Quest Diagnostics

Infectious Disease Update

Medical News

Volume 18, Number 6
August 2011
Pages 67 - 80

In This Issue

We'd Like to Hear from You

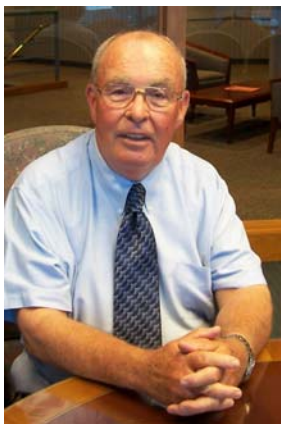
The vast majority of feature articles that appear in our *Infectious Disease Update* come about because somebody asked for them.

Often at meetings or during informal conversations, somebody will say: "Why don't you write something about this particular subject?" Invariably, if it's important enough for one person to be interested in it, then there's an excellent chance that additional readers would like to hear about that subject.

Additionally, you might come across an article in a journal that you feel should be brought to the attention of other professionals. Just let us know the name of the journal, the volume, the month, and the page and we'll try to include it in a forthcoming issue.

To contact the Editor, just click **here.**

William F. Vincent, Ph.D.
Editor



An Overview of *Helicobacter pylori* Infection: A New-Old Disease

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The Name

The name *Helicobacter pylori* is derived from the Greek "*Helico*" signifying a helical or spiral shape. The Greek "*pylori*" refers to the pylorus region of the stomach where *H. pylori* is found.

The Organism

The bacterium is a gram-negative, curved rod about 3 micrometers long with a diameter of about 0.5 micrometers. A polar tuft of flagella allows the bacteria to be highly motile. There are generally four to seven flagella composed of FlaA and FlaB proteins. The shaft is encased within a membranous sheath with a terminal bulb. In addition, there is a hook protein involved in the assembly of the flagella.

H. pylori is a microaerophilic microorganism. This means that it requires oxygen at concentrations lower than

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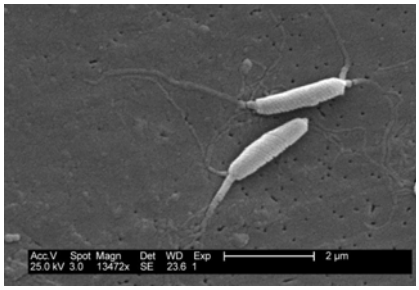
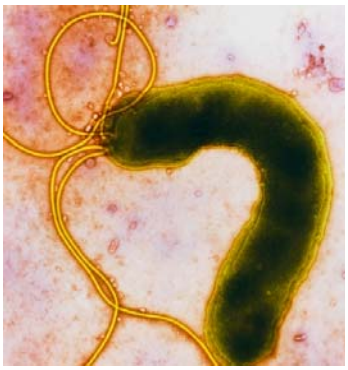
those normally found in the atmosphere.

The internal pH of *H pylori* cytoplasm is 7.0 to 7.3. It contains a hydrogenase, which is used to obtain energy by oxidizing molecular hydrogen that is produced by bacteria found in the gastrointestinal tract. Glucose, amino acids and organic acids can all be used as carbon sources for the organism.



Electron micrograph of *H. pylori* showing polar tuft of flagella
Courtesy of CDC



Colorized electron micrograph of *H. pylori*
Courtesy of the Photo Library, United Kingdom

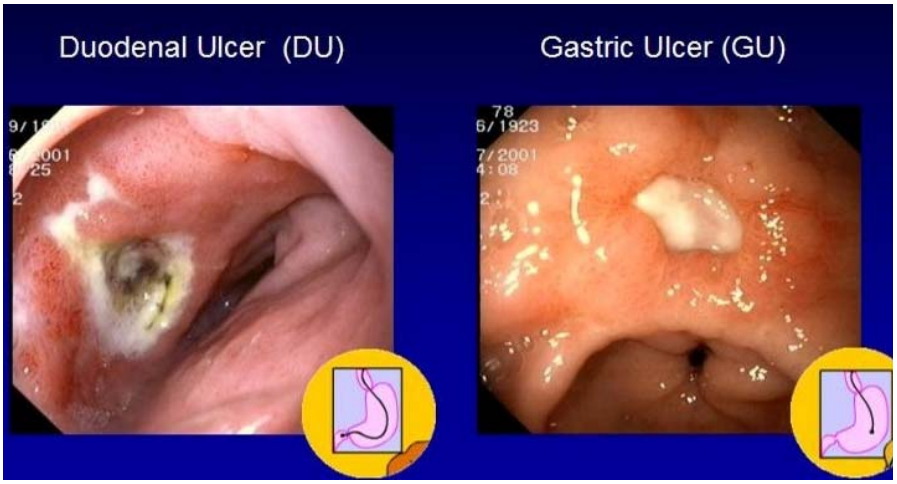
The *H. pylori* genome is very small at about 1.7 Mbp. There is a large diversity in strains; however, only three of these have been completely sequenced. The bacterial strains that have the cagA gene are most often associated with ulcer production.

The Disease

H. pylori infection has been referred to as a "*new-old*" disease. This means that even though it is a newly recognized pathogen it definitely has been around for a long time. A number of diseases previously thought to be incurable such as gastric and duodenal ulcers have been shown to be caused by *H. pylori*.

Gastric adenocarcinoma also has a strong association with a history of *H. pylori* infection. For many years it was believed that the environment of the stomach was too harsh to support any microbial life. However, humans have been colonized with *H. pylori* for at least 50,000 years. In developing countries almost everyone is colonized with *H. pylori*. This occurs early in life and persists for decades. This situation is believed to be associated with poor sanitary conditions. In more developed countries, colonization usually does not occur until later in life.

