The ability of emotional stress to cause various physical symptoms and disorders has been widely recognized since antiquity. This phenomenon is particularly prevalent in primitive peoples, and as Walter Cannon illustrated in "Voodoo" Death, could prove lethal if a taboo was violated, even if this was done unknowingly and only recognized at a much later date. A few centuries ago, disease was frequently viewed as a similar punishment from a divine being for some transgression and there was a firm belief that imagination could also cause disease. Imagination then referred to how the mind might induce various physical or mental disorders rather than our current concepts of creativity, artistic talent or flights of fancy. Certain individuals seem to be more susceptible to stress or to overreact to routine challenges. Others, obsessed with fears of having a serious illness, tend to interpret minor signs and symptoms as being due to a dangerous disease, or become preoccupied with imaginary complaints. Hypochondria is hardly a modern malady. The word comes from hypochōndrios, Greek for "beneath the breast bone cartilage", which is where the heart is located. But this region also includes the upper abdomen, which was believed to be the seat of melancholy due to an excess of black bile (Gr. melās, black + cholē, bile). Galen and other ancient physicians noted that patients with chronic complaints in this area often had no physical illness and tended to be melancholy or depressed.

The ranks of these "worried well" have swelled over the past two decades after direct to consumer drug advertising was allowed. It's difficult to watch TV today without being bombarded by commercials to "Ask your doctor" if some medication "is right for you. As emphasized in a prior Newsletter, this is usually preceded by a list
of symptoms that are commonly experienced by many people and do not necessarily mean that they have a disease or require the drug that is being promoted. Some conditions, such as erectile dysfunction, are not diseases, but normal consequences of aging. Many other ads, like those for Irritable Bowel and Restless Leg Syndromes, exaggerate the magnitude and hype the seriousness of relatively minor conditions. Nevertheless, they are extremely successful in selling drugs whose efficacy is not only dubious, but are sometimes later banned because of serious side effects. To avoid any stigma and to facilitate pushing a product, some disorders are frequently referred to by catchy acronyms like ED, RLS and IBS.

Thus, it would appear that we now also have an epidemic of GERD (Gastroesophageal Reflux Disease). Sales have soared for a class of drugs known as proton pump inhibitors that raked in over $13 billion in 2005 due to aggressive advertising. Almost anyone who watches TV has heard about Nexium, "the healing purple pill". Nexium ($4.4 billion) and Prevacid ($3.8 billion) were the third and fourth best sellers after Lipitor and Zocor for lowering cholesterol. Nexium moved up to second place in 2006 when it raked in more than $5 billion and over the counter sales of Prilosec, the original "purple pill" Nexium replaced, also skyrocketed. The fact is that almost everyone has occasional distress due to acid reflux from the stomach that backs up into the esophagus and most patients get relief from simple antacids or nonprescription drugs like Zantac. If significant heartburn occurs two or more days a week for at least three months, you may have GERD, but most people taking these powerful proton pump inhibitors do not have this degree of frequency or severity of symptoms. Many have no complaints but are arbitrarily started on these drugs for a year to prevent problems because of esophageal inflammation discovered on endoscopy. They are also widely prescribed to prevent ulcerations in arthritis and other patients who take NSAIDs (nonsteroidal anti-inflammatory drugs). However, interactions can occur with common medications like digoxin, coumadin, Valium or iron and there are a variety of adverse allergic reactions and gastrointestinal side effects. Proton pump inhibitors also interfere with calcium absorption and in one recent study, patients over 50 who had taken them for at least a year suffered 44 percent more hip fractures. Risk of hip fracture due to osteoporosis is much greater in senior citizens or people who take higher doses for longer periods.

Prilosec, the original purple pill  Nexium the "healing" purple pill  A bad break for the purple pills

Prilosec, AstraZeneca's original "little purple pill", was the number one selling prescription drug in 2001, when its patent expired. As noted, it was immediately replaced by Nexium, which is almost identical, although a massive advertising blitz touted its superiority and most doctors automatically switched their prescriptions over to this. The AFL-CIO and seniors groups in California filed a false advertising
lawsuit against AstraZeneca alleging that it sought to preserve market share and profits as the Prilosec patent expired by scheming to convince consumers and doctors that studies showed that Nexium was significantly better. Massachusetts consumers also filed a suit claiming that these studies had compared 20 mg. of Prilosec with 40 mg. of Nexium and the company refused to release "detailed descriptions of two studies that showed even the higher dose of Nexium to be no more effective than Prilosec." Prilosec is now marketed by Procter & Gamble over the counter and several companies also make generic versions.

