximum volume of 100 mL. The adjustment of peramivir dosage for adults and adolescents aged 13 years and older with altered creatinine clearance (calculated using the Cockcroft-Gault equation) is as follows:

<table>
<thead>
<tr>
<th>Clearance Creatinine</th>
<th>Recommended Treatment Dose</th>
<th>Recommended Prophy laxis Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60 mL/minute</td>
<td>75 mg BID x 5 days</td>
<td>75 mg QID for at least 10 days</td>
</tr>
<tr>
<td>≤30-60 mL/minute</td>
<td>50 mg BID x 5 days</td>
<td>30 mg QID</td>
</tr>
<tr>
<td>&gt;10-30 mL/minute</td>
<td>30 mg QID x 5 days</td>
<td>30 mg QOD</td>
</tr>
<tr>
<td>ESRD on hemodialysis</td>
<td>30 mg immediately then 30 mg after each dialysis cycle for no more than 5 days</td>
<td>30 mg immediately then 30 mg after alternate hemodialysis cycles</td>
</tr>
<tr>
<td>ESRD on CAPD</td>
<td>Single 30 mg dose</td>
<td>30 mg immediately then 30 mg once weekly</td>
</tr>
</tbody>
</table>

ESRD = end-stage renal disease; BID = twice daily; QID = once daily; QOD = every other day.

**Peramivir (Rapivab)**
Peramivir is an influenza virus NAI indicated for the treatment of acute uncomplicated influenza in patients 2 years old and older who have been symptomatic for no more than 2 days. It is given as a single infusion over 15 to 30 minutes, and it is available as a single-use vial containing 200 mg in a 20 mL (10 mg/mL) vial. The adverse reactions to zanamivir include diarrhea, anaphylaxis, serious skin/hypersensitivity reactions (i.e., Stevens-Johnson syndrome, toxic epidermal necrosis, and erythema), and neuropsychiatric events.

<table>
<thead>
<tr>
<th>Clearance Creatinine</th>
<th>Single Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10-30 mL/minute</td>
<td>600 mg</td>
</tr>
<tr>
<td>30-49 mL/minute</td>
<td>200 mg</td>
</tr>
<tr>
<td>10-29 mL/minute</td>
<td>100 mg</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Administer after dialysis</td>
</tr>
</tbody>
</table>

The clinical trials of peramivir did not include a sufficient number of individuals aged 65 and over to determine whether they respond differently than younger people. However, there have been no reported differences in exposures between older and younger individuals.

The most common adverse reactions to peramivir include diarrhea, anaphylaxis, serious skin/hypersensitivity reactions (i.e., Stevens-Johnson syndrome and erythema multiforme), and neuropsychiatric events. Peramivir is administered as an intravenous infusion and is only indicated for the treatment of influenza, so this medication is not recommended for prophylaxis of influenza in long-term care facilities.

**Zanamivir (Relenza)**
Zanamivir is also an NAI that is indicated for the treatment of acute, uncomplicated influenza types A and B infections in patients age 7 and older who have had symptoms for less than 2 days. It is available as a dry powder inhaler with blister packs that contain the powder. Dosing for the treatment of influenza is 10 mg (two inhalations) twice daily for 5 days. Zanamivir has not been proven effective for influenza prophylaxis in nursing home residents.

No overall differences in safety or effectiveness have been observed between older and younger patients. However, elderly patients may need assistance with using the inhaler device. The adverse reactions to zanamivir include sinusitis, dizziness, fever and/or chills, arthralgia, and infectious arthritis.

For the treatment of influenza, a full course of therapy ranges in price and is approximately the following, based on recent www.goodrx.com pricing (as of April 5, 2019). When comparing the prices of these agents, note that they will vary depending on dosage form, age, weight, renal function, and other factors for the patient.

- Baloxavir marboxil (Xofluza), $515
- Oseltamivir (generic Tamiflu, 30 and 75 mg capsules), $52
- Zanamivir (Relenza), $65
- Peramivir (Rapivab), $317

Many factors need to be considered before choosing the best therapy for an individual patient, but price alone should never be the reason for the final decision.

— Karl Steinberg, MD, CMD, HMDC

**EDITOR’S NOTE:**

Outbreak Prophylaxis
As soon as an influenza outbreak is confirmed, all residents on the same unit with a patient with active illness should be given chemoprophylaxis with an antiviral indicated for this use. Oseltamivir and zanamivir are the only two antivirals indicated for flu prophylaxis; if drug resistance to one

Continued to next page
It seems as if everywhere one looks today, one is confronted with the concept of “The Singularity.” I first heard the term in 2005 when I was asked to review Ray Kurzweil’s book, The Singularity Is Near: When Humans Transcend Biology (New York: Penguin). At the time, the mantra of ‘smaller, faster, cheaper’ was on the lips of every high-tech aspirant. Mr. Kurzweil, one of the latter, took hundreds of complementary therapies per day to “reprogram” his body chemistry to live long enough to reach The Singularity. The Singularity is the point in time — fast approaching, so we have been told — when the fields of engineering, computer science, human physiology, and genomics will come together to bestow at least virtual immortality. Mr. Kurzweil was planning to download his old-fashioned “wet-brain” into a cyborg creation so that he would no longer be bound by the water-based biological maximum life span accorded to humans heretofore.

