PAPER- CC13

BACTERIAL DISEASES

1. RESPIRATORY DISEASE:

Tuberculosis

Tuberculosis -- or TB, as it's commonly called -- is a contagious infection that usually attacks your lungs. It can spread to other parts of your body, like your brain and spine. A type of bacteria called *Mycobacterium tuberculosis* causes it.

In the early 20th century, TB was a leading cause of death in the United States. Today, most cases are cured with antibiotics. But it takes a long time. You have to take meds for at least 6 to 9 months.

CAUSATIVE AGENT

The main cause of TB is *Mycobacterium tuberculosis* (MTB), a small, aerobic, nonmotile bacillus. The high lipid content of this pathogen accounts for many of its unique clinical characteristics. It divides every 16 to 20 hours, which is an extremely slow rate compared with other bacteria, which usually divide in less than an hour.[24] Mycobacteria have an outer membrane lipid bilayer. If a Gram stain is performed, MTB either stains very weakly "Gram-positive" or does not retain dye as a result of the high lipid and mycolic acid content of its cell wall. MTB can withstand weak disinfectants and survive in a dry state for weeks. In nature, the bacterium can grow only within the cells of a host organism, but *M. tuberculosis* can be cultured in the laboratory.

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The *M. tuberculosis* complex (MTBC) includes four other TB-causing mycobacteria: *M. bovis*, *M. africanum*, *M. canetti*, and *M. microti*. *M. africanum* is not widespread, but it is a significant cause of tuberculosis in parts of Africa. *M. bovis* was once a common cause of tuberculosis, but the introduction of pasteurized milk has almost completely eliminated this as a public health problem in developed countries. *M. canetti* is rare and seems to be limited to the Horn of Africa, although a few cases have been seen in African emigrants. *M. microti* is also rare and is seen almost only in immunodeficient people, although its prevalence may be significantly underestimated

Tuberculosis Types

A TB infection doesn't mean you'll get sick. There are two forms of the disease:

Latent TB. You have the germs in your body, but your immune system stops them from spreading. That means you don't have any symptoms and you're not contagious. But the infection is still alive in your body and can one day become active. If you're at high risk for re-activation -- for instance, you have HIV, your primary infection was in the past 2 years, your chest X-ray is abnormal, or your immune system is compromised --- your doctor will treat you with antibiotics to lower the risk for developing active TB.

Active TB. This means the germs multiply and can make you sick. You can spread the disease to others. Ninety percent of adult cases of active TB are from the reactivation of a latent TB infection.

SYMPTOMS:

. Most infections do not have symptoms, in which case it is known as latent tuberculosis. About 10% of latent infections progress to active disease which, if left untreated, kills about half of those affected.

Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis). Extrapulmonary TB occurs when tuberculosis develops outside of the lungs, although extrapulmonary TB may coexist with pulmonary TB.

General signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue.[9] Significant nail clubbing may also occur.[17]

- A cough that lasts more than 3 weeks
- Chest pain
- Coughing up blood
- Feeling tired all the time
- Night sweats
- Chills
- Fever
- Loss of appetite
- Weight loss
- The classic symptoms of active TB are a chronic cough with blood-containing mucus, fever, night sweats, and weight loss. It was historically called "consumption" due to the weight loss. Infection of other organs can cause a wide range of symptoms.

MODE OF TRANSMISSION:

When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious aerosol droplets 0.5 to 5.0 µm in diameter. A single sneeze can release up to

40,000 droplets. Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very small (the inhalation of fewer than 10 bacteria may cause an infection).

People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate. A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year. Transmission should occur from only people with active TB – those with latent infection are not thought to be contagious. The probability of transmission from one person to another depends upon several factors, including the number of infectious droplets expelled by the carrier, the effectiveness of ventilation, the duration of exposure, the virulence of the *M. tuberculosis* strain, the level of immunity in the uninfected person, and others. The cascade of person-to-person spread can be circumvented by segregating those with active ("overt") TB and putting them on anti-TB drug regimens. After about two weeks of effective treatment, subjects with nonresistant active infections generally do not remain contagious to others. If someone does become infected, it typically takes three to four weeks before the newly infected person becomes infectious enough to transmit the disease to others.

Tuberculosis is caused by bacteria that spread through the air, just like a cold or the flu. When someone who has it coughs, sneezes, talks, laughs, or sings, tiny droplets that contain the germs are released. If you breathe in these germs, you can get it.

TB can spread from person to person, but it isn't easy to catch. You usually have to spend a lot of time around someone who has a lot of bacilli in their lungs. You're most likely to catch it from co-workers, friends, and family members.

Tuberculosis germs don't thrive on surfaces. You can't get the disease from shaking hands with someone who has it or by sharing their food or drink.

Pathogenesis

About 90% of those infected with *M. tuberculosis* have asymptomatic, latent TB infections (sometimes called LTBI), with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculous disease. In those with HIV, the risk of developing active TB increases to nearly 10% a year. If effective treatment is not given, the death rate for active TB cases is up to 66%.

TB infection begins when the mycobacteria reach the alveolar air sacs of the lungs, where they invade and replicate within endosomes of alveolar macrophages. Macrophages identify the bacterium as foreign and attempt to eliminate it by phagocytosis. During this process, the bacterium is enveloped by the macrophage and stored temporarily in a membrane-bound vesicle called a phagosome. The phagosome then combines with a lysosome to create a phagolysosome. In the phagolysosome, the cell attempts to use reactive oxygen species and acid to kill the bacterium. However, *M. tuberculosis* has a thick, waxy mycolic acid capsule that

protects it from these toxic substances. *M. tuberculosis* is able to reproduce inside the macrophage and will eventually kill the immune cell.

The primary site of infection in the lungs, known as the "Ghon focus", is generally located in either the upper part of the lower lobe, or the lower part of the upper lobe. Tuberculosis of the lungs may also occur via infection from the blood stream. This is known as a Simon focus and is typically found in the top of the lung. This hematogenous transmission can also spread infection to more distant sites, such as peripheral lymph nodes, the kidneys, the brain, and the bones. All parts of the body can be affected by the disease, though for unknown reasons it rarely affects the heart, skeletal muscles, pancreas, or thyroid.

Tuberculosis is classified as one of the granulomatous inflammatory diseases. Macrophages, epithelioid cells, T lymphocytes, B lymphocytes, and fibroblasts aggregate to form granulomas, with lymphocytes surrounding the infected macrophages. When other macrophages attack the infected macrophage, they fuse together to form a giant multinucleated cell in the alveolar lumen. The granuloma may prevent dissemination of the mycobacteria and provide a local environment for interaction of cells of the immune system. However, more recent evidence suggests that the bacteria use the granulomas to avoid destruction by the host's immune system. Macrophages and dendritic cells in the granulomas are unable to present antigen to lymphocytes; thus the immune response is suppressed. Bacteria inside the granuloma can become dormant, resulting in latent infection. Another feature of the granulomas is the development of abnormal cell death (necrosis) in the center of tubercles. To the naked eye, this has the texture of soft, white cheese and is termed caseous necrosis.

If TB bacteria gain entry to the blood stream from an area of damaged tissue, they can spread throughout the body and set up many foci of infection, all appearing as tiny, white tubercles in the tissues. This severe form of TB disease, most common in young children and those with HIV, is called miliary tuberculosis. People with this disseminated TB have a high fatality rate even with treatment (about 30%).

In many people, the infection waxes and wanes. Tissue destruction and necrosis are often balanced by healing and fibrosis. Affected tissue is replaced by scarring and cavities filled with caseous necrotic material. During active disease, some of these cavities are joined to the air passages (bronchi) and this material can be coughed up. It contains living bacteria, and thus can spread the infection. Treatment with appropriate antibiotics kills bacteria and allows healing to take place. Upon cure, affected areas are eventually replaced by scar tissue.

Tuberculosis Diagnosis

There are two common tests for tuberculosis, but they don’t tell you whether you have latent or active TB:

- **Skin test.** This is also known as the Mantoux tuberculin skin test. A health care worker injects a small amount of fluid into the skin of your lower arm. After 2 or 3 days, they’ll check for swelling in your arm to determine your results. If your

results are positive, you probably have been infected with TB bacteria. But the results can be false positive. If you've gotten a tuberculosis vaccine called bacillus Calmette-Guerin (BCG), the test could say you have TB when you really don't. The results can also be false negative, saying that you don't have TB when you really do, if your infection is recent. You might get this test more than once.

- **Blood test.** These tests, also called interferon-gamma release assays or IGRAs, measure the response when TB proteins are mixed with a small amount of your blood.

If you have a positive skin or blood test, your doctor will probably give you a chest X-ray or CT scan to look for changes in your lungs. They also might test for TB bacteria in your sputum, the mucus that comes up when you cough. These results will help diagnose latent or active TB.