There are additional concerns about the recent surge in prescribing these drugs. A study released a few weeks ago found that over the past four years, "The number of young children on prescription drugs for heartburn and other digestive problems jumped about 56 percent". Researchers found that "557,259 infants and children up to age 4, or about 3 percent of youngsters in that age range, were taking these drugs last year." According to another news report, the use of proton pump inhibitors has become so prevalent, that in 2006, they were prescribed for "an estimated 2 million children in the United States." In commenting on this, a pediatric gastroenterologist at the Hospital for Sick Children in Toronto explained, "Increased use of the treatments could stem from higher rates of obesity and stress, conditions linked with the disorder in adults. It may also mean that children with occasional symptoms are treated as if they have the full-blown disease. The question is whether people are prescribing more medications because they're treating symptoms or whether they're actually treating the disease. . . . Furthermore, children with occasional reflux should not be given drugs because gastroesophageal reflux disease doesn't interfere with their growth, it doesn't cause them pain or irritability." The chief medical officer of the company that conducted the study also warned, "While there are babies that require drug treatments for extreme cases of GERD and other gastrointestinal problems, in some cases, parents and physicians may be looking to medications when non-drug treatments might be adequate."

Reflux symptoms may be due to a hiatus hernia and are apt to be precipitated by lying down or going to bed shortly after eating, particularly in obese people. Spicy or greasy foods, onions, chocolate and peppermint can cause heartburn by stimulating certain gastric hormones that cause the sphincter muscle between the esophagus and stomach to relax. Large meals also cause the muscle to relax by distending the stomach. Alcohol, acidic foods like coffee, orange juice and tomato products can aggravate symptoms by directly irritating the esophagus. Avoiding these problems can often prevent or reduce complaints as can shedding extra pounds if you are significantly overweight. Obesity is a well established risk factor for GERD, particularly in females. This may be due to estrogen, since in one study of obese women, postmenopausal females were much less likely to have reflux symptoms than premenopausal controls with similar weights. In addition, postmenopausal subjects on estrogen replacement therapy also had more symptoms. One explanation for this is that estrogen increases the synthesis of nitric oxide, a chemical that relaxes the lower esophageal sphincter. Support for this comes from a study of over 350 subjects with moderate or severe symptoms of heartburn due to regurgitation. Half were given a cocktail containing melatonin, a readily available sleep aid supplement that inhibits the production of both nitric oxide and stomach acid. The other half received a similar cocktail that replaced the
melatonin with Prilosec, a nonprescription proton pump inhibitor. After seven days, 100 percent of those in the melatonin group reported marked improvement, compared with only 66 percent after nine days on Prilosec.

**Stress, Heartburn, Dyspepsia, Pyrosis And "Agita"**

The first scientific report on physiologic responses to stress was actually Walter Cannon's study of the effects of stress on the esophagus. In 1896, during his first year as a Harvard medical student, he had been assigned to investigate the mechanisms of swallowing by taking advantage of the newly discovered Roentgen rays. These x-rays, as they were later called, could display a faint image of internal body structures using a fluoroscope but it was necessary to sit in a very dark room or wear red goggles to get the best results. Cannon included bismuth in foods since it was opaque and blocked x-rays, which markedly improved his ability to distinguish the peristaltic motion of waves that progressively propelled the contents of the gut forward. Bismuth was subsequently replaced by barium sulfate, which was less toxic, and is still used in GI series, barium enemas and other x-ray imaging procedures. As an aside, medications containing bismuth, like Pepto Bismol, also show up on x-rays and should be avoided for two or three days before any such diagnostic procedures.

