As part of a national campaign, UCLA Health has stepped up its efforts to increase colorectal cancer screening rates both within its own system and in the broader community. It is doing so through initiatives that aim to increase awareness among patients of the importance of screening and through outreach designed to ensure that providers counsel their patients on the issue.

More than 1,500 organizations and health care systems signed on to the National Colorectal Cancer Roundtable’s 80 Percent by 2018 campaign, seeking to raise screening rates among adults 50 years of age and older from approximately 65 percent in 2016 to 80 percent by the end of this year. “Colorectal cancer is the second most common cancer killer in the United States, but unlike other...
UCLA Clinical Updates

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**UCLA establishes CAR T-cell therapy program**

CAR T-cell therapy is an oncologic immunotherapy in which genetically modified T cells recognize a protein found on the surface of antibody-secreting B cells and cancers originating from B cells, initiating an inflammatory response to destroy the malignant cells. The single-dose therapy produced remission at 15 to 24 months in almost half of patients with large B-cell lymphoma, while 83 percent of patients with acute lymphoblastic leukemia attained a complete remission within three months of infusion.

**Limb-sparing surgery for rare bone cancers**

Limb-sparing surgery avoids amputation by removing only the tumor and a small portion of the surrounding soft tissue. Over 90 percent of bone sarcoma cases can be surgically managed by limb-sparing surgery.

**HIPEC offers regional treatment for abdominal cancers**

Hyperthermic intraperitoneal chemoperfusion (HIPEC) is a regional chemotherapy that is paired with cytoreductive surgery to eliminate cancer cells that remain in the abdominal cavity after visible cancer cells have been removed. Because the chemotherapy agent does not circulate through the bloodstream, higher doses can safely be used without the side effects usually associated with systemic chemotherapy.

**New endocrine center offers a streamlined approach to care**

The UCLA Endocrine Center is one of only a handful of centers nationwide offering a full range of consultative, diagnostic and therapeutic endocrinology care — including all diseases of the thyroid, parathyroids and adrenal glands — in a single-visit, one-location setting.

**Clinic treats male-factor fertility issues**

Male-factor fertility problems play a role for about half of all couples having difficulty getting pregnant. When properly identified, most male-factor fertility problems can be overcome, and couples can often succeed in initiating a pregnancy.

**Community pain clinics**

UCLA has established a growing network of community-based pain centers staffed by physicians who are board-certified in anesthesiology and pain medicine. With more than 100 million Americans suffering from acute and chronic pain, there is a need for cost-effective and convenient strategies to help reduce pain while minimizing reliance on narcotics.

**UCLA Scar Treatment Program offers personalized outpatient care**

The UCLA Scar Treatment Program offers treatment for symptomatic or asymptomatic scars from any cause, as well as care for burn injuries.

**Flow diversion stents for unruptured cerebral aneurysms**

Flow diversion is a newer endovascular treatment for brain aneurysm in which a metallic mesh tube is placed across the neck of the aneurysm to divert blood flow. The endothelium then grows onto the stent, sealing off the opening of the aneurysm and healing the blood vessel wall.

To download these and other clinical advances at UCLA Health, go to: uclahealth.org/clinicalupdates

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**News from UCLA Health**

**Potential metabolite therapy to treat C. difficile**

UCLA researchers found that a metabolite therapy was effective in mice for treating Clostridium difficile infection, or C. difficile. Mice treated with an experimental drug called CSA13 were significantly more likely to survive the infection, had lower rates of weight loss and were less likely to have a relapse of the infection. The findings suggest metabolite therapy warrants further research as a possible treatment for C. difficile infection in humans.

uclahealth/cdiffericli3

**Cells contain mitochondria specialized to build fats**

New research by UCLA scientists has found that within each cell a group of specialized mitochondria can be found attached to fat droplets. Rather than burn fat to create energy, these specialized mitochondria are responsible for providing the energy to build and store fat molecules. This discovery of a new function may lead to new treatments for metabolic diseases.

