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in Clinical Practice Today

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To learn more or to refer a patient, call 844-790-2013
**Blood Test Can Indicate When Antibiotics Are Needed**

A rapid blood test during an office visit may soon be able to determine whether a respiratory illness is caused by infection with a virus or bacteria.

A team of infectious diseases and genomics experts at Duke has developed gene signatures that reflect which of a patient’s genes are turned “on” or “off.” These signatures can identify an infection as either viral or bacterial—or something else entirely.

In the study published in *Science Translational Medicine*, the genetic signatures were 87% accurate in classifying more than 300 patients with flu viruses, rhinovirus, strep bacteria, and other common infections, says lead author Ephraim L. Tsaiik, MD, PhD, an assistant professor at Duke’s Center for Applied Genomics & Precision Medicine.

Although the test is currently only being used for research, the Duke team, including senior authors Geoffrey S. Ginsburg, MD, PhD, and Christopher W. Woods, MD, is developing a test that will be widely available in primary care with results received in 1 hour or less.

**Sildenafil Reduces Risk of Harmful Edema in Swimmers**

Swimmers and divers who are prone to sudden swimming-induced pulmonary edema (SIPE) in cold water could benefit from a dose of sildenafil, according to a study by Duke Health researchers in *Circulation*.

Researchers studied 10 athletes who had experienced SIPE while exercising or competing. The SIPE-susceptible athletes had higher pulmonary arterial pressure and pulmonary artery wedge pressure during the simulated cold-water exercise than typical swimmers. When the SIPE-susceptible participants were given sildenafil and swam, their pressures were reduced.

“It appears that the drug, which dilates the blood vessels, could be creating more capacity in the blood vessels in the arms and legs, reducing the tendency for blood to redistribute to the thorax,” says lead author Richard Moon, MD, an anesthesiologist who directs the Duke Center for Hyperbaric Medicine and Environmental Physiology.

**Older Women With Early Breast Cancer Can Benefit From Aggressive Treatments**

Older women with early stage invasive breast cancer had better survival rates than what were estimated by a popular online tool for predicting survival, according to researchers at the Duke Cancer Institute.

The finding provides a strong rationale for women older than 70 years—even those who have additional minor health concerns—to undergo aggressive treatments such as chemotherapy to prevent their cancer from returning.

Gretchen Kimmick, MD, MS, a Duke medical oncologist who presented study findings at the San Antonio Breast Cancer Symposium, says, “This predictive model can help us show patients that they are going to survive long enough to see the benefit of treatment.”
As a clinical social worker specializing in acquired immune deficiency syndrome (AIDS) care since 1992, Gordon Lipscomb, MSW, LCSW, frequently sees patients soon after they learn that they are human immunodeficiency virus (HIV) positive. It never gets any easier, and, in fact, it has gotten less so over the years, he says, because these cases often follow the same discernible patterns.

“One of the most frustrating things for me has been when you look at the medical history of new patients with HIV—there are so many points of intervention that could have happened,” Lipscomb says. “Could the right thing have been said on this trip to the emergency department or that trip to the primary care doctor?”

Now when health care professionals encounter patients exhibiting red-flag HIV risk factors, they have a new treatment option, one with a proven track record of helping such patients avoid contracting the still-incurable virus. It is called pre-exposure prophylaxis (PrEP) and consists of 2 antiretroviral drugs, tenofovir and emtricitabine, taken in a single daily pill. Large clinical trials have shown that fully adherent patients taking tenofovir/emtricitabine demonstrate a defensive protection against HIV infection that exceeds 90%.

Approved for PrEP since 2012, tenofovir/emtricitabine did not gain popularity among primary care providers until the Centers for Disease Control and Prevention published comprehensive treatment guidelines in 2014. So far, however, that popularity has been mostly confined to large metropolitan areas such as New York City, San Francisco, and Chicago, according to Mehri McKellar, MD, an assistant professor of infectious diseases at Duke University.

“The Southeast in particular is a bit behind in terms of uptake of PrEP prescriptions,” she says. “Possibly this is due to concerns that it will undermine the use of condoms, result in transmission of other sexually transmitted infections (STIs), or cause adverse side effects. But, for whatever reason, there remains a general lack of awareness and hesitance on the part of providers.”