Prevention

Prevention of TB involves screening those at high risk, early detection and treatment of cases, and vaccination with the bacillus Calmette-Guérin (BCG) vaccine. Those at high risk include household, workplace, and social contacts of people with active TB. Treatment requires the use of multiple antibiotics over a long period of time.[1] Antibiotic resistance is a growing problem with increasing rates of multiple drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).

Tuberculosis Prevention

To help stop the spread of TB:

- If you have latent TB, take all of your medication so you don't develop active TB, which is contagious.
- If you have active TB, limit your contact with other people at work, school, or home. Cover your mouth when you laugh, sneeze, or cough. Wear a surgical mask when you're around other people during the first weeks of treatment.
- If you're traveling to a place where TB is common, avoid getting close to or spending a lot of time in crowded places with people who have TB.

Children in countries where TB is common often get the BCG vaccine. It isn't recommended in the United States. Other vaccines are being developed and tested.

A number of factors make people more susceptible to TB infections. The most important risk factor globally is HIV; 13% of all people with TB are infected by the virus. Tuberculosis is closely linked to both overcrowding and malnutrition, making it one of the principal diseases of poverty. Those at high risk thus include: people who inject illicit drugs, inhabitants and employees of locales where vulnerable people gather (e.g. prisons and homeless shelters), medically underprivileged and resource-poor communities, high-risk ethnic minorities, children in close contact with high-risk category patients, and health-care providers serving these patients.

Chronic lung disease is another significant risk factor. Silicosis increases the risk about 30-fold. Those who smoke cigarettes have nearly twice the risk of TB compared to nonsmokers.

Other disease states can also increase the risk of developing tuberculosis. These include alcoholism and diabetes mellitus (three-fold increase).

Certain medications, such as corticosteroids and infliximab (an anti-αTNF monoclonal antibody), are other important risk factors, especially in the developed world.

PROPHYLAXIS

Tuberculosis prevention and control efforts rely primarily on the vaccination of infants and the detection and appropriate treatment of active cases. The World Health Organization (WHO) has achieved some success with improved treatment regimens, and a small decrease in case numbers.

Vaccines

The only available vaccine as of 2011 is Bacillus Calmette-Guérin (BCG). In children it decreases the risk of getting the infection by 20% and the risk of infection turning into active disease by nearly 60%.

It is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated. The immunity it induces decreases after about ten years. As tuberculosis is uncommon in most of Canada, the United Kingdom, and the United States, BCG is administered to only those people at high risk. Part of the reasoning against the use of the vaccine is that it makes the tuberculin skin test falsely positive, reducing the test's usefulness as a screening tool. A number of vaccines are in development as of 2011.

Treatment of TB uses antibiotics to kill the bacteria. Effective TB treatment is difficult, due to the unusual structure and chemical composition of the mycobacterial cell wall, which hinders the entry of drugs and makes many antibiotics ineffective.

Active TB is best treated with combinations of several antibiotics to reduce the risk of the bacteria developing antibiotic resistance. The routine use of rifabutin instead of rifampicin in HIV-positive people with tuberculosis is of unclear benefit as of 2007.

Latent TB is treated with either isoniazid or rifampin alone, or a combination of isoniazid with either rifampicin or rifapentine. The treatment takes three to nine months depending on the medications used. People with latent infections are treated to prevent them from progressing to active TB disease later in life.

New onset

The recommended treatment of new-onset pulmonary tuberculosis, as of 2010, is six months of a combination of antibiotics containing rifampicin, isoniazid, pyrazinamide, and ethambutol for the first two months, and only rifampicin and isoniazid for the last four months. Where resistance to isoniazid is high, ethambutol may be added for the last four months as an alternative.

Recurrent disease

If tuberculosis recurs, testing to determine which antibiotics it is sensitive to is important before determining treatment. If multiple drug-resistant TB (MDR-TB) is detected, treatment with at least four effective antibiotics for 18 to 24 months is recommended.

Medication administration

Directly observed therapy, i.e., having a health care provider watch the person take their medications, is recommended by the World Health Organization (WHO) in an effort to reduce the number of people not appropriately taking antibiotics. The evidence to support this practice over people simply taking their medications independently is of poor quality. There is no strong evidence indicating that directly observed therapy improves the number of people who were cured or the number of people who complete their medicine. Moderate quality evidence suggests that there is also no difference if people are observed at home versus at a clinic, or by a family member versus a health care worker. Methods to remind people of the importance of treatment and appointments may result in a small but important improvement.

Medication resistance

Primary resistance occurs when a person becomes infected with a resistant strain of TB. A person with fully susceptible MTB may develop secondary (acquired) resistance during therapy because of inadequate treatment, not taking the prescribed regimen appropriately (lack of compliance), or using low-quality medication. Drug-resistant TB is a serious public health issue in many developing countries, as its treatment is longer and requires more expensive drugs. MDR-TB is defined as resistance to the two most effective first-line TB drugs: rifampicin and isoniazid. Extensively drug-resistant TB is also resistant to three or more of the six classes of second-line drugs. XDR-TB is a term sometimes used to define *extensively resistant* TB, and constitutes one in ten cases of MDR-TB. Cases of XDR TB have been identified in more than 90% of countries.

Progression from TB infection to overt TB disease occurs when the bacilli overcome the immune system defenses and begin to multiply. In primary TB disease (some 1–5% of cases), this occurs soon after the initial infection. However, in the majority of cases, a latent infection occurs with no obvious symptoms. These dormant bacilli produce active tuberculosis in 5–10% of these latent cases, often many years after infection.

The risk of reactivation increases with immunosuppression, such as that caused by infection with HIV. In people coinfected with *M. tuberculosis* and HIV, the risk of reactivation increases to 10% per year Studies using DNA fingerprinting of *M. tuberculosis* strains have shown reinfection contributes more substantially to recurrent TB than previously thought, with estimates that it might account for more than 50% of reactivated cases in areas where TB is common. The chance of death from a case of tuberculosis is about 4% as of 2008, down from 8% in 1995.

2. GASTROINTESTINAL DISEASES

Cholera

Cholera is an infection of the small intestine by some strains of the bacterium *Vibrio cholerae*. Cholera affects an estimated 3–5 million people worldwide and causes 28,800–130,000 deaths a year. Although it is classified as a pandemic as of 2010, it is rare in the developed world. Children are mostly affected. Cholera occurs as both outbreaks and chronically in certain areas. Areas with an ongoing risk of disease include Africa and Southeast Asia The risk of death among those affected is usually less than 5% but may be as high as 50%. No access to treatment results in a higher death rate.

SYMPTOMS

The primary symptoms of cholera are profuse diarrhea and vomiting of clear fluid. These symptoms usually start suddenly, half a day to five days after ingestion of the bacteria. The diarrhea is frequently described as "rice water" in nature and may have a fishy odor. An untreated person with cholera may produce 10 to 20 litres (3 to 5 US gal) of diarrhea a day. Severe cholera, without treatment, kills about half of affected individuals.[14] If the severe diarrhea is not treated, it can result in life-threatening dehydration and electrolyte imbalances. Estimates of the ratio of asymptomatic to symptomatic infections have ranged from 3 to 100. Cholera has been nicknamed the "blue death"because a person's skin may turn bluish-gray from extreme loss of fluids.

Fever is rare and should raise suspicion for secondary infection. Patients can be lethargic, and might have sunken eyes, dry mouth, cold clammy skin, or wrinkled hands and feet. Kussmaul breathing, a deep and labored breathing pattern, can occur because of acidosis from stool bicarbonate losses and lactic acidosis associated with poor perfusion. Blood pressure drops due to dehydration, peripheral pulse is rapid and thready, and urine output decreases with time. Muscle cramping and weakness, altered consciousness, seizures, or even coma due to electrolyte imbalances are common, especially in children.

Transmission

Cholera bacteria have been found in shellfish and plankton.

Transmission is usually through the fecal-oral route of contaminated food or water caused by poor sanitation. Most cholera cases in developed countries are a result of transmission by food, while in the developing world it is more often water. Food transmission can occur when people harvest seafood such as oysters in waters infected with sewage, as *Vibrio cholerae* accumulates in planktonic crustaceans and the oysters eat the zooplankton.

People infected with cholera often have diarrhea, and disease transmission may occur if this highly liquid stool, colloquially referred to as "rice-water", contaminates water used by others. A single diarrheal event can cause a one-million fold increase in numbers of *V. cholerae* in the environment. The source of the contamination is typically other cholera sufferers when their untreated diarrheal discharge is allowed to get into waterways, groundwater or drinking water supplies. Drinking any contaminated water and eating any foods washed in the water, as well as shellfish living in the affected waterway, can cause a person to contract an infection. Cholera is rarely spread directly from person to person*V. cholerae* also exists outside the human body in natural water sources, either by itself or through interacting with phytoplankton, zooplankton, or biotic and abiotic detritus. Drinking such water can also result in the disease, even without prior contamination through fecal matter. Selective pressures exist however in the aquatic environment that may reduce the virulence of *V. cholerae*. Specifically, animal models indicate that the transcriptional profile of the pathogen changes as it prepares to enter an aquatic environment. This transcriptional change results in a loss of ability of *V. cholerae* to be cultured on standard media, a phenotype referred to as 'viable but non-culturable' (VBNC) or more conservatively 'active but non-culturable' (ABNC. One study indicates that the culturability of *V. cholerae* drops 90% within 24 hours of entering the water, and furthermore that this loss in culturability is associated with a loss in virulence.