uclahealth/mitochondriafats

**Two genes likely play role in extreme nausea and vomiting during pregnancy**

A study has identified two genes associated with hyperemesis gravidarum, whose cause has not been determined in previous studies. The genes, known as GDF15 and IGFBP7, are both involved in the development of the placenta and play important roles in early pregnancy and appetite regulation.

uclahealth.org/genespregnancy

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UCLA Health

Clinic treats male-factor fertility issues

UCLA establishes CAR T-cell therapy program

Surgery with HIPEC offers effective regional treatment for select metastatic abdominal cancers

UCLA Health

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MRI, endoscopy being used to screen patients at elevated risk for pancreatic cancer

A diagnosis of pancreatic cancer is dire, but its incidence among the general population remains fairly low. Currently, there are no guidelines for routine screening. However, a consensus is emerging to begin screening certain higher lifetime risk groups annually beginning at age 50 with endoscopic ultrasound and MRI.

Patients who fall into the high-risk category include individuals who have a genetic predisposition that may include several mutations associated with increased risk of pancreatic cancer, the most common of which involves the BRCA2 gene. Other high-risk factors can include a family history, such as having multiple family members with pancreatic cancer, including a first-degree relative diagnosed with pancreatic cancer at a young age.

For the broad population of patients diagnosed with pancreatic cancer, the one-year survival rate is 20 percent and the five-year rate is 7 percent, according to the American Cancer Society. But earlier diagnosis through screening may increase the survival rates for those patients at higher risk, notes Stephen Kim, MD, assistant clinical professor of medicine and a member of the Interventional Endoscopy Service of the Vatche and Tamar Manoukian Division of Digestive Diseases in the David Geffen School of Medicine at UCLA. Currently, only about 10-to-15 percent of patients who are diagnosed with pancreatic cancer are candidates to undergo surgery to resect the tumor. “Too often, by the time it’s detected, it’s too late, and that’s why the outcomes are so poor,” Dr. Kim adds.

In recent years, individuals falling into the high-risk category are being targeted for pancreatic cancer screening through two diagnostic tests that are believed to provide complementary information: MRI and endoscopic ultrasound. Dr. Kim explains that the endoscopic ultrasound is similar to an upper endoscopy: while patients are sedated with anesthesia, a small camera is fed down their throat into their stomach; an ultrasound probe at the end of the endoscope then allows the physician to visualize the pancreas through the wall of the stomach and duodenum. Based on what is seen, fine needle aspiration can be used to biopsy the pancreas.

“This is a very routine procedure for those of us who are trained in it — like any other upper endoscopy,” Dr. Kim says. Unlike colonoscopy, the procedure is purely diagnostic. “It’s analogous to breast cancer screening,” he explains. “We’re trying to pick up cancer at an early stage so that patients can potentially go to surgery, get resected and have a longer life expectancy.”

Dr. Kim notes that pancreatic cancer screening for high-risk patients has its downsides. In some cases, the MRI and endoscopic ultrasound turn up uncertain findings, such as atypical cells that might or might not develop into cancer. “If you’re a patient with a relatively high lifetime risk of pancreatic cancer and you get such a finding, you’re going to surgery, which might or might not turn out to be necessary,” Dr. Kim says. In addition, although the imaging technology has vastly improved, there are still cases in which it fails to detect pancreatic cancer until it has spread.

“We still need to better understand which patients we should be targeting, and we need improved methods for detection and determining when patients should undergo surgery,” Dr. Kim says. “But under our current protocols, high-risk patients are having pancreatic cancer found early enough to be removed successfully. For this high-risk group, the potential benefits of finding a resectable pancreatic cancer in the early stage far outweigh the risks.”
Cancers, we can prevent it in most cases,” says Folasade P. May, MD, PhD, an assistant professor-in-residence in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA. “The problem is that many people are reluctant to take advantage of the prevention tools, which include colonoscopy and home-based screening tests,” says Dr. May, who is helping to spearhead UCLA Health’s effort.