Cannon demonstrated the movement of a pellet through the gullet of a goose using his new technique at a meeting of the American Physiological Society. The results of this and other studies showing the effects of stress on the esophagus and stomach were published in 1898 in the inaugural issue of *The American Journal of Physiology* in a paper entitled "The movements of the stomach studied by means of roentgen rays" He continued his research after graduating in 1900, and in 1906, was appointed Professor and Chairman of the Department of Physiology at Harvard and served in this position for 36 years. In a 1911 publication, "Conditions affecting the activities of the cardia", he explained how acid reflux occurred as a normal phenomenon. The "cardiac sphincter" (now called the lower esophageal sphincter) located at the junction between the esophagus and stomach was a thickened band of circular smooth muscle. When stimulated to contract, it prevented the backup of gastric contents into the esophagus, and provided "pleasant security" from its "nauseating odors and highly disagreeable taste." However, everyone normally experiences some degree of reflux that usually causes no symptoms or damage, and this is particularly common in infants. Cannon described in detail this spontaneous and periodic occurrence of normal reflux as follows, "I noted repeated regurgitation from the stomach into the esophagus.... The animal lay comfortably on a holder, unanesthetized, and was examined by means of the X rays. Each regurgitation was followed at once by a peristaltic wave which pushed the escaped material back again into the stomach. Soon after it was thus restored, the cardia again relaxed and it again rushed out." He reasoned that the ability to temporarily deactivate the cardiac sphincter was particularly important in cattle, sheep and goats that chew a cud consisting of regurgitated, partially digested food. These and other ruminant animals with compartmentalized stomachs need to be able to vent the large volumes of gas that are generated to maintain proper gut function. Reflux and vomiting are also valuable protective mechanisms when toxins are ingested that require a coordinated deactivation of sphincter activity. In 1912 he demonstrated that hunger pangs were due to cramp-like contractions of the stomach.
Cannon had observed early on that peristaltic waves ceased whenever his experimental animals were under stress or excited, which aroused his interest in the autonomic nervous system. Starting in 1911, he and many of his students published numerous papers over the following two decades, showing how stress stimulated the sympathetic system and the adrenal medulla to produce visceral and other changes in body function that could facilitate life saving "fight or flight." As he wrote in his 1945 autobiography, *The Way of an Investigator. A Scientist's Experiences in Medical Research*: "The whole purpose of my effort was to see the peristaltic waves and to learn their effects. Only after some time did I note that the absence of activity was accompanied by signs of perturbation, and when serenity was restored the waves promptly reappeared. This observation, a gift for my troubles, led to a long series of studies on the effects of strong emotions on the body. The idea flashed through my mind that [these changes] could be nicely integrated if conceived of as bodily preparations for supreme effort in flight or in fighting. The inhibition of digestive activity by emotional excitement was an interruption of a process which is not essential in a life-or-death emergency and which uses a supply of blood urgently needed elsewhere."

The earliest recorded use of the term "heartburn" was in the 18th century, to describe a sharp, gnawing or burning pain under the lower sternum that could radiate upwards to the neck. Pain was often worsened by bending or lying down and was usually located in the epigastric region where the esophagus joins the stomach. As noted above, this area had previously been named the cardia, since it was originally believed that such symptoms emanated from the heart. Cardiospasm is still used to refer to a spasm of the lower esophageal sphincter that causes chest pain, regurgitation of food and inability or difficulty in swallowing. It has largely been replaced by achalasia, *(from the Greek α, no or without and khalaísis, relaxation, which comes from khalaín, to loosen)*. Although there may be a physical basis, there is little doubt that this condition can be caused or aggravated by stress. In one study of 25 male and female patients with cardiospasm, all but one stated that the attack had been precipitated by severe emotional stress and that they had previously not been able to "ventilate" their problems. It was not until 1934 that complaints of heartburn were correlated with reflux-induced esophageal inflammation because patients described lower substernal pain that was accompanied by "sour" regurgitation and "belching". Although reflux-induced chest pain is not indicative of heart disease, some overlap still occurs, since indigestion or "dyspepsia", terms that refer to epigastric distress, are complaints that are not uncommon in patients with coronary disease, especially those with impending infarcts.