In the past, the standard treatment for gastric and duodenal ulcers was to administer drugs that helped reduce the gastric acidity and to prescribe a diet that would help reduce irritation of the stomach lining. These treatments worked for a short period of time but they did not prevent reoccurrences. *H. pylori* was first discovered in the stomach of patients diagnosed with gastritis and stomach ulcers in 1982 by Dr. Barry Marshall



Endoscopic views of duodenal and gastric ulcers
Courtesy of the University of Connecticut School of Medicine

and Dr. Robin Warren both of Perth, Australia. Their discovery that the microorganism was responsible for the ulcers meant that treatment with antibiotics would cure the condition as well as prevent reoccurrences.

Barry J. Marshall, MD
Nobel Laureate
Courtesy of the University of Western Australia

Marshall and Warren won the Nobel Prize in Physiology for Medicine in 2005 for their discovery of *H. pylori* and its role in gastritis and peptic ulcer disease.

Since the discovery of the role of *H. pylori* in ulcers, it has been determined that the bacteria causes 95% of duodenal ulcers and 70% of gastric ulcers. *H. pylori* is most commonly transmitted by the fecal-oral route although oral-oral route is also possible. The prevalence of infection is inversely related to the quality of household and public sanitation. It is common for entire families to become infected and infection increases with age. In developing countries, the rate of infection is around 80% whereas in the United States the rate is about 30%. Incidence of infection varies between racial and ethnic groups: 26% of Caucasians, 50% of African-Americans and 60% of Mexican-Americans. Just because there is colonization with *H. pylori*, it does ***not*** mean it will result in disease in all cases. Disease requiring treatment develops in only 10% to 20% of infected individuals. The main risk factors for infection are age and low income.

Ulcers caused by *H. pylori* have been associated with the development of gastric cancer. People infected with these bacteria are three to six times more likely to develop stomach cancer than uninfected individuals. Several studies have demonstrated that inflammation caused by *H. pylori* infection may contribute to the development of adenocarcinoma of the stomach. Infection has also been involved in the development of low-grade B-cell lymphoma of gastric mucosa-associated lymphoid tissue type. It has also been suggested that there is a potential role of *H. pylori* infection in other diseases such as gastroesophageal reflux disease (GERD) as well as some extra-intestinal pathologies like iron deficiency anemia, growth retardation, idiopathic thrombocytopenic purpura, asthma and allergic disorders.

Gastric ulcers are found in the stomach and duodenal ulcers are found in the first part of the small intestine called the duodenum. A general term to describe both of these disorders is "peptic ulcers". Peptic ulcers can cause a variety of symptoms that vary in severity from patient to patient.

Duodenal ulcers generally cause symptoms two to five hours after meals and can usually be improved by eating. Symptoms of gastric ulcers may occur soon after meals. Food will not improve the symptoms of gastric ulcers and usually makes them worse. The most common symptom of an ulcer is a burning pain in the abdomen between the breastbone and the navel.

Symptoms that require immediate attention:

- Vomiting blood,
- Vomiting food that was eaten hours or days before,
- Difficulty in swallowing,
- Nausea,
- Black or tar-like stool (due to occult blood),
- Severe, sudden pain in the abdominal area,
- Pain that radiates to the back,
- Pain that does not go away when you take medications,
- Unusual weakness

Even if the symptoms are mild, peptic ulcers can still develop and a physician should definitely be consulted. If left untreated, peptic ulcers can get considerably worse.

Some of the more severe symptoms may be a sign that an ulcer has broken a blood vessel, gone through, or perforated the stomach or duodenal wall, or has stopped food from moving from the stomach into the duodenum.

Diagnosis

Clinical diagnosis of *H. pylori* is mainly established by the characteristic symptoms. Stomach pain is usually the first signal of a peptic ulcer. In some cases, doctors may treat ulcers without first diagnosing them with specific tests. They will observe if the symptoms are resolved implying that their primary diagnosis was correct.

Gastric ulcers are most often found on the lesser curvature of the stomach. The ulcer is round to oval and usually 2 to 4 cm in diameter with a smooth base and perpendicular borders. In an acute case the borders are not elevated or irregular, however in chronic ulcers, they are regular and may be inflamed.

Duodenal ulcers are found in the duodenum, the first part of the small intestine located between the stomach and the middle part of the small intestine. These ulcers are characterized by a break in the mucosa of the duodenum. Most of these ulcers are less than 1 cm in diameter.

Endoscopy is performed in order to view the ulcer and to collect a tissue specimen for testing. Occasionally, gastric ulcers may be cancerous therefore a biopsy is usually performed. However, almost all duodenal ulcers are benign. There

are many other laboratory tests that may be performed to confirm a diagnosis.

Once a patient has become infected with *H. pylori,* the disease outcome will become dependent on a complex interplay between the bacteria and the host. Most microorganisms are killed in the hostile acidic environment of the gastric lumen. However, *H. pylori* is not cleared by the host immune response and it proliferates in the mucus layer over the epithelium.

The severity of the disease depends upon the characteristics of the colonizing strain, the host immune response and genetics, the level of acid production in the gut and the host diet. *H. pylori* survives because its virulence factors contribute to gastric inflammation, the altering of gastric acid production and the associated tissue destruction it causes.

Humans are the natural host for *H. pylori*. However, a number of animal models have been employed to elucidate the various virulence facto It has been recommended by the America College of Gastroenterology that patients be re-tested 4 weeks post-treatment to confirm eradication. rs associated with this organism. The animals include the mouse, Mongolian gerbil, guinea pig and Rhesus monkeys.