Over the last year, UCLA Health has launched campaigns designed to make patients more aware of colon cancer and the fact that it is preventable, while connecting them with their primary care physicians and gastroenterologists to ensure that they are being screened. Through a collaboration with UCLA Health’s quality initiative and informatics teams, a team that includes Dr. May has obtained information on patients older than 50 who have not received screening and has targeted them through a mailing campaign inviting their participation, either by scheduling a colonoscopy or through a home-based screening test. Both campaigns have resulted in increases in screening uptake.

Dr. May also has collaborated with researchers at the UCLA Fielding School of Public Health on outreach to federally qualified health centers. As part of the initiative, Dr. May has consulted with providers on ways to increase colorectal cancer screening rates among their patients. “One of our main messages is that it doesn’t always have to be a colonoscopy,” she says. “We now have very strong data that supports FIT [fecal immunochemical test], the stool-based home screening kit. Many patients at these centers don’t have access to colonoscopy, so it might be more feasible to give patients this home test, which is still an effective tool for detecting cancer early.”

Dr. May also offers providers advice on how to communicate with patients in ways that will overcome any resistance they might have. “There’s a lot of stigma about any test that requires patients to manipulate their stool, or a procedure that requires instrumentation in the rectum, so we encourage providers to be frank with patients, explaining that it is very common and saves lives,” she says.

In her own research, Dr. May has found that when patients are asked why they aren’t up to date with their colon cancer screening, the leading response is that their doctor hadn’t told them they needed it. “It’s so important for primary care providers to give this messaging to their patients,” she says. “A lot of patients have no idea that colon cancer is so common, or that it’s one of the few cancers we can prevent, but if they hear it from their doctor, they are much more likely to participate in screening.”

Colonoscopy remains the gold standard for colorectal cancer screening. “The advantage is that we’re able to identify the smallest lesions — such as flat polyps that can be more difficult to detect but are potentially higher risk than elevated polyps — and resect them in the same procedure,” says V. Raman Muthusamy, MD, director of endoscopy.

There have been many improvements in colonoscopy over the last decade,
Dr. Muthusamy notes. These include a better understanding of the importance of preparations and an improvement in prep quality, including the recognition that splitting doses between the night before and the morning of the procedure improves the quality of the colon preparation. An increased emphasis on training and quality metrics also has made a difference, as has the growing understanding of the risk of flat polyps and how best to detect them. With new equipment and resection techniques, endoscopists are also able to remove much larger lesions than in the past; at UCLA, approximately 95 percent of benign polyps that were once referred to a surgeon because they were seen as too large to be resected are now removed at the time of the colonoscopy, Dr. Muthusamy notes.

“A lot of patients don’t want to do an invasive procedure just to learn nothing was there,” Dr. Muthusamy says. “But given that colon cancer is such a large burden in this country, and that in at least 20 percent of women and 30 percent of men we will find something — a benign or precancerous polyp — that should be resected, it makes sense to do a test where we can both detect and treat at the same time. On the other hand, if patients are hesitant, they can get a home test, and if that turns up positive, it might be enough to convince the patient to get the colonoscopy. The best test is the one that eventually gets done.”
Hands-on, multidisciplinary approach benefits IBD patients

Due to the relapsing and remitting nature of inflammatory bowel diseases (IBDs) and the complexity of the medications used to treat these conditions, patients with IBD require an intensive, hands-on and multidisciplinary approach to care, says Jenny S. Sauk, MD, clinical director for the UCLA Center for Inflammatory Bowel Diseases.

Approximately 1.6 million people in the U.S. suffer from IBD, which can be diagnosed at any age but is usually first seen in patients between the ages of 15 and 30. The two main forms are Crohn’s disease, a chronic inflammation of any part of the gastrointestinal tract, and ulcerative colitis, which affects the large intestine or the colon. Symptoms — which can include diarrhea, abdominal cramps and pain, bloody stools and formation of ulcers, fever, loss of appetite, fatigue and weight loss — vary from patient to patient, and they tend to change over time.

The chronic inflammation can also lead to complications both inside the GI tract (including abscesses, fistulas, malabsorption and nutritional deficiencies) and outside (including osteoporosis; inflammation of the eyes, joints, mouth and skin; kidney stones; and sclerosing cholangitis).