Both toxic and non-toxic strains exist. Non-toxic strains can acquire toxicity through a temperate bacteriophage.

Susceptibility

About 100 million bacteria must typically be ingested to cause cholera in a normal healthy adult. This dose, however, is less in those with lowered gastric acidity (for instance those using proton pump inhibitors). Children are also more susceptible, with two- to four-year-olds having the highest rates of infection. Individuals' susceptibility to cholera is also affected by their blood type, with those with type O blood being the most susceptible. Persons with lowered immunity, such as persons with AIDS or malnourished children, are more likely to experience a severe case if they become infected. Any individual, even a healthy adult in middle age, can experience a severe case, and each person's case should be measured by the loss of fluids, preferably in consultation with a professional health care provider.

PATOGENICITY

When consumed, most bacteria do not survive the acidic conditions of the human stomach. The few surviving bacteria conserve their energy and stored nutrients during the passage through the stomach by shutting down protein production. When the surviving bacteria exit the stomach and reach the small intestine, they must propel themselves through the thick mucus that lines the small intestine to reach the intestinal walls where they can attach and thrive.

Once the cholera bacteria reach the intestinal wall, they no longer need the flagella to move. The bacteria stop producing the protein flagellin to conserve energy and nutrients

by changing the mix of proteins which they express in response to the changed chemical surroundings. On reaching the intestinal wall, *V. cholerae* start producing the toxic proteins that give the infected person a watery diarrhea. This carries the multiplying new generations of *V. cholerae* bacteria out into the drinking water of the next host if proper sanitation measures are not in place.[

The cholera toxin (CTX or CT) is an oligomeric complex made up of six protein subunits: a single copy of the A subunit (part A), and five copies of the B subunit (part B), connected by a disulfide bond. The five B subunits form a five-membered ring that binds to GM1 gangliosides on the surface of the intestinal epithelium cells. The A1 portion of the A subunit is an enzyme that ADP-ribosylates G proteins, while the A2 chain fits into the central pore of the B subunit ring. Upon binding, the complex is taken into the cell via receptor-mediated endocytosis. Once inside the cell, the disulfide bond is reduced, and the A1 subunit is freed to bind with a human partner protein called ADP-ribosylation factor 6 (Arf6). Binding exposes its active site, allowing it to permanently ribosylate the Gs alpha subunit of the heterotrimeric G protein. This results in constitutive cAMP production, which in turn leads to the secretion of water, sodium, potassium, and bicarbonate into the lumen of the small intestine and rapid dehydration. The gene encoding the cholera toxin was introduced into *V. cholerae* by horizontal gene transfer. Virulent strains of *V. cholerae* carry a variant of a temperate bacteriophage.

Microbiologists have studied the genetic mechanisms by which the *V. cholerae* bacteria turn off the production of some proteins and turn on the production of other proteins as they respond to the series of chemical environments they encounter, passing through the stomach, through the mucous layer of the small intestine, and on to the intestinal wall. Of particular interest have been the genetic mechanisms by which cholera bacteria turn on the protein production of the toxins that interact with host cell mechanisms to pump chloride ions into the small intestine, creating an ionic pressure which prevents sodium ions from entering the cell. The chloride and sodium ions create a salt-water environment in the small intestines, which through osmosis can pull up to six liters of water per day through the intestinal cells, creating the massive amounts of diarrhea. The host can become rapidly dehydrated unless an appropriate mixture of dilute salt water and sugar is taken to replace the blood's water and salts lost in the diarrhea

By inserting separate, successive sections of *V. cholerae* DNA into the DNA of other bacteria, such as *E. coli* that would not naturally produce the protein toxins, researchers have investigated the mechanisms by which *V. cholerae* responds to the changing chemical environments of the stomach, mucous layers, and intestinal wall. Researchers have discovered a complex cascade of regulatory proteins controls expression of *V. cholerae* virulence determinants. In responding to the chemical environment at the intestinal wall, the *V. cholerae* bacteria produce the TcpP/TcpH proteins, which, together with the ToxR/ToxS proteins, activate the expression of the ToxT regulatory protein. ToxT then directly activates expression of virulence genes that produce the toxins, causing diarrhea in the infected person and allowing the bacteria to colonize the intestine.

Antibiotic resistance

In many areas of the world, antibiotic resistance is increasing within cholera bacteria. In Bangladesh, for example, most cases are resistant to tetracycline, trimethoprim-sulfamethoxazole, and erythromycin.[31] Rapid diagnostic assay methods are available for the identification of multi-drug resistant cases.[32] New generation antimicrobials have been discovered which are effective against cholera bacteria in *in vitro* studies.[33]

DIAGNOSIS

A rapid dipstick test is available to determine the presence of *V. cholerae*. In those samples that test positive, further testing should be done to determine antibiotic resistance.] In epidemic situations, a clinical diagnosis may be made by taking a patient history and doing a brief examination. Treatment is usually started without or before confirmation by laboratory analysis.

Stool and swab samples collected in the acute stage of the disease, before antibiotics have been administered, are the most useful specimens for laboratory diagnosis. If an epidemic of cholera is suspected, the most common causative agent is *V. cholerae* O1. If *V. cholerae* serogroup O1 is not isolated, the laboratory should test for *V. cholerae* O139. However, if neither of these organisms is isolated, it is necessary to send stool specimens to a reference laboratory.

Infection with *V. cholerae* O139 should be reported and handled in the same manner as that caused by *V. cholerae* O1. The associated diarrheal illness should be referred to as cholera and must be reported in the United States.

PREVENTION

The World Health Organization (WHO) recommends focusing on prevention, preparedness, and response to combat the spread of cholera. They also stress the importance of an effective surveillance system. Governments can play a role in all of these areas.

Although cholera may be life-threatening, prevention of the disease is normally straightforward if proper sanitation practices are followed. In developed countries, due to nearly universal advanced water treatment and sanitation practices present there, cholera is rare. For example, the last major outbreak of cholera in the United States occurred in 1910–1911. Cholera is mainly a risk in developing countries.

Effective sanitation practices, if instituted and adhered to in time, are usually sufficient to stop an epidemic. There are several points along the cholera transmission path at which its spread may be halted:

- Sterilization: Proper disposal and treatment of all materials that may have come into contact with cholera victims' feces (e.g., clothing, bedding, etc.) are essential. These should be sanitized by washing in hot water, using chlorine bleach if possible. Hands that touch cholera patients or their clothing, bedding, etc., should be

thoroughly cleaned and disinfected with chlorinated water or other effective antimicrobial agents.

- Sewage and fecal sludge management: In cholera-affected areas, sewage and fecal sludge need to be treated and managed carefully in order to stop the spread of this disease via human excreta. Provision of sanitation and hygiene is an important preventative measure. Open defecation, release of untreated sewage, or dumping of fecal sludge from pit latrines or septic tanks into the environment need to be prevented. In many cholera affected zones, there is a low degree of sewage treatment. Therefore, the implementation of dry toilets that do not contribute to water pollution, as they do not flush with water, may be an interesting alternative to flush toilets.
- Sources: Warnings about possible cholera contamination should be posted around contaminated water sources with directions on how to decontaminate the water (boiling, chlorination etc.) for possible use.
- Water purification: All water used for drinking, washing, or cooking should be sterilized by either boiling, chlorination, ozone water treatment, ultraviolet light sterilization (e.g., by solar water disinfection), or antimicrobial filtration in any area where cholera may be present. Chlorination and boiling are often the least expensive and most effective means of halting transmission. Cloth filters or sari filtration, though very basic, have significantly reduced the occurrence of cholera when used in poor villages in Bangladesh that rely on untreated surface water. Better antimicrobial filters, like those present in advanced individual water treatment hiking kits, are most effective. Public health education and adherence to appropriate sanitation practices are of primary importance to help prevent and control transmission of cholera and other diseases.

Handwashing with soap or ash after using a toilet and before handling food or eating is also recommended for cholera prevention by WHO Africa.

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Surveillance and prompt reporting allow for containing cholera epidemics rapidly. Cholera exists as a seasonal disease in many endemic countries, occurring annually mostly during rainy seasons. Surveillance systems can provide early alerts to outbreaks, therefore leading to coordinated response and assist in preparation of preparedness plans. Efficient surveillance systems can also improve the risk assessment for potential cholera outbreaks. Understanding the seasonality and location of outbreaks provides guidance for improving cholera control activities for the most vulnerable. For prevention to be effective, it is important that cases be reported to national health authorities.