Virulence Factors

H. pylori is associated with a number of virulence factors that are described below:

Urease Production

Urease is responsible for the hydrolysis of urea producing carbon dioxide and ammonia; the latter raises the pH of the area immediately surrounding the organism to neutral.

Acid resistance

Though not an acidophile, the organism is able to colonize the acidic gastric environment of the stomach.

H. pylori requires mechanisms to protect itself from acute acid shocks and mechanisms to grow at pH values around 5.5.

Growth at acidic pH induces changes in the lipopolysaccharide (LPS) composition and increases the expression of chaperone-like proteins affecting the expression of several genes at the transcriptional and protein expression levels.

CagA (cytotoxin-associated gene A)

These induces morphological changes, vacuolization and successive degeneration of *in vitro*-cultured cells.

VacA (Vacuolating Cytotoxin)

This is a highly immunogenic protein that induces massive vacuolization in epithelial cells by:

- Membrane channel formation,
- Disruption of endosomal and lysosomal activity,
- effecting the integrin receptor-induced cell signaling
- interference with cytoskeleton-dependent cell functions,
- induction of apoptosis immune modulation.

Adhesins and outer membrane proteins

OipA - may serve as an adhesin but was originally identified as a pro-inflammatory response-inducing protein. There are currently little data with regards to its relevance as a disease-specific marker.

BabA- strongly associated with peptic ulcer disease and gastric adenocarcinoma

SabA - involved during the chronic inflammatory and atrophic disease stages. Appears to be associated with the binding of extracellular matrix protein.

Laminin - gives the organism the ability to penetrate the mucus layer that lines the stomach and access the underlying epithelial cell layer.

Lipopolysaccharides (LPS) - are associated with the cell walls of many microorganisms, especially gram-negative rods. They contain fucosylated oligosaccharide antigens that are structurally and immunologically closely related to human blood group antigens.

Bacterial antigens (Lewis antigens) - display a marked antigenic variation and are thought to contribute to immune evasion.

The Laboratory Diagnosis of *H. pylori*

Laboratory diagnosis of *H. pylori* may involve either invasive or non-invasive techniques. Laboratory culture in most cases is the gold standard for diagnosing bacterial infection. However, it is not generally not recommended for H. pylori because it requires special media and the recovery rate is less than acceptable.

Endoscopic techniques involve examining the gastric mucosa and assessing the level of gastric inflammation or performing a biopsy with urease testing, histology, or culture. Magnified examination of the antral mucosa has been shown to be beneficial in children.

Endoscopy is recommended for patients 55 years and older and those with red-flag signs and symptoms. *H. pylori* may be visualized on histologic examination of biopsies using a variety of staining techniques. Polymerase chain reaction (PCR) and fluorescent *in-situ* hybridization are molecular testing methods being developed for use on biopsy specimens.

Serologic tests detecting IgG antibodies to .*H pylori* are available including Western blot testing, immunochromatography, and enzyme-linked immunosorbent assay (ELISA).

However, when utilizing any serological tests for *H. pylori* disease, one must bear in mind that assay titers will be positive for ***any*** person with a history of .*H pylori* infection and, therefore, serological testing is ***not*** indicated for the evaluation of a treatment response.

Urea Breath Test (UBT)

The noninvasive Urea Breath Test (UBT) can be performed on expired breath. It can be used to assess treatment response. The testing system does not utilize an isotope that generates any ionizing radiation. This method is approved for use in persons over the age of 18 and for pregnant women. A summary of the procedure is follows:

- Urea containing isotopic-labeled carbon is given to the patients,
- When the urea is hydrolyzed by urease produced by *H. pylori*, labeled carbon dioxide is exhaled and measured in the patient's breath,
- The level of labeled carbon dioxide in the patient's breath is associated with the likelihood of infection,
- The usual cutoff point for a positive breath test is a 5 % increase in the level of labeled carbon before and after drinking the urea solution,
- This cutoff value is increased to 8 % in the case of children under 5 years of age.

It has been recommended by the America College of Gastroenterology that patients be re-tested 4 weeks post-treatment to confirm eradication.

Stool Antigen Test

An alternative to the Urea Breath Test is the Stool Antigen Test. This test employs monoclonal antibody toetect *H. pylori* antigen in stool specimens. This test has a sensitivity and specificity approaching 100% and can be used to assess treatment response.

Serology Tests

Serological tests (IgG) are only recommended as screening tests in areas of the world with high prevalence and have little value in diagnosis and evaluating therapy.

Treatment

Drug treatments of *H pylori* disease encounter many problems. The organism demonstrates *in vitro* sensitivity to many antibiotics. However, only a few antibiotics have demonstrated *in vivo* effectiveness. Factors that reduce antibiotic effectiveness include:

- Insufficient tissue penetration into the gastric mucosa due to inactivation of the antimicrobial in the acidic environment,
- Slow growth rate of the organism which makes it difficult for an antimicrobial to be effective.

No single antimicrobial agent is effective as a monotherapy and treatment success is also dependent on acid suppression in the gut.

The efficacy of eradication treatment is significantly lower in actual cases than is reported in controlled studies. This is due for the most part to inadequate patient adherence to the complex antibiotic therapy regime of one proton-pump inhibitor and two antibiotics. This treatment method usually involves clarithromycin and either amoxicillin or metronidazole (Flagyl®). In addition, a bismuth-containing medication is recommended. The duration is usually seven to 14 days. The success rates with the standard triple therapy vary from 60% to 85% dependent upon local antibiotic resistance patterns. Increasing treatment failure rates result from the rising levels of resistance to clarithromycin and metronidazole. Antibiotic resistance can approach 50% in some areas. Failure rates are higher for patients who:

- Are non-adherent with their treatment,
- Have shorter treatment durations,
- Are smokers,
- Are elderly.