She points to a survey of Duke Health primary care providers that found that, although 78% treat men who have sex with men (MSM)—a subpopulation at high risk of acquiring HIV—only 17% had ever prescribed PrEP.
This is particularly troubling in light of the fact that Durham County, home to Duke’s campus, ranks fourth in the state for HIV prevalence and third for incidence of HIV infection, McKellar adds. Moreover, as a region, the southern states lead the nation in numbers of AIDS-related deaths, new AIDS diagnoses, and people living with AIDS. “There is very much a geographic epidemic going on, focused on this part of the country,” she notes.

Promoting PrEP
To help reduce new infections, Duke University has partnered with the Durham County Department of Public Health, Durham Knows (a local public health campaign), and the North Carolina AIDS Training and Education Center to promote PrEP awareness, education, and referrals.

Candidates for PrEP include anyone in a relationship with an HIV-positive partner, MSM who have had anal sex without a condom or been diagnosed with an STD in the past 6 months, and heterosexual men or women who do not regularly use condoms during sex with partners who are at substantial risk of HIV infection (eg, intravenous drug users or bisexual men). PrEP is also a new option for serodiscordant heterosexual couples trying to conceive a child.

Adherence is extremely important. The protective efficacy of tenofovir/emtricitabine drops precipitously if adherence to the daily dosage schedule falters even slightly. In addition, patients must make frequent office visits: every 3 months during the course of treatment. “But it’s also important to remember you might not need this drug forever,” notes McKellar. “I’m a big believer in the idea that patients no longer at risk don’t have to keep taking tenofovir/emtricitabine.”

Risks and Benefits
Adverse effects are relatively minimal. Some patients experience mild nausea, kidney irritation, and a 2% to 4% reduction in bone density, which resolves upon discontinuation of the treatment, according to studies.

A major concern associated with PrEP is whether it might encourage riskier behavior among patients already at a higher risk of HIV infection. For example, MSM might use condoms less frequently. Although McKellar acknowledges that this is a legitimate concern, she points out that risk indices measured among patients enrolled in the PrEP trials remained unchanged.

Some studies found increases in non-HIV STIs among patients taking PrEP. However, it remains unclear whether the treatment itself was causative or whether an unrelated uptick in syphilis and gonorrhea in some geographic areas was to blame.

For the most part, the medical community has greeted PrEP as a breakthrough therapy for a serious condition that has not been granted a fresh clinical strategy for some time. Many have also noted the added benefit of a higher quality of life among some patients. “I’ve seen couples where, even though the positive partner has an undetectable viral load and condom use is part of their routine, offering them PrEP is just extremely liberating and freeing,” says Lipscomb. “More than anything has so far, this helps separate sex from death. It finally lets people exhale and enjoy their sex lives again.” To refer a patient, call 844-790-2013.

(Image of human T lymphocyte on the previous page depicts HIV particles.)
Duke Health has launched the first hand transplant program in North Carolina and is one of fewer than 20 sites in the United States (US) offering this complex, life-altering procedure. Fewer than 150 people have received hand transplants globally.


With Cendales as principal investigator, the Duke Hand Transplant Program is actively recruiting participants for a clinical trial to determine the safety and efficacy of hand transplantation for patients who have lost a limb or limbs below the elbow. The trial will test the effectiveness of the newest immunosuppressive drug in transplantation, belatacept, in preventing rejection of the transplanted hand. The trial will also evaluate how patients engage in activities of daily living before and after the hand transplant at Duke.

The study, funded by the Department of Defense, is open to anyone 18 to 65 years of age with amputations below the elbow—unilaterally or bilaterally—without a time limit from when the individual lost the hand(s), Cendales says.

Hand transplantation is highly complex, involving an intricate process of connecting bone, blood vessels, muscle, nerve, tendons, and skin. Matching the limb from a deceased donor with the recipient includes considering various factors, such as size, age, skin pigmentation, and sex.

The Duke Hand Transplant Program collaborates with referring physicians. “We look forward to working with colleagues through the process,” Cendales says. The program’s multidisciplinary team combines expertise in immunology, transplantation, surgery, occupational therapy, psychology, anesthesia, social work, hospital staff, and nursing.