Vaccine

A number of safe and effective oral vaccines for cholera are available. The World Health Organization (WHO) has three prequalified oral cholera vaccines (OCVs): Dukoral, Sanchol, and Euvichol. Dukoral, an orally administered, inactivated whole cell vaccine, has an overall efficacy of about 52% during the first year after being given and 62% in the second year, with minimal side effects. It is available in over 60 countries. However, it is not currently recommended.

One injectable vaccine was found to be effective for two to three years. The protective efficacy was 28% lower in children less than five years old. However, as of 2010, it has limited availability. Work is under way to investigate the role of mass vaccination. The WHO recommends immunization of high-risk groups, such as children and people with HIV, in countries where this disease is endemic. If people are immunized broadly, herd immunity results, with a decrease in the amount of contamination in the environment.

TREATMENT

Continued eating speeds the recovery of normal intestinal function. The WHO recommends this generally for cases of diarrhea no matter what the underlying cause. A CDC training manual specifically for cholera states: "Continue to breastfeed your baby if the baby has watery diarrhea, even when traveling to get treatment. Adults and older children should continue to eat frequently."

Fluids

The most common error in caring for patients with cholera is to underestimate the speed and volume of fluids required. In most cases, cholera can be successfully treated with oral rehydration therapy (ORT), which is highly effective, safe, and simple to administer.

Electrolytes

As there frequently is initially acidosis, the potassium level may be normal, even though large losses have occurred. As the dehydration is corrected, potassium levels may decrease rapidly, and thus need to be replaced. This may be done by consuming foods high in potassium, like bananas or coconut water.

Antibiotics

Antibiotic treatments for one to three days shorten the course of the disease and reduce the severity of the symptoms. Use of antibiotics also reduces fluid requirements. People will recover without them, however, if sufficient hydration is maintained. The WHO only recommends antibiotics in those with severe dehydration.

Doxycycline is typically used first line, although some strains of *V. cholerae* have shown resistance. Testing for resistance during an outbreak can help determine appropriate future choices. Other antibiotics proven to be effective include cotrimoxazole, erythromycin, tetracycline, chloramphenicol, and furazolidone. Fluoroquinolones, such as ciprofloxacin, also may be used, but resistance has been reported.]

Antibiotics improve outcomes in those who are both severely and not severely dehydrated. Azithromycin and tetracycline may work better than doxycycline or ciprofloxacin.

Zinc supplementation

In Bangladesh zinc supplementation reduced the duration and severity of diarrhea in children with cholera when given with antibiotics and rehydration therapy as needed. It reduced the length of disease by eight hours and the amount of diarrhea stool by 10%.[63] Supplementation appears to be also effective in both treating and preventing infectious diarrhea due to other causes among children in the developing world.

3. GASTROINTESTINAL DISEASES

PEPTIC ULCER

Helicobacter pylori (*H. pylori*) infection occurs when a type of bacteria called *Helicobacter pylori* (*H. pylori*) infects the stomach. This usually happens during childhood. A common cause of peptic ulcers, *H. pylori* infection may be present in more than half the people in the world.

Most people don't realize they have H. pylori infection, because they never get sick from it. If you develop signs and symptoms of a peptic ulcer, your doctor will probably test you for H. pylori infection. If you have H. pylori infection, it can be treated with antibiotics.

Peptic ulcers are acid-induced lesions found in the stomach and duodenum characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria. Lesions that do not reach this depth are called erosions. However, the risk of mortality and need for hospitalizations due to PUD has been decreasing worldwide. This is most likely secondary to a decline in *Helicobacter pylori (H. pylori)* infections due to treatment and improved hygiene. Increased use of prescription and over-the-counter acid-suppressing medications and greater caution with non-steroidal anti-inflammatory drugs (NSAIDs) may account partially for this trend as well.

Symptoms

Most people with H. pylori infection will never have any signs or symptoms. It's not clear why this is, but some people may be born with more resistance to the harmful effects of H. pylori.

When signs or symptoms do occur with *H. pylori* infection, they may include:

- An ache or burning pain in your abdomen

- Abdominal pain that's worse when your stomach is empty
- Nausea
- Loss of appetite
- Frequent burping
- Bloating
- Unintentional weight loss
  - Severe or persistent abdominal pain
  - Difficulty swallowing
  - Bloody or black tarry stools
  - Bloody or black vomit or vomit that looks like coffee grounds

Causes

The exact way *H. pylori* infects someone is still unknown. *H. pylori* bacteria may be passed from person to person through direct contact with saliva, vomit or fecal matter. *H. pylori* may also be spread through contaminated food or water.

Risk factors

H. pylori are often contracted in childhood. Risk factors for *H. pylori* infection are related to living conditions in your childhood, such as:

- **Living in crowded conditions.** You have a greater risk of H. pylori infection if you live in a home with many other people.
- **Living without a reliable supply of clean water.** Having a reliable supply of clean, running water helps reduce the risk of H. pylori.
- **Living in a developing country.** People living in developing countries, where crowded and unsanitary living conditions may be more common, have a higher risk of H. pylori infection.
- **Living with someone who has an H. pylori infection.** If someone you live with has H. pylori, you're more likely to also have H. pylori.

Complications

Complications associated with *H. pylori* infection include:

- **Ulcers.** *H. pylori* can damage the protective lining of your stomach and small intestine. This can allow stomach acid to create an open sore (ulcer). About 10 percent of people with H. pylori will develop an ulcer.
- **Inflammation of the stomach lining.** *H. pylori* infection can irritate your stomach, causing inflammation (gastritis).
- **Stomach cancer.** *H. pylori* infection is a strong risk factor for certain types of stomach cancer.

DISEASE

The main risk factors for PUD are *H. pylori*, however not all individuals infected with *H. pylori* develop PUD. Almost half of the world's population is colonized by *H. pylori.* The organism is usually acquired in childhood and persists until treated. Risk factors for acquiring the infection include a lower socioeconomic status and unsanitary conditions or crowding. The prevalence of *H. pylori* is higher in developing countries and more common in certain ethnicities.

H. pylori causes an inflammatory response with neutrophils, lymphocytes, plasma cells, and macrophages within the mucosal layer and causes epithelial cell degeneration and injury. Gastritis is usually more severe in the antrum, with little or no inflammation in the corpus. All patients found to have peptic ulcers should be tested for *H. pylori.* There are both invasive and noninvasive methods for testing. Of all the noninvasive methods, the urea breath test and stool antigen tests are the most feasible and are more accurate than serologic testing.10 Although invasive, endoscopy allows for biopsy and includes a variety of methods for testing such as histology, culture, or rapid urease test. All methods other than serology are affected by use of acid-suppressing medications such as proton pump inhibitors and may produce false negatives.

About a fifth of PUD cases are not related to *H. pylori*, other etiologies for PUD include ischemia causing stress ulcers, medications (steroids, alendronate, potassium chloride, and chemotherapeutic agents), viral infections (CMV, HSV), gastric bypass surgery, metabolic disturbances, radiotherapy, histamine, eosinophilic infiltration, and basophilia.

DIAGNOSIS

Diagnosis begins with clinical suspicion when patients present with symptoms such as epigastric abdominal pain, burning, post-prandial fullness, or early satiety.1 Classically, patients with duodenal ulcers complain of worsening abdominal pain on an empty stomach and describe hunger or abdominal pain two to three hours after meals or at night. In contrast, patients with gastric ulcers report nausea, vomiting, weight loss and post-prandial abdominal pain. Elderly patients are often minimally symptomatic and

some patients with untreated PUD may have intermittent symptoms due to spontaneous healing and then relapse due to persistence of risk factors, such as continued NSAIDs use or *H. pylori* infection.

If clinical symptoms suggest possible peptic ulcer disease and no alarm symptoms are noted, empiric treatment with anti-secretory therapy can be started. Furthermore, since *H. pylori* is a common cause of PUD, a test and treat strategy with a non-invasive test for *H. pylori* (stool antigen or urea breath test) is recommended in patients less than 55 years of age without alarm features, in geographic regions were gastric cancer is uncommon and the prevalence of *H. pylori* is greater than 20%. In older patients and those with alarm symptoms, endoscopy is recommended to establish a diagnosis. Alarm symptoms include GI bleeding, weight loss, early satiety, dysphagia or odynophagia, family history of upper GI malignancy, iron deficiency anemia or new upper GI symptoms in patients older than 55. Esophagogastroduodenoscopy (EGD) or upper endoscopy is the gold standard for the diagnosis of PUD. It is can be used to detect *H. pylori* with gastric biopsies and can also rule out malignancy.

Prevention

In areas of the world where H. pylori infection and its complications are common, doctors sometimes test healthy people for H. pylori. Whether there is a benefit to treating H. pylori when you have no signs or symptoms of infection is controversial among doctors.