The medical term for heartburn is pyrosis, *(from pyrōsis, the Greek word for burning)*. This can be severe at times, since gastric acid can be stronger than the acid in car batteries. In French, heartburn is *brûlure épigastrique* *(burning or searing sensation in the upper abdomen)*, in Spanish and Italian, *arder de estómago* and *bruciore di stomaco* *(burning in the stomach)* and in Yiddish, it is *harz-brenenisch*, *(heart burning)*, which reflects its American roots. In that regard, there is also "agita", an Italian-American slang word of uncertain origin. Some linguists believe this comes from *agitare*, Italian for "to agitate' or "to trouble", which is derived from the Latin *agitare*, meaning "to stir up." To be *agitato* is to
be very excited and a musical score marked "agitato" is intended to be played at a frenzied pace. Others suggest that the source is "acido" (pronounced Ah-chee-do), Italian for "stomach acid," which later became "agita" (Ah-jih-ta). In either case "agita" seems to have arrived in New York with Italian immigrants around the turn of the last century. It has been in constant use since then, especially in New York City and other metropolitan areas, where it is often more synonymous with stress than heartburn. Comedian Jackie Mason explained "agita" as "when you have been aggarvated to the point where it feels like you have a serious migraine headache throughout your whole body." Woody Allen, nominated for an Academy Award for his 1984 film, Broadway Danny Rose, made the song "Agita" it's centerpiece. The setting was the Carnegie Delicatessen, a famous Jewish eatery and gathering place in Manhattan. Although the song dealt with indigestion, its thrust was that "agita" is the Italian-American equivalent of "tsuris", which is Yiddish for "misery".

**Stress, GERD, Gastritis, Stomach And Duodenal Ulcers**

It is estimated that more than 40 percent of U.S. adults have heartburn at least once a month and that 7 percent experience it daily. How many actually suffer from GERD is more difficult to determine since these terms are frequently used as synonyms, especially in TV ads for drugs. Patients are also confused and are likely to refer to their complaints as GERD, since this may have more of the connotation of a disease over which they have little control. Having heartburn is less socially acceptable because it can result from overindulgence, eating the wrong foods and other faulty and preventable habits that imply some defect in character such as lack of will power. As noted previously, an association between heartburn and stress has long been recognized. A recent Gallup poll found that 64 percent of respondents with heartburn reported that stress increased their symptoms. To verify this, researchers studied sixty subjects with current heartburn symptoms and rated the frequency and severity of stressful life change events that had been experienced over the preceding 6 months. They were then followed for 4 months, during which symptom severity and quality of life were recorded in a daily diary and levels of anxiety and depression were measured. The results confirmed that severe and/or sustained stress during the previous 6 months significantly predicted an increase in heartburn symptoms during the 4 month follow-up period. Heartburn severity correlated best with major life stress events rather than an accumulation of minor stresses or change in mood, although chronically depressed patients reported taking more heartburn medications.

It was initially assumed that stress induced heartburn resulted from an increase in the frequency and or duration of acid reflux events. However, one study found that when heartburn patients were subjected to acute stress in a laboratory setting, there was no evidence of increased acid measured by a probe placed at the end of the esophagus. Moreover, acid concentrations were similar when those patients who reported increased symptoms during stress were compared to others who had no change in complaints. Other attempts to demonstrate increased acid in the esophagus during stress have also yielded negative results, despite higher concentrations of acid in the stomach. In another experiment, GERD patients were stressed by being forced to do mental arithmetic tasks and compete in a difficult computer video game under time pressure. Although participants reported increased subjective ratings of anxiety and heartburn symptoms during these
stressful challenges, there was no corresponding change in esophageal acid concentrations. To evaluate the effect of stress reduction, patients were taught a progressive muscular relaxation technique during which they alternately tensed and relaxed 16 muscle groups in sequence. Those who practiced this regularly reported lower subjective ratings of anxiety and acid reflux symptoms. It was noted that during relaxation there was also a reduction in the concentration of acid in the esophagus. So what's going on? How does this help to explain the relationship between stress, heartburn and GERD?

