SEPSIS IS A DISEASE that kills more than 258,000 Americans each year—that is more than prostate cancer, breast cancer and AIDS combined. It is the leading cause of death in hospitals, however nearly 80 percent of sepsis cases develop outside of a hospital. Yet, for a disease that is so common and deadly, less than half of Americans have ever heard of sepsis.

“There has never been a major public education campaign for sepsis, so it has always flown under the radar,” says Michael Filbin, MD, MGH Emergency Medicine physician and leader of the MGH Sepsis Care Redesign and Partners HealthCare sepsis initiatives.

CAUSES, SIGNS AND SYMPTOMS
Sepsis can be caused by any type of bacterial, viral or fungal infection in the body, such as a cut or scrape, pneumonia, ulcers or a urinary tract infection. Sepsis is when the body’s response to fighting the infection goes wrong and overresponds, causing the immune system to attack its own organs and tissues.

“One of the issues with sepsis is the patient doesn’t always present with clear symptoms of infection,” Filbin says. “It can manifest in vague and insidious ways. In most cases patients are older or chronically ill, but it can just as easily hit the young and healthy.”

Though often difficult to pinpoint as sepsis, some of the warning signs include a fever, chills, rapid breathing, extreme pain, pale or mottled skin, elevated heart rate, and confusion or disorientation. If a person is experiencing any of these symptoms, Filbin says, they should ask

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**Research Roundup**

RESEARCH at the MGH is interwoven throughout more than 30 departments, centers and units and is conducted with the support and guidance of the MGH Research Institute. The Research Roundup is a monthly series highlighting studies, news and events. This month’s column includes new insights into cystic fibrosis, genetic risk factors for heart attacks, and potential connections between anxiety and Alzheimer’s disease.

**NEWLY DISCOVERED CELL TYPE APPEARS TO PLAY A KEY ROLE IN CYSTIC FIBROSIS**

A team from the MGH and the Broad Institute has found a new cell type in the lung that appears to play a key role in cystic fibrosis. Using a new sequencing technology, the team made an organ map of specialized cell types in the airway and they found an exceedingly rare cell type that specializes in balancing hydration at surface of the lung, which is important in staving off infections. They named this intriguing new cell type “pulmonary ionocytes,” and found that the cells also produce most of the gene product that, when mutated, causes cystic fibrosis. Ionocytes are now the most promising cellular target for therapeutic efforts to cure cystic fibrosis.

**IDENTIFYING GENETIC RISK FACTORS FOR HEART ATTACK**

Researchers from the MGH Center for Genomic Medicine and the Broad Institute have identified a new genetic risk factor that could help to identify millions of people at more than triple the normal risk for heart attack – and millions more at high risk for type 2 diabetes, breast cancer or atrial fibrillation. This approach involves newly developed scores that tally genetic risk information from millions of sites in DNA where one patient differs from another. Most importantly, these high-risk individuals are currently flying under the radar within clinical practice, but if identified, would benefit from targeted prevention efforts.

**TESTING THE LONG-TERM EFFICACY OF A CHOLERA VACCINE**

MGH researchers and their Haitian colleagues found that two doses of an oral cholera vaccine (OCV) were effective in protecting individuals in Haiti against cholera for at least four years. The research team collaborated with Haitian public health officials to vaccinate more than 50,000 people against cholera in 2012 and studied cases of diarrhea for the subsequent four years. This is the first study showing OCV has long-term effectiveness when used in a cholera outbreak, and the first study of the long-term effectiveness of OCV in a country like Haiti, where the disease was newly introduced. The results add to the evidence needed to improve prevention and control of cholera globally.

**A CONNECTION BETWEEN ANXIETY AND THE RISK OF ALZHEIMER’S DISEASE?**

Alzheimer’s disease is characterized by the accumulation of abnormal brain proteins – amyloid-beta and tau – a process that begins when older adults are cognitively unimpaired. Researchers at the MGH are working to define very early neurobehavioral and biological markers of Alzheimer’s disease prior to cognitive impairment. In a neuroimaging study of normal older adults, researchers found that high amyloid-beta in subcortical structures, a region of advanced accumulation, was associated with higher levels of anxiety and particularly in carriers of the APOE ε4 genetic marker. These findings point to anxiety and specific genetic and regional biomarkers that may identify individuals at highest risk of cognitive decline.

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**Clinic provides hope for moms in recovery**

**TO IMPROVE THE HEALTH of infants and mothers, the MGH has opened the HOPE Clinic, assisting pregnant women like Aryana Moschitto, who is recovering from substance use disorder.**

Like other expectant mothers, the 25-year-old is debating names for her daughter, laughing about her baby shower and worrying about her upcoming delivery. But she’s also seeing clinicians in obstetrics, family medicine, addiction medicine, pediatrics and psychiatry, as well as a substance use recovery coach and a social worker at the HOPE (Harnessing support for Opioid and substance use disorder in Pregnancy and Early childhood) Clinic.