If you're concerned about H. pylori infection or think you may have a high risk of stomach cancer, talk to your doctor. Together you can decide whether you may benefit from H. pylori screening.

People who have symptoms of an ulcer, gastritis, or another stomach issue may be tested for *H. pylori* or other problems.

H. pylori can be detected with blood, breath, or stool tests.

Ulcers, gastritis, and stomach cancer are often diagnosed with a combination of the following tests:

- Medical history: past medical problems and symptoms are discussed.
- Physical exam: examining and listening to the belly.
- Special X-rays that show the inside of the stomach.
- Endoscopy: doctors view the inside of the stomach with a special instrument while the patient is sedated or put to sleep.

If an ulcer is found, patients may be treated with a variety of medications, including some or all of the following:

- Antibiotics to kill *H. pylori*.
- Medicines that reduce stomach acid called proton pump inhibitors (PPIs) or histamine receptor blockers.
- Medicines that coat the ulcer and help it heal.

Sometimes, a peptic ulcer can come back after treatment. To help avoid this, experts recommend:

- Stop NSAIDs or take a much smaller dose.
- Only take NSAIDs with special medicines that protect the stomach.
- Avoid alcohol.
- Do not smoke.

TREATMENT

Treatment is usually directed at identifying the factors that lead to PUD. For *H. pylori*-associated PUD, eradication alone will lead to ulcer healing and prevent further mucosal injury. However, due to rising antibiotic resistance in *H. pylori*, treatment has become more difficult. First line therapy for *H. pylori* eradication includes a proton pump inhibitor (PPI), clarithromycin and amoxicillin or metronidazole (for penicillin-allergic patients) for seven to 14 days. PPIs work synergistically with antibiotics to eradicate *H. pylori.* Due to increasing antibiotic resistance, the efficacy of triple therapy has fallen below 70% in many countries. As susceptibility testing is often not available in clinical practice, clarithromycin-based regimens should be avoided when local clarithromycin resistance rates are greater than 15%. Clarithromycin resistance rates are high (>20%) across the United States. When using clarithromycin-based triple therapy, eradication rates can be increased with use of high dose PPI and by extending the duration of treatment from seven to 14 days. For areas with high clarithromycin resistance, bismuth-containing quadruple therapy with a PPI, bismuth, tetracycline and a nitroimidazole (metronidazole or tinidazole) for 14 days or PPI, clarithromycin, amoxicillin, and a nitroimidazole for 14 days is the preferred as first line treatment. There have been issues with the cost and availability of tetracycline and the data have been mixed on whether doxycycline can be substituted. The regimens discussed above yield eradication rates greater than 90%.

All patients treated for *H. pylori,* should be tested to confirm eradication at least four weeks after completing therapy. Second line therapy should be prescribed if a first line regimen fails and should not include repeating metronidazole or clarithromycin. Furthermore, susceptibility testing should be considered after two

treatment failures or after one treatment failure when endoscopy is performed (for other reasons such as follow up of gastric ulcer). If culture for *H. pylori* is not available to evaluate for resistance or after three recommended treatments have failed, rifabutin-based triple therapy (PPI, rifabutin, and amoxicillin) for 10 days can be considered. If symptoms do not improve after *H. pylori* eradication, endoscopy should be pursued if not already performed.

Antibiotic resistance

Most *H. pylori* infections can still be successfully treated with antibiotics. However, research suggests that some *H. pylori* infections are becoming resistant to certain antibiotics. This means *H. pylori* is able to survive antibiotic treatment and the patient may need another drug to kill the bacteria.

Antibiotic resistance is a growing problem across the globe. The CDC say that more than 23,000 people die each year as a result of an antibiotic-resistant infection. Many people may have heard of methicillin-resistant *Staphylococcus aureus* (MRSA), but there are many other types of bacteria that have become resistant to antibiotics.

Everyone can do their part to help fight the problem of antibiotic resistance. The CDC say that people should:

- Use antibiotics only when prescribed by a doctor.
- Never use antibiotics for colds or the flu – these are viruses and antibiotics won't work against these illnesses.
- Take the entire course of antibiotics if they have been prescribed.
- Never share antibiotics with others.
- Never use old or leftover antibiotics.

Fortunately, *H. pylori* is still treatable with several different antibiotics. Quick treatment will help prevent damage to the stomach and the possible problems of ulcers, gastritis, and stomach cancer.

4.TETANUS

Tetanus, also known as **lockjaw**, is a bacterial infection characterized by muscle spasms. Tetanus is caused by an infection with the bacterium *Clostridium tetani*, Tetanus can be prevented by immunization with the tetanus vaccine. Tetanus occurs in all parts of the world but is most frequent in hot and wet climates where the soil contains a lot of organic matter.

Causes

Bacteria called *Clostridium tetani* cause tetanus. Tetanus is an international health problem, as *C. tetani* endospores are ubiquitous. Endospores can be introduced into the body through a puncture wound (penetrating trauma). Due to *C. tetani* being an anaerobic bacterium, it and its endospores thrive in environments that lack oxygen, such as a puncture wound.

Spores of the bacteria can be found in dust, dirt, and animal droppings. Spores are small reproductive bodies produced by certain organisms. They're often resistant to harsh environmental conditions, such as high heat.

A person can become infected when these spores enter the bloodstream through a cut or deep wound. The bacteria spores then spread to the central nervous system and produce a toxin called tetanospasmin. This toxin is a poison that blocks the nerve signals from your spinal cord to your muscles. This can lead to severe muscle spasms.

Tetanus infection has been associated with:

- crush injuries
- injuries with dead tissue
- burns
- puncture wounds from piercings, tattoos, injection drug use, or injury (such as stepping on a nail)
- wounds contaminated with dirt, feces, or saliva

Less commonly, it's been associated with:

- animal bites
- dental infections
- insect bites

- chronic sores and infections

Tetanus is not contagious from person to person. The infection occurs worldwide, but is more common in hot, damp climates with rich soil. It’s also more common in densely populated areas.

Tetanus is often associated with rust, especially rusty nails. Although rust itself does not cause tetanus, objects that accumulate rust are often found outdoors or in places that harbor anaerobic bacteria. Additionally, the rough surface of rusty metal provides a habitat for *C. tetani*, while a nail affords a means to puncture skin and deliver endospores deep within the body at the site of the wound. An endospore is a non-metabolizing survival structure that begins to metabolize and cause infection once in an adequate environment.

Symptoms

Tetanus affects the nerves that control your muscles, which can lead to difficulty swallowing. You may also experience spasms and stiffness in various muscles, especially those in your jaw, abdomen, chest, back, and neck.

Other common tetanus symptoms are:

- fast heart rate
- fever
- sweating
- high blood pressure

The incubation period — the time between exposure to the bacteria and the onset of illness — is between 3 and 21 days. Symptoms typically appear within 14 daysTrusted Source of initial infection. Infections that occur faster after exposure are typically more severe and have a worse prognosis.

Tetanus often begins with mild spasms in the jaw muscles—also known as lockjaw or trismus. The spasms can also affect the facial muscles resulting in an appearance called *risus sardonicus*. Chest, neck, back, abdominal muscles, and buttocks may be affected. Back muscle spasms often cause arching, called opisthotonos. Sometimes the spasms affect muscles that help with breathing, which can lead to breathing problems. Prolonged muscular action causes sudden, powerful, and painful contractions of muscle groups, which is called "tetany". These episodes can cause fractures and muscle tears. Other symptoms include fever, headache, restlessness, irritability, feeding

difficulties, breathing problems, burning sensation during urination, urinary retention and loss of stool control.

Even with treatment, about 10% of people who contract tetanus die. The mortality rate is higher in unvaccinated people and people over 60 years of age.

Incubation period

The incubation period of tetanus may be up to several months, but is usually about ten days. In general, the farther the injury site is from the central nervous system, the longer the incubation period. The shorter the incubation period, the more severe the symptoms. In neonatal tetanus, symptoms usually appear from 4 to 14 days after birth, averaging about 7 days. On the basis of clinical findings, four different forms of tetanus have been described.

Generalized tetanus

Generalized tetanus is the most common type of tetanus, representing about 80% of cases. The generalized form usually presents with a descending pattern. The first sign is trismus, or lockjaw, and the facial spasms called *risus sardonicus*, followed by stiffness of the neck, difficulty in swallowing, and rigidity of pectoral and calf muscles.

Tetanus neurotoxin (TeNT) binds to the presynaptic membrane of the neuromuscular junction, is internalized and is transported back through the axon until it reaches the central nervous system. Here, it selectively binds to and is transported into inhibitory neurons via endocytosis. It then leaves the vesicle for the neuron cytosol where it cleaves vesicle associated membrane protein (VAMP) synaptobrevin, which is necessary for membrane fusion of small synaptic vesicles (SSV's). SSV's carry neurotransmitter to the membrane for release, so inhibition of this process blocks neurotransmitter release.