For more information, call 844-790-2013 or visit our Web site at www.dukemedicine.org/treatments/transplant-program/hand-transplant.
Best Apps for Primary Care Physicians

By Meredith Lidard Kleeman

Most physicians use their smartphones and tablets for professional reasons, according to a 2015 study from Kantar Media. Additionally, the Manhattan Research’s 2014 Taking the Pulse US study found that nearly one-half use their devices to share information with patients.

Thus, mobile applications can not only help doctors simplify daily tasks, but they can also enhance patient care. Apps can be used to check drug interactions and side effects, stay current with clinical guidelines, and connect with doctors across the country. Here are some of the best apps available for iOS and Android devices.

**Epocrates:** A perennial favorite among physicians, this app has been around for almost 20 years—it was introduced in 1998 for PalmPilots. The free version allows clinicians to review drug prescribing and safety information for thousands of brand and generic drugs, identify pills by imprint code and physical characteristics, and perform dozens of calculations. The premium version, currently available for $174.99 for a 1-year subscription, offers clinical practice guidelines, guidance on infectious disease treatment, and more.

**Turboscan:** This free app turns your smartphone into a scanner and lets you scan documents to send as a PDF or image. Mark Seigel, MD, an OB/GYN based in Rockville, MD, says he uses this app almost every day. “I get lots of requests from patients asking me to sign forms,” he says. “I sign the form, scan it, and email it right back—patients love that.”

**UpToDate:** This app requires a paid subscription, but it earns high marks among physicians for its wealth of evidence-based clinical information. Michele Casey, MD, a practice medical director for Duke Primary Care, says this app is one of many that she relies on to access information quickly and keep up with ever-changing clinical recommendations. Subscriptions currently start at $499 per year.

**Doximity:** The largest medical professional network in the country is available on mobile and Web platforms and allows users to connect with doctors nationwide. Members can use a dedicated fax number to send and receive secure faxes in compliance with the Health Insurance Portability and Accountability Act. They can also get the latest specialized news and journal articles.

**NEJM This Week:** *The New England Journal of Medicine*, one of the most trusted medical journals in the world, offers access to recent articles, medical images, weekly audio summaries, and procedure videos in this free app. It’s currently only available for iOS devices.
A 61-year-old woman presented to Duke Health in July 2012 with advanced, low-grade serous carcinoma of the ovary. The patient first noticed lower-left quadrant pain in 2010, and the finding on computed tomography (CT) was negative, except for a small adrenal mass. Her symptoms progressed and, in May 2012, follow-up CT revealed an omental cake and carcinomatosis.

A general surgeon at Duke performed laparoscopy and biopsies that demonstrated extensive, unresectable cancer involving all peritoneal surfaces. The patient was referred to Fidel Valea, MD, a gynecologic oncologist at Duke, who recommended paclitaxel and carboplatin chemotherapy. He hoped to surgically debulk her cancer after 3 chemotherapy cycles.

The patient underwent exploratory laparotomy in December 2012; however, her slow-growing, low-grade disease had not responded and was still unresectable.

She was offered the choice to undergo further conventional chemotherapy or try a less conventional biologic drug called bevacizumab. She considered bevacizumab because chemotherapy was not effective the first time and she experienced severe side effects. She also considered end-of-life hospice care.

Valea suggested that her tumor be tested for genetic mutations and alterations that might be exploited for therapy. Her tumor was sent to FoundationOne, an oncologic genomic-profiling company, for evaluation.

After a unique mutation in the tumor’s estrogen receptors was detected, Valea recommended using fulvestrant, a first-in-its-class estrogen-receptor antagonist that has no known agonist effects. Unlike chemotherapy, fulvestrant doesn’t eradicate tumors, but it also doesn’t let cells reproduce. The patient opted to try fulvestrant, aware that no data existed on the use of the drug in ovarian cancer.

The patient began taking monthly 500-mg injections of fulvestrant in January 2014. Her cancer antigen 125 tumor marker level, once elevated to 43.2 units/mL, dropped and ultimately stabilized within the normal range to 8.9 units/mL. CT in July 2015 revealed she still had some scattered calcifications that were probably related to her disease but no omental caking. The patient is now living a fully functional life without any clinical evidence of disease. (Colored magnetic resonance imaging scan above shows ovarian cancer.)