“To provide the highest quality of care, our goal is to treat patients with effective medications early in the course of disease to prevent bowel damage that can occur with uncontrolled chronic inflammation,” Dr. Sauk explains.
“IBD can cause major lifestyle disruptions, the symptoms can be very unpredictable, and when they are left unchecked they can quickly worsen and, in some cases, lead to the need for surgery,” Dr. Sauk adds. “While many of our medications are effective, it is not always clear who will respond to various therapies. Closely following up with the patients is crucial to know whether our treatment strategies are effective enough to lead to our goal of mucosal healing.”

Flare-ups after periods of sustained clinical remission remain a possibility, so ongoing follow-up is beneficial, even when the disease does not appear to be active. “It is important to make sure we look for signs of increasing disease activity and control the inflammation as soon as we detect it,” Dr. Sauk says. She also notes that the medications used to treat IBD should be closely managed because there can be rare but serious side effects.

At UCLA’s IBD center, gastroenterologists with expertise in IBD collaborate closely with specialists, including pathologists, radiologists and colorectal surgeons, to design an individualized care program for each patient. The multidisciplinary team meets every two weeks to discuss and strategize the most challenging cases. In some cases, surgical management preceding medical management is the optimal strategy to treat IBD, and these multidisciplinary conferences allow gastroenterologists and surgeons to review and discuss imaging and biopsy results simultaneously. A registered dietitian with expertise in gastrointestinal disorders is a key member of the team, providing advice on optimal diet to minimize symptoms that the patient is experiencing. The center’s nursing and administrative staff are also specially trained in IBD, understanding the intricacies of specialty pharmacies and the insurance prior to the authorization process unique to many of the medications used to treat the disease.

To make it easier for patients to adhere to their treatment regimens, the UCLA IBD center has established a dozen infusion therapy centers in UCLA oncology offices across Southern California. “We have many physicians within the UCLA group who are positioned throughout Los Angeles, and we are all working together in an effort to make it convenient for our patients to get quality care,” Dr. Sauk says. “With infusion centers throughout Los Angeles, patients no longer have to go back and forth to Westwood for all of their appointments. These medications are typically provided in tertiary care centers, but we are making them more accessible.”

Meanwhile, UCLA IBD center researchers are taking a systematic approach to understanding the mechanisms by which IBD develops, including a focus on systems biology and exploring the complex microbial ecosystem involved in Crohn’s disease and ulcerative colitis. The sharp increase in IBD incidence — up as much as 20 percent over the last two decades — indicates that environmental factors, along with genetics, are playing a pivotal role in triggering the disease. Environmental contributors have been studied far less than genetic and mechanistic pathways in the past, but are now a major focus of UCLA IBD center research. In particular, the studies are focusing on the role of the microbiome and epigenome — how, for instance, IBD develops through changes in the gut bacteria, as well as through changes in microRNAs, long non-coding RNAs, DNA methylation and chromatin. The UCLA researchers are also looking at the connection between IBD and the brain.

“We are using patient samples to learn about how genetics, the microbiome, stress and other factors affect IBD. With our strong team of basic and clinical researchers, we think UCLA is uniquely positioned to gain insights into ways we can better understand the disease and intervene to affect its trajectory.”

“We are using patient samples to learn about how genetics, the microbiome, stress and other factors affect IBD,” Dr. Sauk says. “With our strong team of basic and clinical researchers, we think UCLA is uniquely positioned to gain insights into ways we can better understand the disease and intervene to affect its trajectory.”
Including a registered dietitian is essential to properly manage a broad range of gastrointestinal disorders, experts at UCLA say. “Diet is a very important part of gastrointestinal diseases, whether it’s the impact of eating certain foods that cause an immune or allergic response or simply alterations in gut function that can be exacerbated by a particular diet,” says Lin Chang, MD, a professor in the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA. Dr. Chang notes that among patients with irritable bowel syndrome (IBS), nearly 70 percent report that their symptoms worsen after meals. “Unlike many aspects of their disease, diet modification is something a patient can control, and this empowers them,” she says.