Tetanus toxin specifically blocks the release of the neurotransmitters GABA and glycine from inhibitory neurons. These neurons keep overactive motor neurons from firing and also play a role in the relaxation of muscles after contraction. When inhibitory neurons are unable to release their neurotransmitters, motor neurons fire out of control and muscles have difficulty relaxing. This causes the muscle spasms and spastic paralysis seen in tetanus infection.

The tetanus toxin, tetanospasmin, is made up of a heavy chain and a light chain. There are three domains, each of which contribute to the pathophysiology of the toxin. The heavy chain has two of the domains. The N-terminal side of the heavy chain helps with membrane translocation, and the C-terminal side helps the toxin locate the specific receptor site on the correct neuron. The light chain domain cleaves the VAMP protein once it arrives in the inhibitory neuron cytosol.

DIAGNOSIS

There are currently no blood tests for diagnosing tetanus. The diagnosis is based on the presentation of tetanus symptoms and does not depend upon isolation of the bacterium, which is recovered from the wound in only 30% of cases and can be isolated from people without tetanus. Laboratory identification of *C. tetani* can be demonstrated only

by production of tetanospasmin in mice. Having recently experienced head trauma may indicate cephalic tetanus if no other diagnosis has been made.

The "spatula test" is a clinical test for tetanus that involves touching the posterior pharyngeal wall with a soft-tipped instrument and observing the effect. A positive test result is the involuntary contraction of the jaw (biting down on the "spatula") and a negative test result would normally be a gag reflex attempting to expel the foreign object.

Prevention

Vaccination can prevent tetanus infections, but only if you receive your booster shots on schedule. In the United States, the tetanus vaccine is given to children as part of the diphtheria-tetanus-pertussis shot, also called the DTap shot. This is a three-in-one vaccine that protects against diphtheria, pertussis, and tetanus. However, it doesn't provide lifelong protection. Children need to get a booster shot at 11 or 12 years of age. Adults then need a booster vaccine called the Td vaccine (for tetanus and diphtheria) every 10 years after that. Check with your doctor if you aren't sure if you're up to date on your shots.

Proper treatment and cleaning of wounds can also help prevent the infection. If you're injured outside and think your injury has made contact with soil, call your healthcare provider and ask about your risk of tetanus.

Unlike many infectious diseases, recovery from naturally acquired tetanus does not usually result in immunity to tetanus. This is due to the extreme potency of the tetanospasmin toxin. Tetanospasmin will likely be lethal before it will provoke an immune response.

Tetanus can be prevented by vaccination with tetanus toxoid. The CDC recommends that adults receive a booster vaccine every ten years, and standard care practice in many places is to give the booster to any person with a puncture wound who is uncertain of when he or she was last vaccinated, or if he or she has had fewer than three lifetime doses of the vaccine. The booster may not prevent a potentially fatal case of tetanus from the current wound, however, as it can take up to two weeks for tetanus antibodies to form.

In children under the age of seven, the tetanus vaccine is often administered as a combined vaccine, DPT/DTaP vaccine, which also includes vaccines against diphtheria and pertussis. For adults and children over seven, the Td vaccine (tetanus and diphtheria) or Tdap (tetanus, diphtheria, and acellular pertussis) is commonly used.

Post-exposure prophylaxis

Tetanus toxoid can be given in case of a suspected exposure to tetanus. In such cases, it can be given with or without tetanus immunoglobulin (also called *tetanus*

antibodies or *tetanus antitoxin*). It can be given as intravenous therapy or by intramuscular injection.

Treatment

Treatment depends on the severity of your symptoms. Tetanus is typically treated with a variety of therapies and medications, such as:

- antibiotics such as penicillin to kill the bacteria in your system
- tetanus immune globulin (TIG) to neutralize the toxins that the bacteria have created in your body
- muscle relaxers to control muscle spasms
- a tetanus vaccine given along with the treatment
- cleaning the wound to get rid of the source of the bacteria

In some cases, a surgical procedure called debridement is used to remove dead or infected tissue. If you have difficulty swallowing and breathing, you may need a breathing tube or ventilator (a machine that moves air in and out of the lungs).

Mild tetanus

Mild cases of tetanus can be treated with: tetanus immunoglobulin (TIG), also called *tetanus antibodies* or *tetanus antitoxin.* It can be given as intravenous therapy or by intramuscular injection.

- metronidazole IV for 10 days
- diazepam oral or IV

Severe tetanus

Severe cases will require admission to intensive care. In addition to the measures listed above for mild tetanus:

- Human tetanus immunoglobulin injected intrathecally (increases clinical improvement from 4% to 35%)
- Tracheotomy and mechanical ventilation for 3 to 4 weeks. Tracheotomy is recommended for securing the airway because the presence of an endotracheal tube is a stimulus for spasm
- Magnesium sulfate, as an intravenous (IV) infusion, to control spasm and autonomic dysfunction
- Diazepam as a continuous IV infusion

- The autonomic effects of tetanus can be difficult to manage (alternating hyper- and hypotension hyperpyrexia/hypothermia) and may require IV labetalol, magnesium, clonidine, or nifedipine

Drugs such as diazepam or other muscle relaxants can be given to control the muscle spasms. In extreme cases it may be necessary to paralyze the person with curare-like drugs and use a mechanical ventilator.

In order to survive a tetanus infection, the maintenance of an airway and proper nutrition are required. An intake of 3,500 to 4,000 calories and at least 150 g of protein per day is often given in liquid form through a tube directly into the stomach (percutaneous endoscopic gastrostomy), or through a drip into a vein (parenteral nutrition). This high-caloric diet maintenance is required because of the increased metabolic strain brought on by the increased muscle activity. Full recovery takes 4 to 6 weeks because the body must regenerate destroyed nerve axon terminals.

The antibiotic of choice is metronidazole. It can be given as intravenously, by mouth, or by rectum. Of likewise efficiency is penicillin, but some raise the concern of provoking spasms because it inhibits GABA receptor, which is already affected by tetanospasmin.

5. TREPONEMA PALLIDUM

Treponema pallidum is a spirochaete bacterium with various subspecies that cause the diseases syphilis, bejel, and yaws. It is transmitted only amongst humans. *Treponema pallidum* is the causative organism of syphilis. It is a motile spirochete that is generally acquired by close sexual contact and which enters host tissue by breaches in squamous or columnar epithelium. Disease is marked by a primary chancre (an area of ulceration and inflammation) seen in genital areas, which manifests soon after the primary infection. Progression to secondary and tertiary syphilis is marked by maculopapular rashes and eventual granulomatous response with CNS involvement. Nonvenereal treponemal diseases include pinta, caused by *Treponema* carateum, and disfiguring yaws, caused by *Treponema pallidum* ssp. *pertenue*.

ORGANISM

It is a helically coiled microorganism usually 6–15 μm long and 0.1–0.2 μm wide.[2] *T. pallidum*'s lack of metabolic pathways (tricarboxylic acid cycle, oxidative phosphorylation) results in minimal metabolic activity. The treponemes have a cytoplasmic and an outer membrane. Using light microscopy, treponemes are visible only by using dark field illumination. *Treponema pallidum* consists of 3 subspecies, *T. p. pallidum, T. p. endemicum,* and*T. p. pertenue,* each of these subspecies has a distinct disease associated with them. Three subspecies of *T. pallidum* are known:

- *Treponema pallidum pallidum*, which causes syphilis
- *T. p. endemicum*, which causes bejel or endemic syphilis
- *T. p. pertenue*, which causes yaws

The three subspecies causing yaws, pinta, and syphilis are morphologically and serologically indistinguishable. These bacteria were originally classified as members of separate species, but DNA hybridization analysis indicates they are members of the same species. *Treponema carateum*, the cause of pinta, remains a separate species because no isolate is available for DNA analysis. Subspecies *T. p. endemicum* and *T. p. pertenue,* disease transmittance is considered non-venereal. *T. p. pallidum* is the most invasive pathogenic subspecies while *T. p. carateum* is the least invasive of the subspecies. *T. p. endemicum* and *T. p. pertenue* are intermediately invasive.

Ultrastructure

Treponema pallidum is a helically shaped bacteria comprised of an outer membrane, peptidoglycan layer, inner membrane, protoplasmic cylinder, and periplasmic space. It is often described as Gram negative, but its outer membrane lacks lipopolysaccharide, which is found in the outer membrane of other Gram-negative bacteria. It has an endoflagella (periplasmic flagella) comprised of 4 main polypeptides, a core structure, and a sheath. The flagella is located within the periplasmic space and wraps around the protoplasmic cylinder. *T. pallidum*'s outer membrane has the most contact with host cells and contains few transmembrane proteins, limiting antigenicity while its cytoplasmic membrane is covered in lipoproteins. The outer membrane's treponemal ligands main function is attachment to host cells, with functional and antigenic relatedness between ligands. The genus *Treponema* has ribbons of cytoskeletal cytoplasmic filaments that run the length of the cell just underneath the cytoplasmic membrane. They are composed of the intermediate filament-like protein CfpA (cytoplasmic filament protein A). Although the filaments may be involved in chromosome structure and segregation or cell division, their precise function is unknown.