Other regimens are available when these standard triple treatmentd fail. These include: triple-drug regimen of pantoprazole, amoxicillin, and levofloxacin; proven to be effective in 70% of patients in whom standard triple therapy failed. A second-line therapy with omeprazole, amoxicillin, and rifabutin is also suggested or a standard quadruple therapy (omeprazole, bismuth, metronidazole, and tetracycline) for seven days. Unfortunately, there is a high recrudescence and reinfection rate reported from areas with high levels of transmission. Also, since only symptomatic patients are treated, asymptomatic subjects remain at-risk for developing severe complications of a *H. pylori* infection and developing atrophic gastritis and gastric cancer.

Common treatment side effects of eradication treatment include: abdominal pain, nausea and diarrhea.

Vaccine Development

Vaccine development for this disease has somewhat stagnated. Evidence exists that demonstrates that protection against *H. pylori* infection can be achieved prophylactically and therapeutically in animal models.

The types of vaccines studied thus far include:

- Inactivated whole-cell *H. pylori* vaccines,
- *H. pylori* vaccines utilizing soluble recombinant urease,
- *H. pylori* vaccines based on multiple antigen administered parenterally,
- *H. pylori* vaccines based on *Salmonella*-vectored urease.

A large body of clinical data has been acquired through animal studies. However, few clinical trials have been carried out so far in humans to test the safety, immunogenicity and possible efficacy of potential vaccines against *H. pylori.*

Mucosally delivered vaccines have consistently given suboptimal results. It is thought that better vaccine formulations, better antigen preparations, better adjuvants, and better delivery/vector systems need to be developed and tested for safety and immunogenicity in humans. The drawbacks of pharmaceutical therapy could be overcome by efficacious vaccines. Prophylactic vaccination against *H. pylori* is projected to be cost effective if it had 55% efficacy. If targeted to all infants, the vaccine would significantly reduce the prevalence of *H. pylori*, thereby reducing the prevalence cases of peptic ulcer and gastric cancer. Unfortunately, most of the pharmaceutical companies that were involved in the development of a vaccine stopped their efforts; the major bottleneck of the anti-*H. pylori* vaccine is the lack of major investments in its research and development.

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Other Infectious Disease News

Quest Diagnostics launches Hepatitis C Virus Therapy Test based on IL28B Gene Variants

AccuType(R) IL28B test now available to physicians and for clinical trials research

Quest Diagnostics Incorporated recently announced the availability of its AccuType® IL28B test for aiding in the prediction of patient response to peginterferon alpha-based therapy for hepatitis C virus (HCV) infection. Quest Diagnostics is now offering the test to physicians and other healthcare providers in the U.S. and to pharma-ceutical companies for use in clinical trials research.

The test was developed through a global non-exclusive license agreement under which Schering Corporation, a Merck affiliate, licensed certain patent rights claiming Interleukin (IL) 28B genetic markers to Quest Diagnostics. These genetic markers have been shown to provide an indicator of potential response to peginterferon alpha-based therapy for HCV. Additional terms were not disclosed.

"Our AccuType IL28B test will give physicians greater insights for treating individual patients infected with the most common form of HCV using standard antiviral therapies," said Rick L. Pesano, M.D., Ph.D., medical director, infectious diseases, Quest Diagnostics. "AccuType IL28B testing will also help physicians consider alternative therapies, which in the future may include HCV protease inhibitors."

Combination interferon-ribavirin therapy administered over several months is considered standard of care in treating HCV, although experimental HCV protease inhibitors are

now under priority review by the U.S. Food and Drug Administration.[1,2] Side effects, such as fatigue, depression and nausea, affect the majority of patients, and an estimated 10% to 14% of people discontinue therapy.[3,4] Moreover, as many as one in two patients fail to eradicate the virus, as indicated by blood tests, after a full course of therapy.[5]

A certain polymorphism of the IL28B gene found in individuals infected with the most common type of HCV, HCV genotype 1, aids in identifying those patients who are twice as likely to eliminate the HCV virus on a sustained basis when treated with pegylated interferon-ribavirin combination therapies.[6] Other factors, including age and gender, may affect treatment response.

HCV infection is the most common chronic blood borne infection in the United States, chronically infecting approximately 3.2 million people.

Left untreated, chronic HCV can lead to liver cancer or cirrhosis requiring liver transplantation. Chronic HCV infection accounts for an estimated 8,000 to 10,000 deaths each year in the United States.[7]

About Quest Diagnostics

Quest Diagnostics is the world's leading provider of diagnostic testing, information and services that patients and doctors need to make better healthcare decisions. The company offers the broadest access to diagnostic testing services through its network of laboratories and patient service centers, and provides interpretive consultation through its extensive medical and scientific staff. Quest Diagnostics is a pioneer in developing innovative diagnostic tests and advanced healthcare information technology solutions that help improve patient care.

Quest Diagnostics' broad hepatitis C and B virus testing menu includes hepatic function tests to help determine HCV exposure and identify abnormal liver function; Heptimax® viral RNA quantitative testing to monitor viral load during therapy; and HCV genotyping to aid in predicting treatment duration and success. Quest Diagnostics also offers tests, such as HepaScore™, to help physicians identify and stage liver fibrosis.

References

[1] Merck press release, 6 January 2011; Vertex Pharmaceuticals press release.

[2] HCSP Fact Sheet, Hepatitis C Support Project (HCSP);2008; ver 3. [click **here** to go to website].

[3] Manns, M.P. *et al*. 2001. Peginterferon alfa-2b plus ribavirin compared to interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomized trial. *Lancet* **358**: 958-965. [Click **here** to go to abstract]

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[7] Centers for Disease Control and Prevention. 2010. Hepatitis C FAQs for Health Professionals. [click **here** to go to website].