Nonconventional Treatment Saves Patient With Ovarian Cancer

By Karen Appold
Spouse-Run Practices: Lessons From a Successful Team

By Meredith Lidard Kleeman

The couple that plays together stays together, or so the saying goes. But what about the couple that works together?

Working with a spouse who manages your office may seem like a great idea, but separating your personal life from your professional life can be tricky. Duke surgeon Chris Watters, MD, and his wife Ginny Watters, RN (pictured above), have worked together for 14 years. Ginny was hired by Duke as the nurse manager at her husband’s surgical practice, a position that she’s held for the last 4 years; before that, she worked as a nurse in the practice.

The couple met 30 years ago when Chris was a resident at Duke Health and Ginny was working as a nurse in the intensive care unit. They both credit that time as the foundation for their current working relationship. “It’s easier for us because we worked together before we became a couple,” Chris says.

Both husband and wife agree that they have similar personalities, which works in their favor. “We tend to have a pretty cohesive approach,” Ginny says.

Their complementary working styles help keep the practice running smoothly. “Generally, we have the same vision for what we want,” Ginny explains. “When there’s something [Chris] wants done, I end up being the go-between with the staff to execute it.”

That said, there are times when personal tensions creep into the workplace, despite their best efforts. “We try hard not to let [personal issues] affect the office,” Ginny notes. “But some days, it is hard… and on those days, I just remove myself from the situation, walk around the building for a few minutes, and clear my head.”

They find that the most challenging aspect of working together is separating their work life from their personal life. As self-confessed workaholics, they often find themselves discussing patient schedules when they return home. “We’re not very good at taking time out of the office,” Ginny admits.

Despite the challenges, the couple enjoys spending time during the day together. “I’ve always considered Ginny my best friend,” Chris says. “It’s nice that we can share… at the workplace instead of having to save it up and wait until we get home.”

And everyone at the office—patients and staff—knows who’s really in charge: Ginny. “I let her tell me what to do, and it works out pretty well,” Chris says. 
In the fall of 2014, a 31-year-old otherwise healthy, athletic woman in Raleigh, NC, coughed up blood and reported to a nearby emergency department. Eventually, the woman, the mother of a toddler, received a diagnosis after bronchoscopy. She had a tumor in the upper lobe of her left lung, which was growing into and nearly obstructing the airway.

A surgeon informed her that, although the tumor was a low-grade carcinoid—a well-differentiated neuroendocrine carcinoma—she would need her entire left lung removed. He told her that he could perform the surgery as a minimally invasive procedure.

A SECOND OPINION
The patient, who felt well and was disturbed by the gravity of the surgical suggestion, sought further medical advice. She consulted thoracic surgeon David White, MD, at Duke for a second opinion.

White explained that the best solution would be to remove the entire upper lobe of the left lung, along with a “sleeve” of the left mainstem bronchus, but not the whole...
lung. White performed the sleeve lobectomy and reattached the lower lobe by suturing the airway back together.

A carcinoid is rare in the general population, but White says he typically sees 5 to 6 such tumors each year.

“This was a case in which going to a high-volume center with thoracic surgeons was the right decision for the patient, so that she would not be negatively impacted by living with only 1 lung for the next 30 to 40 years,” White explains.

When to Refer

“Any time referring physicians or one of their patients is not entirely comfortable with an opinion or recommended treatment for a lung mass or condition, they should consider referral to a higher-volume center.”

Although the repair was performed in an open operation, Duke offers many options for less invasive lung surgeries when appropriate. In particular, Duke performs a large number of minimally invasive chest surgeries, including thoracoscopic and robotic-assisted surgeries.

Duke also offers endobronchial ultrasound to perform biopsies without an incision. The endobronchial approach allows surgeons to identify small lymph nodes by ultrasound that previously would have been removed through surgery (or possibly missed).

Now, they can be biopsied with a tiny needle through the wall of the airway in a less invasive fashion, which can often provide the same level of specificity as a more invasive biopsy. White says, “We are more aggressive about getting to the precise diagnosis and, when we can, learning about genetic mutations.” For example, a patient whose tumor contains an EGFR mutation can be treated with a pill such as erlotinib, a targeted therapy that acts selectively on the cancer cells, rather than traditional cytotoxic chemotherapy, which affects all cells and may be associated with more adverse effects.