The clinical features of syphilis, yaws, and bejel occur in multiple stages that affect the skin. The skin lesions observed in the early stage last for weeks or months. The skin lesions are highly infectious, and the spirochetes in the lesions are transmitted by direct contact. The lesions regress as the immune response develops against *T. pallidum*. The latent stage that results lasts a lifetime in many cases. In a minority of cases, the disease exits latency and enters a tertiary phase, in which destructive lesions of skin, bone, and cartilage ensue. Unlike yaws and bejels, syphilis in its tertiary stage often affects the heart, eyes, and nervous system as well.

Transmission

T. p. pallidum is a motile spirochaete that is generally acquired by close sexual contact, entering the host via breaches in squamous or columnar epithelium. The organism can also be transmitted to a fetus by transplacental passage during the later stages of

pregnancy, giving rise to congenital syphilis. The helical structure of *T. p. pallidum* allows it to move in a corkscrew motion through mucous membranes or enter minuscule breaks in the skin. In women the initial lesion is usually on the labia, the walls of the vagina, or the cervix; in men it is on the shaft or glans of the penis. It gains access to the host's blood and lymph systems through tissue and mucous membranes. In more severe cases, it may gain access to the host by infecting the skeletal bones and central nervous system of the body.

The incubation period for a *T. p. pallidum* infection is usually around 21 days, but can range from 10 days to 90 days.

Treponema pallidum is a corkscrew-shaped (spirochete) bacterium. It thrives in moist regions of the body and will survive and reproduce only where there is little oxygen present. It is killed by heat, drying, and sunlight. Therefore, one cannot catch syphilis from contact with toilet seats, bath towels, or bedding. It can, however, live in collected blood for up to 24 h at 4 °C and thus, in rare cases, is transmitted during blood transfusion. Nine out of 10 cases of syphilis transmission occur during sexual intercourse, although it can also be introduced into an open wound in the skin. Fortunately, only about 1 in 10 people exposed to the bacterium develops syphilis. People infected with syphilis can acquire the HIV virus more easily and transmit it to others.

Pathophysiology

Treponema pallidum causes a chancre at the inoculation site (primary syphilis). A maculopapular rash and lymphadenopathy are prominent in the second stage of syphilis. Fever, malaise, nausea, headache, joint pain, and anorexia may also be present. Next, a latent stage occurs in which the organism invades vital organs. A final, tertiary stage may display gummas, cardiovascular disease, and neurosyphilis. Other *Treponema* species cause open lesions of the skin. Borreliosis, caused by *B. burgdorferi* and related species, cause an initial ‘bull's eye’ lesion at the site of the arthropod bite. The disease causes fever, malaise, and anorexia and, after a period of years, serious central nervous system symptoms. *Leptospira* causes flu-like symptoms, including fever, muscle weakness and aches, backpain, headache, and malaise.

TREATMENT

During the early 1940s rabbit models in combination with the drug penicillin allowed for a long term drug treatment. These experiments establish the ground work that modern scientists use for syphilis therapy. Penicillin can inhibit *T. pallidum* in 6–8 hours though the cells still remain in lymph nodes and regenerate. Though penicillin is not the only drug that can be used to inhibit *T. pallidum*, it has also been found that any β-lactam antibiotics or macrolides can also be used. The *T. pallidum* strain 14 has built resistance to some macrolides, including erythromycin and azithromycin. Resistance to macrolides in *T. Pallidum* strain 14 is believed to derive from a single point mutation that increased the organisms livability. Many of the syphilis treatment therapies only lead to bacteriostatic results, unless larger concentrations of penicillin are used for bactericidal effects. Penicillin overall is the most recommended antibiotic by the CDC

as it shows the best results with prolonged usage, it can inhibit and may even kill *T. Pallidum* at low to high doses with each increase in concentration being more effective.

No vaccine for syphilis is available. The outer membrane of *T. pallidum* has too few surface proteins for an antibody to be effective. Efforts to develop a safe and effective syphilis vaccine have been hindered by uncertainty about the relative importance of humoral and cellular mechanisms to protective immunity, and because *T. pallidum* outer membrane proteins have not been unambiguously identified. In contrast, some of the known antigens are intracellular, and antibodies are ineffective against them to clear the infection.

6. *Staphylococcus aureus*

Staphylococcus aureus is a Gram-positive, round-shaped bacterium and it is a usual member of the microbiota of the body, frequently found in the upper respiratory tract and on the skin. It is often positive for catalase and nitrate reduction and is a facultative anaerobe that can grow without the need for oxygen. Although *S. aureus* usually acts as a commensal of the human microbiota it can also become an opportunistic pathogen, being a common cause of skin infections including abscesses, respiratory infections such as sinusitis, and food poisoning. Pathogenic strains often promote infections by producing virulence factors such as potent protein toxins, and the expression of a cell-surface protein that binds and inactivates antibodies. The emergence of antibiotic-resistant strains of *S. aureus* such as methicillin-resistant *S. aureus* (MRSA) is a worldwide problem in clinical medicine. Despite much research and development, no vaccine for *S. aureus* has been approved

An estimated 20% to 30% of the human population are long-term carriers *S. aureus* which can be found as part of the normal skin flora, in the nostrils, and as a normal inhabitant of the lower reproductive tract of women. *S. aureus* can cause a range of illnesses, from minor skin infections, such as pimples,[7] impetigo, boils, cellulitis, folliculitis, carbuncles, scalded skin syndrome, and abscesses, to life-threatening diseases such as pneumonia, meningitis, osteomyelitis, endocarditis, toxic shock syndrome, bacteremia, and sepsis. It is still one of the five most common causes of hospital-acquired infections and is often the cause of wound infections following surgery. Each year, around 500,000 patients in hospitals of the United States contract a staphylococcal infection, chiefly by *S. aureus*. Up to 50,000 deaths each year in the USA are linked with *S. aureus* infections.

ORGANISM

S. aureus "grape-cluster berry", Latin aureus, "golden" is a facultative anaerobic, Grampositive coccal (round) bacterium also known as "golden staph" and "oro staphira". *S. aureus* is nonmotile and does not form spores. In medical literature, the bacterium is often referred to as *S. aureus*. *S. aureus* appears as staphylococci (grape-like clusters) when viewed through a microscope, and has large, round, golden-yellow colonies, often with hemolysis, when grown on blood agar plates. *S. aureus* reproduces asexually by binary fission. Complete separation of the daughter cells is mediated by *S. aureus* autolysin, and in its absence or targeted inhibition, the daughter cells remain attached to one another and appear as clusters. *S. aureus* is catalase-positive (meaning it can produce the enzyme catalase). Catalase converts hydrogen peroxide (H2O2) to water and oxygen. Catalase-activity tests are sometimes used to distinguish staphylococci from enterococci and streptococci. Previously, *S. aureus* was differentiated from other staphylococci by the coagulase test.

However, not all *S. aureus* strains are coagulase-positive and incorrect species identification can impact effective treatment and control measures. Staphylococcus is different from the similarly named and medically relevant genus Streptococcus. Natural genetic transformation is a reproductive process involving DNA transfer from one bacterium to another through the intervening medium, and the integration of the donor sequence into the recipient genome by homologous recombination. *S. aureus* was found to be capable of natural genetic transformation, but only at low frequency under the experimental conditions employed. Further studies suggested that the development of competence for natural genetic transformation may be substantially higher under appropriate conditions, yet to be discovered.

PATHOGENOCITY

The carriage of *S. aureus* is an important source of hospital-acquired infection (also called nosocomial) and community-acquired MRSA. Although *S. aureus* can be present on the skin of the host, a large proportion of its carriage is through the anterior nares of the nasal passages and can further be present in the ears. The ability of the nasal passages to harbour *S. aureus* results from a combination of a weakened or defective host immunity and the bacterium's ability to evade host innate immunity. Nasal carriage is also implicated in the occurrence of staph infections.

DISEASE

While *S.aureus* is a commensal bacterium, asymptomatically colonizing about 30% of the human population, it can sometimes cause disease. In particular, *S. aureus* is one of the most common causes of bacteremia and infective endocarditis. Additionally, it can cause various skin and soft-tissue infections, particularly when skin or mucosal barriers have been breached. *S. aureus* infections can spread through contact with pus from an infected wound, skinto-skin contact with an infected person, and contact with

objects used by an infected person such as towels, sheets, clothing, or athletic equipment. Joint replacements put a person at particular risk of septic arthritis, staphylococcal endocarditis (infection of the heart valves), and pneumonia. Preventive measures include washing hands often with soap and making sure to bathe or shower daily. *S. aureus* is a significant cause of chronic biofilm infections on medical implants, and the repressor of toxins is part of the infection pathway. *S. aureus* can lay dormant in the body for years undetected. Once symptoms begin to show, the host is contagious for another two weeks, and the overall illness lasts a few weeks. If untreated, though, the disease can be deadly. Deeply penetrating *S. aureus* infections can be severe.