The integrated care model aims to help women from pregnancy through their child’s second birthday.

“I have been using since I was 13, and trying to get clean since I was 17,” says Moschitto, who is in recovery from opioid use. “But I have never had the support I have gotten through the HOPE Clinic.”

Pediatrician Davida Schiff, MD, medical director of the HOPE Clinic, says, “Pregnancy can provide a window of hope to many women who are struggling with substance use disorder. At that moment of hope, it’s critical to provide the right support that will help these women succeed.”

Jessica R. Gray, MD, HOPE Clinic’s clinical director, says the early parenting years can be very motivating for entering and maintaining recovery from opioid use.

At the clinic, the bond between mothers and infants is carefully nurtured. For example, a child experiencing withdrawal symptoms after birth can be soothed through cuddling, skin-to-skin time and breastfeeding, Schiff says. The HOPE Clinic works with parents to support their infants’ health and well-being after delivery and to promote a strong parent-child bond from the first hours of life.

“The complexity of our patients’ medical, psychological and social needs is profound,” Schiff says. The clinic’s patients are often homeless or living in residential treatment centers. They may be struggling with more than one substance use disorder. Many have been physically or psychologically abused and have ongoing legal issues.

Schiff says many patients are inspired by Katie Raftery, the HOPE Clinic’s recovery coach.

“At this clinic,” Raftery says, “we want to be more than just doctors treating a medical condition. We want to create a sense of stability and security, help them take care of their babies and build a foundation for a healthy family they can take forward on their recovery journey.”

Raftery, who has two children, says she went into recovery when she was pregnant with her son, and found it was essential to build a “tribe” of people to support her. She decided to become a recovery coach to help do the same for those like Moschitto.

“She’s always there for me to talk over things I find overwhelming,” Moschitto says. “There’s so much stigma around this disease, but in the HOPE Clinic everyone is accepting and welcoming. Jan. 6, is my ‘recovery date,’ because it’s the day I found out I was pregnant. I’m looking at life differently because someone is going to depend on me. But I also know how powerful this disease is and I am so grateful to the HOPE Clinic for helping me be vigilant with my recovery.”
Turning lemons into lemonade

ON AUG. 31, 9-year-old Liam Doherty organized his second annual lemonade stand. He wasn’t raising funds for a new bike or video game, but to support the research of Jess Kaplan, MD, clinical director of the MassGeneral Hospital for Children Inflammatory Bowel Disease (IBD) Center.

Liam has Crohn’s disease, an autoimmune disease that attacks the intestines, causing swelling and ulcers. In 2017, he experienced a flare up, making the positive and active young boy feel tired and worn out. His parents, Lauren and Russ Doherty, stressed the need to find ways to turn the experience into something positive.

“Sometimes when life hands you lemons, you have to make lemonade,” says Lauren. That is when the idea was born – Liam would help find a cure for IBD through a lemonade stand.

With support from family, friends and the community – including Canton’s Department of Public Works, Fire Department and Police Department – Liam raised $10,000 this year, bringing his total to more than $18,000. Liam hopes to raise $60,000 by the time he turns 15.

Tornado preparedness: MGH unveils new protocol

THE MGH WILL SOON roll out its newly developed Tornado Protocol. Developed by the Center for Disaster Medicine – which oversees all preparedness and emergency management efforts at the MGH – the protocol outlines hospital plans and procedures in the event of the unexpected weather emergency.

“Forecasting tornadoes is still very difficult, so there are usually only a few minutes of warning – or less – when we recognize that one has formed,” says Rob Krupa, planning, training and exercise program manager for the Center for Disaster Medicine. “Because of this, it’s especially important to have a detailed response plan that we can use in a moment’s notice to ensure rapid action. The safety and security of our patients, their families and all of our staff is of greatest concern during a tornado, so we will be hosting training sessions and exercise drills throughout the hospital to review precautions, shelter options and how to recover after the storm hits.”

While still fairly uncommon in New England, more than 1,200 tornadoes occur in the United States every year, including one reported in Iowa earlier this week. And, in recent years, Massachusetts has been hit with multiple tornadoes, including a twister confirmed in Webster this past August. Four years ago, on June 28, 2014, a tornado damaged 65 homes and businesses in Revere, Massachusetts with its 120-mph winds, and on June 1, 2011, one touched down in Springfield, resulting in three deaths and an estimated $140 million worth of damages.