At the UCLA Digestive Health and Nutrition Clinic in Westwood and the UCLA Health GI Clinic in Santa Monica, registered dietitians with specialized training in GI conditions such as celiac disease, IBS and other functional bowel disorders, esophageal motility disorders and inflammatory bowel diseases work closely with physicians and their patients to manage illnesses and improve symptoms.

“Patients are very interested in learning more about the proper diet,” says Nancee Jaffe, MS, RDN, a dietitian specializing in digestive health in the Westwood clinic. “We all have to eat, and when food is either contributing to symptoms or can help with symptom reduction, getting the information to make good decisions is very empowering. And given the importance of dietary interventions in conditions like celiac disease and functional bowel disorders, having a well-trained dietitian work with these patients can make a big difference in ensuring a successful remission of symptoms.”

Jaffe notes that patients are exposed to a lot of advice on diet and nutrition from media sources, but much of it is conflicting and/or not informed by sound evidence. Moreover, a diet that’s healthy for the general population isn’t necessarily optimal for patients with a gastrointestinal disorder.

“Given the importance of dietary interventions in conditions like celiac disease and functional bowel disorders, having a well-trained dietitian work with these patients can make a big difference in ensuring a successful remission of symptoms.”

Many gastroenterologists lack the training and the time to provide the type of extensive nutrition counseling these patients need, Dr. Chang adds. In the past, she and her colleagues often referred patients to a dietitian outside of the clinic. But appointments often were difficult to obtain and the dietitians typically lacked specialized GI expertise. Now the more than 80 gastroenterologists in UCLA's GI division can refer to specially trained GI dietitians in Westwood and Santa Monica.

Prior to meeting with patients for the first time, Jaffe looks through their medical history and labs and consults with their physicians. During the hour-long first session, she goes over the patient’s diet and begins to design an intervention. “We’re looking at the specifics, down to which types of sugars and fats are in their diet and whether or not their GI tract
is able to handle it given their disease state,” she explains. Patients often are asked to keep a journal of what they eat and when they experience symptoms in an effort to detect patterns. They leave with practical solutions: Beyond the dietary plan, Jaffe provides packets of information that can include meal plans, recipes and brand names that have the proper ingredients, along with tips on how to follow the plan when dining out.

Beyond the benefits to the patients, the gastroenterologists at UCLA have appreciated what the dietitians have brought to the care of their patients. “The dietitian has become an integral part of the overall care we provide,” Dr. Chang says. “Having a GI dietitian who is knowledgeable and accessible can significantly improve the management of GI symptoms and the disease overall, and it results in patients being much more satisfied with their care.”
Achalasia is a rare disorder that affects the nerve and muscle function of the esophagus and lower esophageal sphincter (LES), making it difficult for food and liquid to pass into the stomach. The hallmark features include chest pain, dysphagia and regurgitation. The dysphagia — difficulty swallowing — can manifest as a food-sticking sensation or a feeling of delay of food passage into the throat, chest or upper abdomen. Although the exact cause of achalasia is not known, the condition is believed to result from an immune-mediated response affecting the nerves that regulate muscle function of the esophagus and the lower esophageal sphincter.

Per-oral endoscopic myotomy, or POEM, represents a paradigm shift in endoscopic intervention to treat achalasia. Although the exact cause of achalasia is not known, the condition is believed to result from an immune-mediated response affecting the nerves that regulate muscle function of the esophagus and LES. POEM procedure offers relief for patients with achalasia

A new procedure that blurs the boundaries between endoscopy and surgery has joined the armamentarium of treatments for achalasia, an esophageal disease that can have severe quality-of-life impacts for patients, and which, in its later stages, can be life-threatening.