Quest Diagnostics launches Simplexa® *Clostridium difficile* Universal Direct Test in Europe

First test from the Focus Diagnostics Simplexa® product line for the hospital-acquired infection (HAI) market

Quest Diagnostics, announced recently the availability in Europe of the Simplexa® *C. difficile* Universal Direct test on the 3M(TM) Integrated Cycler. The new CE marked *in vitro* diagnostic (IVD) Simplexa® test enables fast, high volume lab testing, eliminating the traditional extraction step and allowing for processing of up to 94 patient specimens in about an hour.

Focus Diagnostics, a business unit of Quest Diagnostics and the developer of the Simplexa® product line, will unveil the new test as well as the Simplexa® Epstein Barr (EBV) and BK Virus tests, which were "CE" marked in May 2011, during the European Congress of Clinical Microbiology and Infectious Disease Tradeshow in Milan (Exhibit number 241). A CE mark is a regulatory requirement to sell products in about 35 countries in Europe.

Simplexa® tests, running on the 3M(TM) Integrated Cycler, employ real-time polymerase chain reaction (RT-PCR) to qualitatively and quantitatively detect viruses, bacteria and other agents. The Simplexa® *C. difficile* Universal Direct test is performed on liquid or unformed human stool samples and detects toxin producing strains of *Clostridium difficile*, including NAP1/B1/027.

"*Clostridium difficile* is a common cause of antibiotic-associated diarrhea and an extremely important and serious hospital-acquired infection," said Jay M. Lieberman, M.D., Medical Director for Quest Diagnostics and Focus Diagnostics. "*C. difficile* infections (CDI) range in severity from mild diarrhea to life-threatening pseudomembranous colitis, and result in significant suffering and deaths. Timely diagnosis is essential for clinicians when treating patients presenting with possible *C. difficile* disease."

"Our Simplexa® *C. difficile* Universal Direct test will help physicians make a fast, reliable diagnosis of CDI," says Dr. John Hurrell, General Manager at Focus Diagnostics. "This is vital to treating patients and reducing the threat of transmission to other patients."

CDI is a bacterial infection that most commonly affects patients on prolonged use of broad spectrum antibiotics, over 65 in age, and those who have recently undergone gastro-intestinal surgery or are immuno-compromised. In major European Union (EU) countries, such as Belgium, Denmark, France, Germany, Italy, Netherlands, Spain and the United Kingdom, CDI is estimated to be responsible for 1.1 in 1,000 hospital admissions and is expected to double over the next four decades.[1] The European Center for Disease Prevention and Control estimates the financial impact of each CDI case in England can cost euro 5,000 to 15,000. With a European population of 457 million, the potential cost to the Union may exceed euro 300 million annually.[2]

Focus Diagnostics launched the Simplexa® molecular product line in 2009 with a focus on influenza and respiratory syncytial virus. Since that time, the Simplex®a product line has expanded to include tests for detecting Flu A/B and Respiratory Syncytial virus, EBV, BK virus and *Bordetella pertussis*. Simplexa® tests run on the 3M Integrated Cycler, a compact, portable testing platform that can provide results in as few as 60 minutes following sample extraction, as part of an exclusive worldwide agreement with 3M.

In April 2011, the Simplexa®/3M technology won a 2011 Edison Award for new science and medical diagnostic products, based on criteria that included technological innovation and marketplace success.

To order the Simplex® EBV or BKV tests, please contact Focus Diagnostics at 800-445-0185 (U.S.) or +49-6026-9499540 (Europe). You may also visit us at FocusDiagnostics.com or Simplexadx.com.

About Focus Diagnostics

Focus Diagnostics, Inc. is an infectious disease diagnostics company, providing infectious disease reference laboratory services to hospitals and laboratories nationwide, and manufacturing and distributing diagnostic products worldwide. Focus Diagnostics develops innovative tests and products to assist physicians in diagnosing infectious diseases, and often provides the first diagnostic tests in the U.S. for emerging diseases, such as West Nile virus and SARS. HerpeSelect® type-specific HSV serology and West Nile Virus DxSelect(TM) are top-selling Focus Diagnostics products used in laboratories worldwide. Focus Diagnostics is a wholly owned subsidiary of Quest Diagnostics. Visit Focus Diagnostics by clicking **here**.

[1] Kuijper E.J. *et al*. 2006. Emergence of *Clostridium difficile*-associated disease in North America and Europe. *Clinical Microbiology and Infection* **12**(s6): 2-18. Click **here** to go to abstract.

[2] European Center for Disease Prevention and Control website on *Clostridium difficile* infection, accessed on May 2, 2011. Click **here** to go to website

Giving The Shingles and Pneumococcal vaccines at The Same Time

The initial labeling on these vaccines warned against giving them at the same time. New studies, however, refute this recommendation. This, of course, is a "study" - not a recommendation or change *per se*. Any change will have to wait until the manufacturer or a governmental agency makes it.

Oxman, M.N. *et al.* 2011. Zoster vaccine recommendations: the importance of using a clinically valid correlate of protection. *Vaccine* **29**: 3625-3627.

NEW FEATURE!

Need Assistance with Infectious Disease Issues?

We are the world's leading provider of diagnostics testing services with a medical and scientific staff of approximately 900 MDs and PhDs possessing considerable experience in infectious disease, infection control and clinical microbiology.

Through a new service, we offer you access to our experience and expertise.

If you have a question in any of these areas, please feel free to contact us by email.

In your email, state your question as clearly as possible. Also, please furnish us with your name, position, affiliation, phone number and email address. ***All*** requests will be kept confidential!