Krupa says the MGH Center for Disaster Medicine worked closely with city and state officials to create the hospital’s response plan, and received valuable insight from leaders at St. John’s Regional Medical Center in Joplin, Missouri, which was destroyed during a 2011 multi-vortex tornado.

“September marks National Emergency Preparedness Month, so it’s the perfect opportunity to continue the conversation about the best ways to prepare for, respond to and recover from disasters,” Krupa says.

TORNADO WATCHES AND WARNINGS

Tornado Watch:
- Conditions are favorable for the development of tornadoes in and close to the watch area.
- Size can vary.
- Duration: 4 to 8 hours.
- Normally issued well in advance of severe weather.

Tornado Warning:
- A tornado is indicated by radar and people in the affected area should seek safe shelter immediately.
- Stay away from windows, doors and walls that face the building’s exterior.
- Duration: Roughly 30 minutes.

WHAT TO DO DURING A TORNADO WARNING:

Clinical Areas:
- Move ambulatory patients into their bathroom, into the hallway or other internal location away from windows.
- Bed-bound patients will be placed in the flat position, as tolerated. Turn bed so headboard is between patient and any windows. Protect patient with blankets or pillows.
- Maintain accountability of all patients and employees until Tornado Warning has expired.

Non-Clinical Areas:
- Go to a shelter area, such as a basement or the lowest level in the building.
- If you cannot get to shelter area, go to the center of an interior room – such as a closet or interior hallway – away from corners, windows, doors and outside walls.
- Put as many walls as possible between you and the outside.
- Stay away from windows.
Sepsis
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themselves “could this be sepsis?” If diagnosed early, sepsis can be treated with antibiotics, IV fluids and close monitoring.

TREATMENT OPTIONS
Early identification and diagnosis of sepsis is critical. For every hour that sepsis diagnosis and treatment is delayed, the risk of death increases considerably, Filbin says.

“As doctors, we are taught to base our decisions off diagnostic information,” he says. “With sepsis, it is not always possible to wait for that information. The tricky part sometimes is knowing when to pull the trigger on preemptive treatments.”

Sepsis also can lead to tissue damage and organ failure, and the patient may be dehydrated or have low blood pressure – all conditions that need to be taken into consideration during treatment.

Antibiotics are the one intervention proven to decrease morbidity in sepsis patients,” Filbin says. “However, there is a whole suite of treatments that may be needed to fix organ dysfunction, among other things, so a lot of challenging decisions are involved in the process.”

STEPS FORWARD
“One thing that really strikes me is the tools we have to diagnose sepsis, treat it and monitor it have not changed in all my years in health care,” says Filbin. Although treatment is essentially the same as it was many years ago, there have been processes at the MGH to improve sepsis diagnosis.

Starting in 2014, Filbin partnered with other MGH clinicians and a Massachusetts Institute of Technology biomedical engineering team to analyze sepsis signs and create an algorithmic warning system to alert clinicians when a patient might have sepsis.

This cut the length of time it takes to diagnose sepsis in half, leading to earlier antibiotic treatment.

As a result of this work, a purple flag appears in Epic to alert emergency clinicians to the possibility of sepsis. A best practice alert also was built into the electronic medical record, as well as a sepsis specific order set to help clinicians order the correct treatments. Filbin also is a co-chair of the MGH Sepsis Steering Committee – along with Emily Aaronson, MD, of Emergency Medicine; Kathryn Hibbert, MD, of Pulmonary and Critical Care Medicine; Colleen Snydeman, RN, PhD, director of the Nursing & Patient Care Services Office of Quality and Safety; and Michael Phillips, of the Center for Quality and Safety. The group of dedicated sepsis champions from each clinical department was formed two years ago and regularly meets to review sepsis care at the MGH with the goal of setting and improving standards of care for patients with sepsis.

“The most important thing we can do is educate everybody – the public, doctors, physician assistants, nurse practitioners and, most importantly, frontline nurses – to recognize the signs of sepsis and to understand how deadly it can be if not treated promptly,” Filbin says.

IN RECOGNITION OF SEPSIS AWARENESS MONTH, MGH WILL HOST:

- Sept. 18, Noon – 1 pm: Filbin and Hibbert will speak to advanced practice providers about sepsis in the O’Keeffe Auditorium.
- Sept. 19, 9 am - 2 pm: A “Meet the Expert” table at Eat Street Café will provide an opportunity for staff, patients and visitors to learn more about sepsis from MGH experts.

CELEBRATING 50 YEARS

MGH CHARLESTOWN HEALTHCARE CENTER will celebrate its 50th anniversary Sept. 28 from 4-7 pm at the health center. Speakers, activities and a multimedia presentation highlighting the history of the health center’s contributions to Charlestown will be featured. Light refreshments and swag bags will be available and Doc McStuffins will greet children. All are welcome.