Achalasia affects the nerve and muscle function of the esophagus and lower esophageal sphincter, making it difficult for food and liquid to pass into the stomach. Although the exact cause of achalasia is not known, the condition is believed to result from an immune-mediated response affecting the nerves that regulate muscle function of the esophagus and LES.
Vatche and Tamar Manoukian Division of Digestive Diseases

With nearly 94 faculty physicians and scientists, the Vatche and Tamar Manoukian Division of Digestive Diseases is a world leader in the diagnosis and treatment of disorders of the gastrointestinal tract, as well as research to find new cures. In addition to its programs at Ronald Reagan UCLA Medical Center and UCLA Medical Center, Santa Monica, the division has physicians in community offices throughout the Los Angeles region.

To learn more about the UCLA Vatche & Tamar Manoukian Division of Digestive Diseases, go to uclahealth.org/gastro

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Diagnosis of achalasia can be challenging. “We get quite a few referrals of patients in whom it is not clear why they can’t swallow,” says Jeffrey Conklin, MD, medical director of the UCLA Center for Esophageal Disorders. Cancers and other motility disorders can mimic symptoms of achalasia, he notes. Patients with reflux can develop strictures at the bottom of their esophagus, which can also produce similar symptoms.

High-resolution esophageal manometry — a test during which a thin catheter is passed through the nose into the esophagus to record pressure changes during swallowing — is the gold standard for achalasia diagnosis. “On the manometry, the diagnosis is made by demonstrating that the lower esophageal sphincter does not relax and there is failure of peristalsis in the esophagus,” Dr. Conklin explains. This usually requires referral to a specialized center. The urgency of the diagnosis and treatment of the disorder goes beyond the quality-of-life impact. “At the end-stage of the disease, patients start to aspirate at night because the esophagus is full of food,” Dr. Conklin notes. “As the aspirated contents from the esophagus get into the lungs, this can become life-threatening, leading to pneumonia and chronic lung disease.”

Achalasia treatments aim to relax or disrupt the muscle of the esophagus in order to allow food to enter the stomach more easily. Dilating the esophagus with a large-bore balloon can be used as an alternative to surgery, but this approach has been found to be marginally less safe and less durable than other treatments, Dr. Conklin says. Similarly, botulinum toxin injections can provide relief, but given that the effects are temporary, it is offered only to patients who would be unable to tolerate other therapies.

The mainstay of treatment is myotomy, which cuts the abnormal LES muscle at the junction between the stomach and esophagus. It is accomplished by a laparoscopic surgery called Heller myotomy. The procedure typically involves adding a Dor fundoplication, in which a small piece of the stomach is partially wrapped around the esophagus to decrease the risk of reflux.

More recently, UCLA and a select number of centers have begun performing per-oral endoscopic myotomy, or POEM, which aims to recreate the Heller myotomy in a less-invasive way. POEM became possible through advances in endoscopic techniques, including submucosal endoscopy and natural orifice transluminal endoscopic surgery, or NOTES. “This represents a paradigm shift in endoscopic intervention,” says Alireza Sedarat, MD, interventional endoscopist at the UCLA Center for Esophageal Disorders. “Traditionally, with endoscopy we stay within the lumen. In this case, an incision is made to enter the esophageal wall and expose the muscle. It’s blurring the boundaries between an endoscopic procedure and surgery, with great safety and success.”

Dr. Sedarat notes that POEM causes minimal disruption of the body’s anatomy in accessing the spastic muscle, and it results in a faster recovery and return to swallowing than the Heller myotomy. “This is one of the most gratifying procedures that I do,” he says. “Patients return with big smiles on their faces because they’re able to eat and drink what they want. It has a dramatic impact.”

Any patient with symptomatic achalasia who is a candidate for laparoscopic Heller is also a candidate for POEM, Dr. Sedarat says. The endoscopic procedure is particularly advantageous for patients with type III achalasia, in which there is an esophageal body spasm in addition to the lower esophageal sphincter relaxation impairment. For these patients, it can be more difficult to provide an adequate myotomy through laparoscopic surgery because of the physical limitations imposed by the diaphragm, whereas POEM allows precise tailoring of the myotomy length in the esophagus. For other types of achalasia, the anti-reflux component of the surgery may offer an advantage. At UCLA, patients see both the surgeon and the endoscopist before making a decision. Success rates for both procedures are greater than 90 percent.