The authors of the study believe that stress causes an increase in esophageal sensitivity to smaller amounts of acid in certain patients. Support for this comes from studies in their laboratory in symptoms when acid is infused into the esophagus of GERD patients who were simultaneously subjected to psychological stress. Preliminary results confirm that the threshold for experiencing symptoms is markedly lowered during stress and that this increased sensitivity to acid occurs regardless of whether or not there is any evidence of esophageal inflammation. The mechanism by which stress causes this hypersensitivity to acid is not clear. Most of the GERD patients that were studied seemed to be psychologically similar to controls without evidence of esophageal inflammation. However, those who tended to be anxious and were exposed to sustained periods of stress during their daily activities, were much more likely to notice a worsening of their symptoms at such times. Heartburn patients who did not have significant esophageal inflammation also had a greater tendency to exhibit symptoms of anxiety and hysteria. What may be equally important is that both groups had less social support from family and friends and were deprived of the powerful stress reduction benefits that this provides.

There has been heightened interest in reflux disease because of a study showing that GERD workers cost their employers an annual average of $3,355 due to medical care, prescription drugs and other expenses such as a 10 percent reduction in productivity. Decreased productivity alone is estimated to cost U.S. employers up to $75 billion a year. As indicated previously, you might have GERD if you have heartburn two or more days a week for at least three months. However, the diagnosis can only be confirmed by endoscopic examination of the esophagus and a biopsy of the affected area to rule out other pathology. Many patients in whom the diagnosis is established have no heartburn symptoms but are arbitrarily put on proton pump inhibitors for a year to treat or prevent Barrett's esophagus, a precancerous but asymptomatic lesion. Unfortunately, no drugs have been shown to reduce the likelihood of cancer and this complication is uncommon, if not rare. One report indicated "a physician would have to follow almost 50 patients with Barrett's esophagus for 10 years to have a chance of finding a single cancer." Surgery can eradicate Barrett's, the most popular being a procedure that involves taking the top of the stomach and wrapping it around the bottom of the esophagus. This creates a one-way valve so that food can go down but acid can't back up. Since there are adverse side effects as well as complications that occur with all abdominal surgery, this is likely to be replaced by the new outpatient "Halo 360" procedure. It consists of inserting an expandable balloon device into the esophagus and inflating it at the site of the lesion. Short bursts of radiofrequency energy are then delivered that burn away the top diseased layer of the esophagus, allowing healthy tissue to grow back. The procedure takes 15 to 25 minutes, is
effective in eradicating Barrett's in 90 percent of cases with minimal discomfort, and patients can return home within two hours.

Gastritis refers to inflammation of the lining of the stomach that is usually manifested by a burning sensation in the upper abdomen and occasionally bloating, belching or nausea. It can be caused by the regular use of aspirin and other pain relief medications that reduce levels of prostaglandin, a chemical that normally preserves the protective lining of the stomach. Gastritis can also result from infection with *H. Pylori*, the bacterium associated with stomach and duodenal ulcers. The important role of stress was emphasized by Hans Selye over 70 years ago, in his initial description of what he called "The Alarm Reaction". He had observed that when experimental animals were subjected to severe stress, the first evidence of changes in the body were inflammation of the lining of the stomach, atrophy of the thymus and lymphatic tissues, and enlargement of the adrenal glands. These three responses occurred whether the animals were exposed to frigid temperatures, excessive heat, shining bright lights in their eyes while the eyelids were sewn back, prolonged exercise by being forced to keep swimming to stay alive, unbearable frustration, painful stimuli and other forms of torture that researchers previously used that would not be permitted today. While excesses of temperature might cause specific damage such as frostbite or a burn, these and other potent stressors all produced the same pathological triad of superficial stomach inflammation with tiny ulcerations, thymus and lymphoid tissue atrophy and enlarged adrenals.

This led to Selye's definition of stress as "the nonspecific response of the body to any demand for change". This was in sharp contrast to the prevailing concept that every disease had a specific cause. Tuberculosis was caused by the tubercle bacillus, anthrax by the anthrax bacillus, scurvy by a lack of vitamin C, rickets by a lack of vitamin D, etc., etc. What Selye was proposing was the opposite, namely that the identical pathology could have many different causes due to the nonspecific effects of stress. In addition to the immediate responses seen in the "Alarm Reaction", which Selye viewed as a call to arms of the body's defenses, he found that when animals continued to be subjected to stress, they entered a "Stage of Resistance", during which defense mechanisms were maximized, and subsequently a "Stage of Exhaustion", characterized by dwindling or disappearance of defenses and eventually death. He called this three-phased response to stress "The General Adaptation Syndrome". During the course of this syndrome he noted pathological changes in the gastrointestinal tract, heart, blood vessels, kidneys and other organs similar to those seen in patients with peptic ulcers, ulcerative colitis, heart attacks, hypertension, kidney damage and other diseases. He suggested that nonspecific stress could also cause these disorders in humans and referred to them as "Diseases of Adaptation".