Contact us by clicking **here**!

Thank you for letting us be of assistance to you!

Can Bedbugs transmit Diseases?

Most readers probably know that there has been a dramatic resurgence in infestations by these creatures in many parts of the country (particularly here in the Northeast). New York City and Boston have been particularly hard hit.

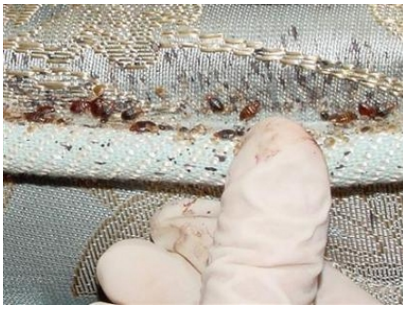
A dorsal view of the bedbug,
Cimex lectularis
Courtesy of CDC

In the literature there are a number of articles stating that bedbugs have never been associated with the transmission of diseases unlike the situation wtih many other insects (ticks, cockroaches, mosquitoes, *etc*,)

A very short report (actually a letter to the editor) recently appeared in *Emerging Infectious Diseases* which was entitled "Bedbugs as Vectors for Drug-resistant Bacteria". This was a report on three persons from Vancouver, Canada's Eastside (an impoverished community) who went into the hospital and were found to be infested with bedbugs. Five bedbugs were collected, ground up and tested for the presence of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE).

From two of the five patients, VRE was isolated from one bedbug each. From the third patient, MRSA was isolated from three bedbugs. Based on this study, it was suggested that maybe bedbugs could transmit MRSA and VRE among these patients especially considering the scratching and itching associated with bedbug bites.

This report immediately went "viral" on the Net (wish they could come up with another word for this phenoenon) on both medical and lay internet sites. What bothers this writer is that the study only involved three patients and five bedbugs.



Bedbugs, bedbug eggs and feces along the edge of a mattress. This is the best place to look for them in a hotel room
Courtesy of CDC

Lowe, C.F. and Romney. 2011. Bedbugs as vectors for drug-resistant bacteria (letter). *Emerging Infectious Diseases* . June 2011. E-published ahead of print. Click **here** for entire article.

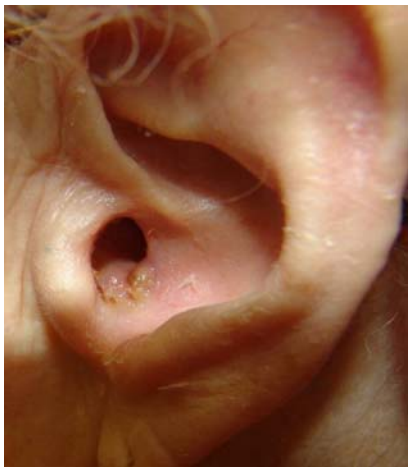
Incidence of Surgical Site Infection in Obese Patients undergoing Colorectal Surgery

Investigators at Johns Hopkins School of Medicine have concluded that obesity leads to a 60 % increase in surgical site infections (SSIs) in patients undergoing colorectal surgery. In terms of cost, the mean rate increased from $ 14,608 to $ 31,933 with obese patients.

Wick, E.C. *et al*. 2011. Surgical site infections and costs in obese patients undergoing colorectal surgery. *Archives of Surgery* Published online May 16, 2011. Click **here** to go to complete article.

Little Problem - Big Bucks: Swimmer's Ear

Probably most of us have had "swimmer's ear" (otitis externa) especially when we were kids. I swam in the local brooks since we didn't have the benefit of nice, chlorinated pools 60 years ago. We were always told to keep water out of our ears. When I go down to the pool at the YMCA, I see all these children with ear plugs. This is a good idea since most cases of otitis externa are associated with swimming and are preventable through the simple use of effective ear plugs.



Symptoms of swimmer's ear
Courtesy of CDC

Most cases of otitis externa are generally mild and easily treated with common antimicrobials. Researchers recently reported in Morbidity and Mortality Weekly Report that in 2007, there were about 2.4 million cases of otitis externa in the U.S. The rates were the highest among children in the age range of five to nine (18.6 cases per 1,000). By the time children had reached the age of 15 to 19, the infection rate drops to 8.8 per 1,000.

It has been estimated that otitis externa is responsible for about 597,000 ambulatory care visits annually and $ 489 million in direct healthcare payments.

The article also included some suggestions for preventing otitis externa as follows:

- Keep water out of ears as much as possible when swimming,
- Dry ears thoroughly after swimming and showering,

- Do ***not*** put objects, such as cotton-tip swabs and fingers, in ears,
- Do ***not*** remove ear wax - let a healthcare professional do it,
- Consult a healthcare professional about using ear drops after swimming,
- Consult a healthcare professional if ears become itchy, flaky, swollen, painful or have drainage,
- Ask the pool or hot tub operator if pH levels are checked at least twice daily.

Piercefield, E.W. *et al*. 2011. Estimated burden of acute otitis externa - United States, 2003-2007. *Morbidity and Mortality Weekly Report* **60**: 605-609. Click **here** to go to entire article at the CDC website.

What's Your Gut Bug Type?

People can be divided into groups all different ways - color of hair, racial background, ethnic background, blood types and the list goes on and on.

Researchers in Heidelberg, Germany recently found that humans can be divided into three distinct groups, called "enterotypes" based on the microorganisms that normally live in their gut.

They found that these enterotypes have no connection with sex, weight, health, age or ethnic background. They can't really explain this but it may be that the gut become initially colonized by a "pioneering organism" which paves the way for other organisms.

The long-term effects of a person's enterotype are unknown.