Teamwork is a key to the success of the Duke thoracic program. Programs like Duke’s offer a multidisciplinary approach that has been widely recognized over the past few years, particularly in thoracic surgery and other types of cancer surgery. White says, “We use this approach at Duke Raleigh Cancer Center, where we hold a weekly multidisciplinary lung cancer clinic. Patients can often see several specialists during 1 visit because of coordinated communication among the specialists.”

To refer a patient with thoracic disease, call 844-790-2013
10 Tips for Implementing and Improving Care Coordination

By Emily Paulsen

Care coordination is like the air traffic control of health care, says Yul Ejnes, MD, an internist based in Rhode Island who helped develop the High Value Care Coordination Toolkit for the American College of Physicians (ACP). Medical practices have done this for years but may not have had the time or resources to focus on it. Now payers are offering incentives for practices to add care coordination. Here are some tips to make the transition.

1. Embrace it. Overloaded physicians may feel that participating in care coordination is more trouble than it’s worth. But evidence suggests that it can improve care, increase patient satisfaction, and reduce costs—something that Ejnes has seen in his own practice. “You have to believe it’s important, or it won’t happen,” he says.

2. Start out slowly. Tracy Watrous, vice president of organizational content management for MGMA, says it’s often not necessary to hire a dedicated care coordinator. Practices can start by shifting job responsibilities so that staff can devote time to care-coordination activities.

3. Involve staff members at all levels. Staff can share ideas about how to efficiently integrate care-coordination tasks into their workdays.

4. Explore what other practices are doing. Physicians can learn a lot by talking to colleagues at local medical societies or visiting other practices.

5. Focus on areas of biggest impact. Chronic care management, transitions between care settings, and referrals offer the biggest opportunities for quality improvement and cost reduction.

6. Open lines of communication. Make sure referring physicians and local hospitals know how to relay when one of your patients is admitted, treated, or discharged.

7. Recognize the patient’s role. Patient engagement plays a big role in care coordination, says Watrous. Find ways to involve patients in treatment planning and ensure that they have the information and support they need to carry out the plan between visits.

8. Make small changes. Watrous says 1 internal medicine practice improved diabetic foot care by asking patients with diabetes to take off their shoes and socks at office visits. This way, physicians could quickly check their feet.

9. Use technology. Most electronic health records can generate lists of patients who are due for preventive care. Reduce duplicate testing by using your state Health Information Exchange to check for laboratory results and studies ordered for your patients by other physicians.

10. Take advantage of available tools. ACP, MGMA, and other state and national physician groups and payers offer free and low-cost resources for training staff and implementing care coordination.
It can be challenging to know when a person is in cardiogenic shock because the physical manifestations can vary widely. Treatment must be swift and effective, or patients won’t recover; even with care, some cannot recover and require cardiac transplantation.

Thus, the Duke Heart Center launched a pilot program with CarolinaEast Medical Center based in New Bern, NC, to devise effective cardiogenic shock treatment protocols.

Each center uses a broad protocol and customizes it to the partner site. This way, workloads become aligned to safely benefit patients who experience cardiogenic shock, says Chet Patel, MD, a cardiologist and heart failure specialist who is medical director of the Cardiac Transplant Program at Duke.

David Jessup, MD, an interventional cardiologist and subspecialty clinic director at CarolinaEast, helped develop the new protocols after chairing the STEMI Data Collection Reporting Committee for the Washington State Department of Health. When he moved back to North Carolina, he realized the need for coordinated, systematic transportation to and treatment at a tertiary center and began working with Duke.

“Deciding on terms and definitions was key to speeding up communication safely and effectively,” Jessup says. “If I say we have a class II cardiogenic shock patient, then the Duke team knows the patient has an Impella device and knows the steps we have taken. Thus, there is no need—at 3 in the morning—to report the details. It also means steps won’t be repeated upon arrival at Duke.” The enhanced communication could save time and improve patient safety, Jessup says.

Patel notes the partners have been working to identify the highest-yield information needed at the outset. “This helps us avoid focusing on noncritical details,” Patel says. “The bottom line is early recognition and stabilization, even before knowing exactly what is happening for a particular patient. We have had to adapt to this new process because it’s best for the patients.”