The significance of the pathological changes seen in the "Alarm Reaction" and why they only involved the stomach, lymphatic system and adrenals was not clear at the time. Decades before, Walter Cannon previously described his "fight or flight" responses to acute stress as being due to a stimulation of sympathetic nervous system activity and an outpouring of adrenaline from the adrenal medulla. Unlike Cannon, Selye was an accomplished pathologist, and noted that the enlargement of the adrenal was due to an increase in its outer shell or cortex, rather than the
medulla it surrounded. Being a superb biochemist, he knew that this is where steroid hormones were manufactured. Some of these, like cortisone, had anti-inflammatory effects while others, such as desoxycorticosterone, caused sodium and fluid retention and there were some with weak androgenic actions. Symptoms related to all of these hormones are seen in patients where there is hyperactivity of the adrenal cortex due to stimulation from a benign pituitary tumor. This is known as Cushing's disease, since it was first described by Harvey Cushing, the father of brain surgery, who demonstrated that everything returned to normal after the tumor was removed.

Cushing also noted that increased intracranial pressure from any cause was often associated with ulcerations in the stomach, and occasionally the esophagus and duodenum, that are still referred to as Cushing ulcers. This is sometimes confused with Curling's ulcer, an acute ulcer of the duodenum that results from the stress of severe burns and is named after Thomas Curling, the physician who described ten such patients in 1842. Both of these disorders are likely due to increased production of anti-inflammatory hormones like cortisone. When cortisone became available for the treatment of rheumatoid arthritis in 1948, the immediate response was often dramatic. However, it soon became apparent that patients on long term treatment often had GI complications, including bleeding from severe peptic ulceration, activation of previously quiescent tuberculosis, decreased resistance to other infections as well as delayed wound healing. Not much was known about the immune system when Selye described the "Alarm Reaction", although it is now evident that atrophy of the thymus and lymphoid tissues markedly reduces the production of the T and B cells they manufacture that allow us to resist bacteria, viruses or any perceived foreign intruder. This also helps to explain the role of stress in autoimmune disorders like rheumatoid arthritis, lupus and multiple sclerosis, in which the immune system attacks normal tissue, because it is somehow interpreted as being foreign.

As emphasized in a prior Newsletter, **it is not generally recognized that in addition to the brain in our skull, we have a "second brain" in the gut, and that the two are in constant communication.** The reason for this is that during early fetal development, both the brain and the gut (esophagus, stomach, small intestine and colon) developed from the same clump of embryonic tissue. This subsequently divided with one section growing into the central nervous system (brain and cranial nerves) and the other into an enteric nervous system that contains a "gut brain". Later on, these two brains then became connected via the massive vagus nerve. Nearly every brain-regulating hormone and neurotransmitter found in the brain has also been found in this "gut brain", which also has more nerve cells than the total of all nerves connecting the rest of your body to the brain. Because of this, the state of your gut has a profound influence on your brain, as well as vice versa. That's why you have "gut feelings" about something that may differ from rational appraisal and why you feel "butterflies in the stomach" if you are very anxious or nervous. This two way conversation helps to explain why the feeling of a full stomach stops your appetite and why stress can cause GI symptoms ranging from diarrhea and constipation as well as its role in functional disorders like irritable bowel syndrome, as well as ulcerative colitis, terminal ileitis and other inflammatory bowel diseases.
This is also why **many drugs used to treat gastrointestinal diseases were originally designed to act on the brain**, like Imitrex for migraine and clonidine, which is prescribed for various psychiatric disorders. Antidepressants like Prozac that increase brain serotonin to relieve depression can cause abdominal cramps due to gut spasms. Both Lotronex, which is derived from an anti-anxiety medication, and Zelnorm, another drug used to treat irritable bowel syndrome, work by effects on serotonin in the gut. Scientists have discovered that some Alzheimer's and Parkinson's patients accumulate the same type of tissue damage in their bowels as they do in their skulls, raising the possibility that these disorders might someday be diagnosed by routine rectal biopsy.