Arumugam, M. *et al*. 2011. Enterotypes of the human gut microbiome. *Nature* **473**: 174-180. Click **here** to go to abstract.

Cases of Dengue Fever in U.S. Triple during Last Decade

Investigators at the University of Iowa Carver College of Medicine sifted through data on cases of dengue fever occurring in the U.S. in the last decade and found that the incidence has tripled in the U.S. Most of the cases have come in from other areas of the world but a significant number of cases occurred among persons who have not traveled. Most of these cases have been in Florida and surrounding states.

Dengue fever can be caused by any one of four closely related viruses and is transmitted in North America by the *Aedes aegypti* mosquito .

Streit, J. *et al*. 2011. Upward trend in Dengue incidence among hospitalized patients, United States. *Emerging Infectious Diseases* **5**: 914-916. Click **here** to go to complete article.

Four Pills or One for Tuberculosis?

Researchers for the World Health Organization recently tested the use of a single tablet containing four drugs for tuberculosis. Studies were carried out in Africa, South America and Asia and the four drugs used in this study were rifampicin, isoniazid, pyrazinamide and ethambutol.

They found that the results were comparable whether the patient received the 4-drug pill or if the medications were given separately.

The combination therapy dropped the number of pills the patient had to take from 9 to 16 to 3 to 4. This is a real plus when it comes to compliance and should lead to reduced development of resistance.

Lienhardt, C. *et al.* 2011. Efficacy and safety of a 4-drug fixed-dose regimen compared with separate drugs for treatment of pulmonary tuberculosis. The Study C randomized controlled trial. *Journal of The American Medical Association* **305**: 1415-1423. Click **here** to go to abstract.

Intensive Care Units in Many Michigan Hospitals go Two or More Years without A Bloodstream Infection

Central line-associated bloodstream infections (CLABSIs) in the intensive care unit represent very dangerous events with associated high morbidity and mortality. It has been estimated that at any given time, roughly one in 20 patients in ICUs in the U.S. will have one. Additionally, treatment of such infections is very expensive and increases the cost of taking care of these patients.

As part of a Federal program named the Keystone Project, hospitals in Michigan instituted an initiative known as the Comprehensive Unit-Based Safety Program or CUSP, in an attempt to reduce or hopefully eliminate CLABSIs for an extended period of time (up to two years or more).

The investigators found that 60 % of the 80 Michigan ICUs evaluated went one year or more without a bloodstream infection. 25 % were able to achieve two years or more. Smaller hospitals were able to achieve better results than larger ones.

The next thing that crossed the writer's mind was what is the CUSP program? It must be something really tough and complex in order to reduce CBABSIs like this.

We found that the program actually only consisted of five steps as follows:

Step 1. The staff are educated on the science of safety,

Step 2. The staff complete an assessment of patient safety culture,

Step 3. A senior hospital executive partners with the unit to improve communications and educate leadership,

News Credits

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Step 4. The staff learn from unit defects,

Step 5. The staff use the tools, including checklists, to improve teamwork, communication, and other systems of work.

In the Michigan CUSP study, it was estimated that more than 1,500 lives and $ 200 million were saved in the first 18 months.

Agency for Healthcare Research and Quality. ICUs in Michigan sustain zero blood stream infections for up to 2 years. Press release date May 9, 2011. Click **here** to go to press release.

Agency for Healthcare Research and Quality. Using a comprehensive unit-based safety program to prevent healthcare-associated infections. Click **here** to go to website.

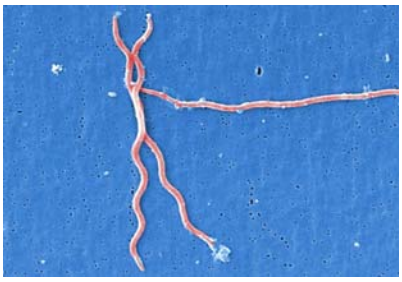
Lipitz-Snyderman, A. *et al*. 2011. The ability of intensive care units to maintain zero central line-associated bloodstream infections. *Archives of Internal Medicine* **171**: 856-858. No abstract available.

New Test Offerings from Quest Diagnostics

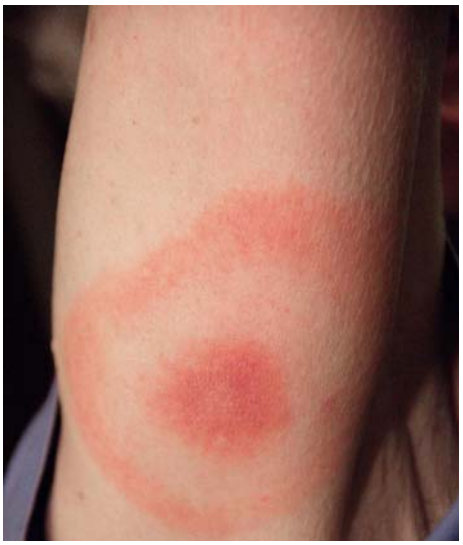
Lyme Disease (*Borrelia* spp.) DNA, Qualitative Real-Time PCR

Clinical Significance

The diagnosis of Lyme disease (borreliosis) is most often made by clinical examination combined with evidence of a tick bite or exposure in endemic areas. Amplification of *Borrelia* genomic DNA from blood, fluids or tissues can be used to support the diagnosis



Digitally-colorized electron micrographs of *Borrelia burgdorferi*
Courtesy of CDC



The erythema migrans or "bull's eye rash associated with Lyme borreliosis

Specimens for Testing

1 mL of whole blood (EDTA or ACD), synovial fluid or CSF can be submitted. 4 mL of a random urine specimen is required. Specimens should be kept refrigerated and are stable for up to 7 days. Frozen specimens are stable up to 30 days.