At the time I read his book I was 57 years old, deep into my practice career, caring for hundreds of the old, old-old, and oldest-old. My father was seven years into his Alzheimer’s dementia, and my mother, after a stroke and fractured hip, was following in his footsteps. I was much too involved in what I will call “The Particularity” of my individual patients — their myriad medical, psychosocial, pharmaceutical, and insurance issues — to worry very much about Mr. Kurzweil and his ilk’s quest for personal lifetime maximization.

I also noticed there were no bioethicists in his orbit, and so in my review of his book, I wrote, “Technology without wisdom is like a runaway horse. It may take us very quickly to somewhere we don’t want to go. Our elderly need people — friends, family members, and health care workers who understand and value them as individuals — all of them crucial to providing quality care to our aging loved ones. We must work together to decide when to embrace the latest technological advance and when to turn away” (Memory Lessons: A Doctor’s Story, New York: Hyperion, 2009, p. 144).

Well, many years have passed since Mr. Kurzweil’s book came out. Once a medical backwater paddled by crackpot theorists, the field of longevity research has since come into its own. Money is being pumped into research and clinical trials like water pouring from the mythical fountain of youth. These dollars are coming from venture capitalists and the multimillionaire/billionaire investor class, all hoping to take advantage of any discoveries to boost their own life spans. And maybe that could help some others along the way — if the unwashed masses can come up with the money.

Last year at least $1.3 billion was invested in all this by just a few companies: CBInsights, Samumed (regenerative medicine), Celularity (stem cells), Unity Biotechnology (senolytics), Alkahest (“young blood”) (“Is Research on Aging Finally Growing Up?” Endpoints, Jan. 1, 2019; http://bit.ly/2UBD9PN). As Aubrey DeGrey, PhD, an antiaging pioneer and chief science officer of the SENS Research Foundation and vice president of New Technology Discovery at AgeX Therapeutics, said, “I think you could say that 2018 was the year in which the industry became un-ignoreable. We’ve had a complete explosion of private sector interest in stuff that’s actually plausible.”

“Like what?” you, my fellow geriatricians, might ask as you make your nursing home rounds, as you try, day in and day out, to deal with pressure ulcers, dementia behaviors, frailty, worried and angry family, facilities closing, the Medicare utilization ghouls, and on and on. But perhaps you also have experience with the diaper that triggers an alarm (another one?) when it gets wet, as marketed by the company ElderSens. How’s that for high-tech’s practical input into the long-term care field?

So now we all have developing antiaging breakthroughs to look forward to, and they are just about to make our jobs obsolete. For example,:

• In case you have trouble determining whether your patients are aging, you can soon count on the “epigenetic clock” — a true test of biological age based on DNA methylation. You will be able to order this test at your facility soon. (Counting telomeres is so passé.)

• Rejuvance Bio is looking to reverse aging in spaniels and Dobermans prone to arrhythmias and then apply these findings to that chronic heart failure patient you keep sending back and forth to the hospital, as you get stung again and again by Medicare. (Perhaps we can enjoy having these dogs around our facilities once their work in the lab is done.)

• The Mayo Clinic is developing “transgenes” — a way to eliminate senescent cells in the brains of mice that might otherwise develop Parkinson’s or Alzheimer’s disease. (Well, one can hope.)

• The “Young Blood” movement is one more reason for the grandkids to visit the facility! Ambrosia collects $8,000 per patient for infusions from young people. Alkahest is doing similar work and launched a small clinical trial in 2016: they reported in JAMA Neurology that “the treatment was safe, well-tolerated, and feasible” (2019;76:35–40), though they didn’t have much to say about effectiveness. (Sorry, not yet covered by Medicare.)

• Celularity is using placental stem cells to treat cancer, Crohn’s disease, and diabetic peripheral neuropathy. (Well, as long as that port from the last ICU admit is still in place.)

• The field of “senolytics,” another area of active aging research, focuses on compounds that can eliminate senescent cells. Aged mice treated with the leukemia drug dasatinib and flavanol quercetin cleared senescent cells and showed improved health and life span. (And so many of us had mistakenly been thinking that we might be overtreating our aging patients with chemotherapy and other drugs…) I could go on and on. All these unproven complementary therapies — how about that “jellyfish” aid for dementia? — suck about $80 billion dollars a year out of consumer’s wallets, money that could be put to much better purposes.

Also metformin is extending life in rodents and nematodes; rapamycin is already being used and reduces infections in human volunteers; sirtuins affect NAD+ levels, which decline with age; minocycline prevents the protein buildup characteristic of neurodegenerative disease; atrial and brain natriuretic peptides can slow aging in mice and may be effective against Alzheimer’s disease. There are more, but I tire, and I am running out of column inches. Exciting or ho-hum? In the years since Mr. Kurzweil published The Singularity, exactly what has the high-tech industry done to help you and me care for our patients? Oh, I forgot: the electronic medical record!

Maybe we are at an inflection point; I’m just not smart enough to know. But I urge us to look around. Life expectancy is actually declining in America primarily due to the social ills of our nation. Long-term care facilities — places whose mission it is to care for the elderly and infirm, here and now — are closing due to lack of funding. Pharmaceuticals that we know can help the many conditions geriatricians treat are in many instances unaffordable to our patients.

The best antiaging advice that we know is live well, maintain a normal body weight, exercise appropriately, keep the mind active, and stay socially engaged. But I guess there is just not that much money to be made in proffering these tried-and-true therapies.