The ability of stress to produce peptic ulcers was unequivocally demonstrated by Stewart Wolf in his study of Tom, which was featured in a 1943 *Time* magazine cover story. Tom was a patient with an esophagogastric fistula that allowed direct visualization of the stomach, so that it was possible to see and photograph changes in secretory and motility patterns that correlated with his emotional status. On one occasion, when Tom was extremely upset, Stewart painstakingly documented the progressive development of a peptic ulcer due to increased gastric secretions and diminished blood flow to the stomach that also damaged its lining. As Walter Cannon commented, "The functions of the stomach have never been investigated with the detailed care, the skill and ingenuity displayed in the research on Tom's stomach". However, this and other supportive studies confirming the relationship between stress and ulcers seemed to go out the window when it was discovered that the vast majority of ulcer patients had an *H. pylori* infection and that antibiotics effectively eradicated the ulcer. Although this seemed to be solid proof that ulcers were due to *H. pylori* infection, as emphasized in a previous Newsletter devoted to this, at least half the world's population harbors *H. pylori* by the age of 10. The organism lives only in the gut, where it lies dormant and usually causes no symptoms, since only a tiny fraction of those that have it develop ulcers.

What seems most likely is that stress induced anti-inflammatory hormones like cortisone impair defense mechanisms that normally prevent ulcers. As noted previously, peptic ulcers and activation of asymptomatic tuberculosis is not uncommon in patients who take cortisone to treat chronic conditions like rheumatoid arthritis. A similar situation is seen with other quiescent microorganisms like herpes simplex virus, which causes recurrent cold sores during periods of stress. Finally, those who are dubious about the effect of stress on the gut, should be aware that the stomach might be a more sensitive barometer than the heart in some instances. Standard lie detector polygraph tests utilize changes in the electrocardiogram (ECG) and blood pressure to help in reaching an evaluation. However, a recent comparison study revealed that an electrogastrogram (EGG), which records changes in stomach motility and contractions, might be a superior indicator to detect lying. As the senior author noted, "We concluded that the addition of the EGG to standard polygraph methods has clear value in improving the accuracy of current lie detectors. The communication between the big brain and the little brain in the stomach can be complex and merits further study."
Stress, Irritable Bowel Syndrome And Inflammatory Bowel Disease

Irritable Bowel Syndrome (IBS) is characterized by chronic abdominal pain, discomfort, and irregular bowel movements. Researchers believe that this is due to the fact that nerves in the intestinal wall do not react normally to food and gas passing by, causing muscles in the colon contract erratically. As a result, food travels too slowly or too rapidly, causing constipation or diarrhea. IBS patients often experience both these symptoms regularly, in addition to abdominal pain, gas and bloating. The diagnosis requires a year's history of at least 12 weeks (not necessarily consecutive) of pain or abdominal discomfort that is relieved with defecation and/or is associated with a change in stool frequency or form. However, the diagnosis is difficult to make since unlike other gastrointestinal diseases, there are no structural changes. This, as well as the fact that symptoms are usually related to stress, has led many doctors to dismiss complaints as being psychosomatic in origin. In addition, up to 40 percent of patients have increased anxiety levels similar to those reported in other presumed "functional" disorders like fibromyalgia and chronic fatigue syndrome. IBS has also become a wastebasket diagnosis for anyone with unexplained abdominal distress or significant change in bowel habit, which is why it is the most common disorder reported by gastroenterologists.