Turnaround Time

Testing is performed Monday through Sunday and reports are available in 1 to 3 days.

Performing Laboratory

Focus Diagnostics

Please note: these tests are not available for New York patient testing.

Examination of Ticks for Lyme Disease (*Borrelia* spp.) DNA by Real-Time PCR

Specimens for testing

One tick should be submitted to the laboratory in 70 % ethanol or in a wet tissue in a sterile screw cap container. Specimens should be transported at room temperature.

Turnaround Time

Testing is performed Monday through Sunday and reports are available in 1 to 3 days.

Performing Laboratory

Focus Diagnostics

Aspergillus DNA, Qualitative Real-Time PCR

Clinical Significance

Detection of *Aspergillus* species DNA in clinical specimens can be useful in the diagnosis of invasive aspergillosis. Identification of the particular *Aspergillus* species can be useful in determining treatment. This assay tests for *Aspergillus* spp., *Aspergillus fumigatus* and *Aspergillus terreus*.

Specimens for Testing

3 mL of bronchoalveolar lavage, sputum or whole blood (EDTA or ACD) should be submitted to the laboratory refrigerated.

3 mm sections of tissue should be submitted frozen.

Turnaround Time

Testing is performed Monday through Sunday and reports are available in 1 to 3 days.

Performing Laboratory

Focus Diagnostics

Please Note: This test is not available for New York patient testing. There is ***no*** recommended alternative for New York patient testing at this time.

Clients desiring additional information on these or any other tests offered by Quest Diagnostics should contact their local Quest Diagnostics service representative.

From The Editor's Desk

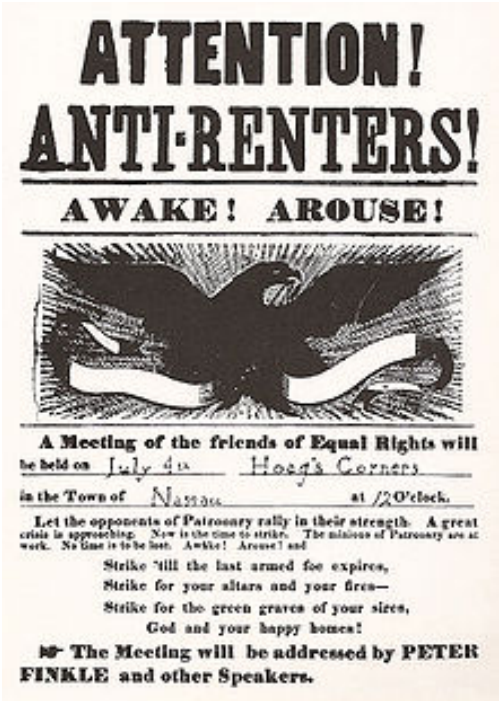
WHEN AMERICAN "SERFS" ROSE UP AGAINST THEIR FEUDAL LORDS!

Most Americans, seeing this title for the first time, would be startled since we just never associate serfdom and feudal landlords with our country especially into the 19th century. But it really did happen!

Starting in the 1600s and going right into the beginning of the 19th century, almost all of the land in upper New York State was owned by a select few persons known by the Dutch name of "Patroons". The Patroons owned all the land on which the tenants in the Hudson Valley lived and used feudal leases to maintain control (very tight control we might add).

Then in the early 1840s, all hell broke loose when the Van Rensselaer Patroon decided that his family needed more money from the leases and jacked all the rents up. The region literally exploded with rallies and violence against the landlords.

One of the biggest rallies occurred in the little village of Hoag's Corners, New York, about 20 miles outside Albany on July 4, 1844. The event was named "Big Thunder". To the right is the flier announcing it.



ATTENTION!

ANTI-RENTERS!

AWAKE! AROUSE!

A Meeting of the friends of Equal Rights will be held on July 4th Hoag's Corners in the Town of Nassau at 2 O'clock.

Let the opponents of Patroonry rally in their strength. A great crisis is approaching. Now is the time to strike. The minions of Patroonry are at work. No time is to be lost. Awake! Arouse! and

Strike 'till the last armed foe expires,
Strike for your altars and your fires—
Strike for the green graves of your sires,
God and your happy homes!

☞ The Meeting will be addressed by PETER FINKLE and other Speakers.

Hundreds of farmers for many miles around arrived dressed as Indians and had a big rally with speakers and a great deal of enthusiasm. They wore calico dresses with a belt around them and leather face masks adorned with feathers so they wouldn't be recognized.

One of the participants in Big Thunder was Orrin Vincent, this writer's great grandfather.

After many years of feuding and generally raising hell, the Patroons finally gave in and sold the farms to the farmers. It did not happen, however, until the New York State legislature ordered it.

Believe it or not, Big Thunder was held on Orrin's property since there was a natural amphitheater behind it! My grandfather (Frank Vincent) would take me for walks behind the farm house (where both he and my father were born). He used to tell me that my great grandfather, Orrin, rode dressed as an Indian in the fields back there. Incidentally, when I asked him why, he didn't know why. One of my older cousins as a small child had actually seen the calico dress and mask that Orrin wore.

A calico Indian complete with a leather mask. This outfit was made and worn at a reenactment of one of the Anti-rent war rallies

Historic marker in front of the Vincent homestead in Hoag's Corners, NY.

The Vincent homestead in Hoag's Corners, NY. The writer's father was born in the room upstairs to the left with the lower curtain in it. About 20 years ago, the present owners thoroughly searched the lot behind it using a metal detector and found about 20 coins all dating before 1844! The owner has them in a shadow box in the front room. Every time I've seen them, I ask myself "did my great grandfather, Orrin, drop one of these coins on July 4, 1844?"