Duke previously initiated successful protocols for 2 other acute conditions: myocardial infarction and aortic dissection. “We have learned from each of those processes to develop protocols for a condition like cardiogenic shock,” Patel says. Duke has just launched a Heart Center app that provides a 1-touch contact information system so that referring physicians in any setting can call a Duke specialist on a 24/7 basis. (X-ray above shows pulmonary embolism with a massive thrombus in the right and left pulmonary arteries in a patient who experienced cardiac arrest.)
CASE STUDY

First-of-Its-Kind Retinal Repair for Refractory Macular Hole

By Catherine Lewis

A new approach confers surprising outcomes.

A highly myopic, 53-year-old woman underwent pars plana vitrectomy with internal limiting membrane (ILM) peel to treat a macular hole in one of her eyes. Six months later, she developed a refractory macular hole and retinal detachment. To treat the retinal detachment, the patient underwent therapy with a scleral buckle and repeat pars plana vitrectomy. Still, the macular hole persisted.

To prevent the patient’s vision from further deteriorating, local surgeons referred her to the Duke Eye Center. Initially, Tamer Mahmoud, MD, a vitreoretinal surgeon, planned to use the ILM as a flap to repair the hole and prevent future detachments. However, he soon discovered that she had an open posterior capsule preventing lens capsule harvest and insufficient ILM for use as a flap, severely limiting her treatment options.

In a first-of-its-kind transplant, the patient received an autologous retinal transplant, which not only repaired the macular hole but also significantly improved the patient’s visual acuity.

Macular holes that are associated with myopic traction maculopathy or retinal detachment tend to have high reopening rates, and patients with these types of impairment have few treatment options. In general, commonly used procedures require positioning an ILM flap inside the macular hole, which may cause iatrogenic trauma to the retinal pigment epithelium and has limited potential to improve vision.

In contrast, the neurosensory retinal flap is thicker, easier to handle, and may also offer some functional benefits. In this case, after Mahmoud

OCT imaging of the macular hole before surgery (top) and 1 month after it was closed with the transplant (bottom).
performed the autologous retinal transplant surgery using silicone oil to keep the transplant in place, the patient’s eye did not exhibit retinal detachment or reopening of the macular hole (see figure on the previous page). In addition, the harvest site did not show any complications.

Following the surgery, the patient noticed a progressive reduction of her central scotoma. Most surprisingly, the patient experienced increased retinal sensitivity, and, after only 3 months, her visual acuity improved from a corrected acuity of 20/200 to 20/80, suggesting that the transplant also retained the patient’s retinal function.

“That was very exciting and entirely unexpected,” says Mahmoud. “We tested the sensitivity of the retina using microperimetry and found that her sensitivity had indeed significantly improved.”

To prevent future complications, Mahmoud removed the silicone oil after several months using Duke’s state-of-the-art intraoperative optical coherence tomography (OCT) technology, which allowed him to avoid disrupting the transplant.

The technology also revealed that, in contrast to the thin piece of transplanted peripheral retina, the transplant had begun to develop layers, similar to the thicker, central retinal tissue. This development generates further questions as to how the transplanted peripheral retinal tissue can acquire the morphologic and functional characteristics of the central retina.

Mahmoud and colleagues are working to understand the mechanism and the long-term outcomes of this type of transplantation to further refine the technique. This approach may represent a viable alternative for patients who previously did not have surgical options.

“It is incredibly gratifying to have success, not only in developing a new way to close macular holes but also to see this completely unanticipated functional improvement in retinal sensitivity and vision,” Mahmoud remarks. “Now we need to understand more about those cells because the surgery itself isn’t very complicated, but the implications go far beyond macular holes.”

The procedure may also benefit patients with other retinal conditions, he says. “If the retina from the periphery starts changing behavior, then there may be applications for other types of retinal diseases where the central vision is lost. That’s what’s truly exciting.”

Duke is one of few centers to offer the Argus II Retinal Prosthesis System.

Since the initial transplant, Mahmoud has completed 2 additional successful transplants and has published the case as a surgical technique in JAMA Ophthalmology. Mahmoud is part of a team of Duke retinal specialists who use the latest diagnostic, medical, and surgical advances to diagnose and manage the most complex retinal diseases. Duke is one of few centers to offer the Argus II Retinal Prosthesis System and, in 2014, completed the seventh such transplant, restoring levels of vision. ☝️

To refer a patient, call 844-790-2013
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