IBS is estimated to affect one in five Americans, including 2.5 million children. The disorder tends to run in families since three out of four kids with IBS have at least one parent or sibling with gastrointestinal problems. Symptoms can start as early as five years of age but more often begin around the age of 10. Although they may temporarily disappear during early adolescence, there is usually a recurrence a few years later and the condition becomes chronic with intermittent periods of relief that vary in duration. IBS may follow an infection, suggesting that the immune system may play a role. The disorder can be managed but not cured by adding fiber to the diet and avoiding certain triggers. Lotronex was hailed as a breakthrough drug when it was released in 1999 but had to be withdrawn less than a year later because of severe side effects and several possible deaths. Zelnorm, another IBS drug introduced in 2002 with a massive publicity blitz, was also banned earlier this year for similar reasons. Because of numerous complaints, the FDA reversed itself and both drugs have since been reapproved for severe diarrhea or constipation not responsive to other medications, but with strict warnings and restrictions. Unfortunately, Lotronex worsens constipation and Zelnorm causes diarrhea. Most IBS patients suffer from both complaints, so that these drugs are two-edged swords with limited benefits and significant risks. Since there is no effective treatment, the most effective way to manage IBS is to prevent attacks. Various risk factors, triggers and influences shown below emphasize the important role of stress.
How stress can affect the development and modulation of IBS symptoms. Different stressors may trigger the onset of symptoms as well as contribute to their persistence depending on genetics and other factors. (From Mayer et al. Am J Physiol Gastrointest Liver Physiol 280: G519-G524, 2001)

For all these reasons, stress reduction approaches should be instituted in the management of all IBS patients. Options include various meditative and progressive muscular relaxation procedures, regular exercise (walking, jogging, yoga), insuring regular sleep, providing counseling and support and avoiding foods and stressful situations that have been found to trigger attacks. It is believed that the basic problem is that the brain and autonomic nervous system respond excessively or erratically to normal gastrointestinal sensations. A large NIH study is currently in progress to test this hypothesis in IBS patients with similar disease severity. Those in the first group are taught progressive muscle relaxation techniques to reduce tension and stress. A second group focuses on identifying situations and thought processes that aggravate their symptoms so they can learn not to overreact to challenges or "catastrophize" perceived threats. They can learn not to react overly anxiously to events in their lives--or "catastrophize". The third group is given educational materials on the physiology of IBS to determine if an understanding of this might reduce attacks. Volunteers in all three groups receive 10 weekly sessions with a psychologist and a follow-up meeting after six months. Researchers will also use sophisticated brain imaging and other techniques to investigate feedback mechanisms between the GI tract and the brain, since some studies suggest that activation of the limbic system is associated with flare-ups.

Inflammatory bowel disease (IBD) refers to a group of disorders that include ulcerative colitis, Crohn's disease, and bacterial infections. More then 600,000 Americans a year suffer from IBD symptoms such as abdominal pain, severe cramps, nausea, diarrhea or loose stools containing blood, pus and excess mucus. Ulcerative colitis causes ulcers in the lower part of the large intestine, often starting at the rectum, that frequently bleed. Crohn's disease patients have similar ulcerations throughout the small intestine, especially the ileum, and although the colon can be involved, the rectum is usually spared. What causes these disorders has not been determined but it is believed that both result from exaggerated immune system responses to normal bacteria and food in the gut that are
mistakenly perceived as being foreign. In an attempt to attack and destroy these presumed invaders, white blood cells accumulate in the lining of the bowel wall producing chronic inflammation, ulcerations and tissue damage.

There is little doubt that stress can aggravate and precipitate attacks of IBD. One study found a significant relationship between exacerbation of ulcerative colitis and long-term stress as rated on the Perceived Stress Questionnaire. In another, researchers studied patients with inactive ulcerative colitis and healthy controls. Both groups were told they were participating in a study to assess the relationship between their intelligence and their responses to stress. They were then given an IQ test to complete in 50 minutes that should have taken an hour or more while contrasting types of music were played into each ear. They were also reminded, at increasingly frequent intervals, to increase their effort to finish the test. Blood pressure, heart rate, and blood- and mucus-levels of inflammatory markers were measured before, during and after completing the test. While the cardiovascular responses were similar, systemic and mucosal inflammation were greater in the ulcerative colitis group as assessed by interleukin-6, tumor necrosis factor, natural killer cells, platelet activation, and other markers of increased immune system activity. Lifetime psychiatric diagnoses are associated with an increased incidence of Crohn's disease. Further proof of the influence of the brain comes from the observation that if the spinal cord is severed above the level of T4, where nerves to the gut begin, ulcerative colitis patients have a complete remission. Similarly, large studies show that patients with spinal cord transection at this level, but not below, never develop ulcerative colitis. All of the above confirm René Dubos' assertion,

"What happens in the mind of man is always reflected in the diseases of his body."

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