Skin infections

Skin infections are the most common form of *S. aureus* infection. This can manifest in various ways, including small benign boils, folliculitis, impetigo, cellulitis, and more severe, invasive soft-tissue infections. *S. aureus* is extremely prevalent in persons with atopic dermatitis, more commonly known as eczema. It is mostly found in fertile, active places, including the armpits, hair, and scalp. Large pimples that appear in those areas may exacerbate the infection if lacerated. This can lead to staphylococcal scalded skin syndrome, a severe form of which can be seen in newborns. The presence of S. aureus in persons with atopic dermatitis is not an indication to treat with oral antibiotics, as evidence has not shown this to give benefit to the patient. However, topical antibiotics combined with corticosteroids have been found to improve the condition. Colonization of *S. aureus* drives inflammation of atopic dermatitis; *S. aureus* is believed to exploit defects in the skin barrier of persons with atopic dermatitis, triggering cytokine expression and therefore exacerbating symptoms.

Food poisoning

S. aureus is also responsible for food poisoning. It is capable of generating toxins that produce food poisoning in the human body. Its incubation period lasts one to six hours, with the illness itself lasting from 30 minutes to 3 days. Preventive measures one can take to help prevent the spread of the disease include washing hands thoroughly with soap and water before preparing food. Stay away from any food if ill, and wear gloves if any open wounds occur on hands or wrists while preparing food. If storing food for longer than 2 hours, keep the food below 5 or above 63 °C.

Bone and joint infections

S. aureus is the bacterium commonly responsible for all major bone and joint infections. This manifests in one of three forms: osteomyelitis, septic arthritis, and infection from a replacement joint surgery.

Bacteremia

S. aureus is a leading cause of bloodstream infections throughout much of the industrialized world. Infection is generally associated with breaks in the skin or mucosal membranes due to surgery, injury, or use of intravascular devices such as catheters,

hemodialysis machines, or injected drugs. Once the bacteria have entered the bloodstream, they can infect various organs, causing infective endocarditis, septic arthritis, and osteomyelitis. This disease is particularly prevalent and severe in the very young and very old. Without antibiotic treatment, *S. aureus* bacteremia has a case fatality rate around 80%. With antibiotic treatment, case fatality rates range from 15% to 50% depending on the age and health of the patient, as well as the antibiotic resistance of the *S. aureus* strain.

Medical implant infections

S. aureus is often found in biofilms formed on medical devices implanted in the body or on human tissue. It is commonly found with another pathogen, Candida albicans, forming multispecies biofilms. The latter is suspected to help *S. aureus* penetrate human tissue. A higher mortality is linked with multispecies biofilms. *S. aureus* biofilm is the predominant cause of orthopedic implant-related infections, but is also found on cardiac implants, vascular grafts, various catheters, and cosmetic surgical implants. After implantation, the surface of these devices becomes coated with host proteins, which provide a rich surface for bacterial attachment and biofilm formation. Once the device becomes infected, it must by completely removed, since S. aureus biofilm cannot be destroyed by antibiotic treatments. Current therapy for S. aureus biofilm-mediated infections involves surgical removal of the infected device followed by antibiotic treatment. Conventional antibiotic treatment alone is not effective in eradicating such infections. An alternative to postsurgical antibiotic treatment is using antibiotic-loaded, dissolvable calcium sulfate beads, which are implanted with the medical device. These beads can release high doses of antibiotics at the desired site to prevent the initial infection. Novel treatments for *S. aureus* biofilm involving nano silver particles, bacteriophages, and plant-derived antibiotic agents are being studied. These agents have shown inhibitory effects against *S. aureus* embedded in biofilms. A class of enzymes have been found to have biofilm matrix-degrading ability, thus may be used as biofilm dispersal agents in combination with antibiotics.

Animal infections.

S. aureus can survive on dogs, cats, and horses, and can cause bumblefoot in chickens. Some believe health-care workers' dogs should be considered a significant source of antibiotic-resistant S. aureus, especially in times of outbreak. In a 2008 study by Boost, O'Donoghue, and James, it was found that just about 90% of S. aureus colonized within pet dogs presented as resistant to at least one antibiotic. The nasal region has been implicated as the most important site of transfer between dogs and humans. S. aureus is one of the causal agents of mastitis in dairy cows. Its large polysaccharide capsule protects the organism from recognition by the cow's immune defenses.

VIRULENCE FACTOR

S. aureus produces various enzymes such as coagulase (bound and free coagulases) which clots plasma and coats the bacterial cell, probably to prevent phagocytosis. Hyaluronidase (also known as spreading factor) breaks down hyaluronic acid and helps in spreading it. S. aureus also produces deoxyribonuclease, which breaks down the DNA, lipase to digest lipids, staphylokinase to dissolve fibrin and aid in spread, and beta-lactamase for drug resistance.

Toxins

Depending on the strain, S. aureus is capable of secreting several exotoxins, which can be categorized into three groups. Many of these toxins are associated with specific diseases.

Superantigens

Antigens known as superantigens can induce toxic shock syndrome (TSS). This group includes the toxins TSST-1, and enterotoxin type B, which causes TSS associated with tampon use. Toxic shock syndrome is characterized by fever, erythematous rash, low blood pressure, shock, multiple organ failure, and skin peeling. Lack of antibody to TSST-1 plays a part in the pathogenesis of TSS. Other strains of S. aureus can produce an enterotoxin that is the causative agent of a type of gastroenteritis. This form of gastroenteritis is self-limiting, characterized by vomiting and diarrhea 1–6 hours after ingestion of the toxin, with recovery in 8 to 24 hours. Symptoms include nausea, vomiting, diarrhea, and major abdominal pain.

Exfoliative toxins

Exfoliative toxins are exotoxins implicated in the disease staphylococcal scalded skin syndrome (SSSS), which occurs most commonly in infants and young children. It also may occur as epidemics in hospital nurseries. The protease activity of the exfoliative toxins causes peeling of the skin observed with SSSS. Other toxins Staphylococcal toxins that act on cell membranes include alpha toxin, beta toxin, delta toxin, and several bicomponent toxins. Strains of S. aureus can host phages, such as the prophage Φ-PVL that produces Panton-Valentine leukocidin (PVL), to increase virulence. The bicomponent toxin PVL is associated with severe necrotizing pneumonia in children. The genes encoding the components of PVL are encoded on a bacteriophage found in community-associated MRSA strains.

TREATMENT

The treatment of choice for S. aureus infection is penicillin. An antibiotic derived from some Penicillium fungal species, penicillin inhibits the formation of peptidoglycan crosslinkages that provide the rigidity and strength in a bacterial cell wall. The four-membered β-lactam ring of penicillin is bound to enzyme DD-transpeptidase, an enzyme that when functional, cross-links chains of peptidoglycan that form bacterial cell

walls. The binding of β-lactam to DD-transpeptidase inhibits the enzyme's functionality and it can no longer catalyze the formation of the cross-links. As a result, cell wall formation and degradation are imbalanced, thus resulting in cell death. In most countries, however, penicillin resistance is extremely common, and first-line therapy is most commonly a penicillinase-resistant β-lactam antibiotic (for example, oxacillin or flucloxacillin, both of which have the same mechanism of action as penicillin). Combination therapy with gentamicin may be used to treat serious infections, such as endocarditis. but its use is controversial because of the high risk of damage to the kidneys.[87] The duration of treatment depends on the site of infection and on severity. Adjunctive rifampicin has been historically used in the management of S aureus bacteraemia, but randomised controlled trial evidence has shown this to be of no overall benefit over standard antibiotic therapy.

Antibiotic resistance in *S. aureus* was uncommon when penicillin was first introduced in 1943. Indeed, the original Petri dish on which Alexander Fleming of Imperial College London observed the antibacterial activity of the Penicillium fungus was growing a culture of *S. aureus*. By 1950, 40% of hospital *S. aureus* isolates were penicillinresistant; by 1960, this had risen to 80%. Staphylococcal resistance to penicillin is mediated by penicillinase (a form of betalactamase) production: an enzyme that cleaves the β-lactam ring of the penicillin molecule, rendering the antibiotic ineffective. Penicillinase-resistant β-lactam antibiotics, such as methicillin, nafcillin, oxacillin, cloxacillin, dicloxacillin, and flucloxacillin are able to resist degradation by staphylococcal penicillinase. Resistance to methicillin is mediated via the mec operon, part of the staphylococcal cassette chromosome mec (SCCmec). SCCmec is a family of mobile genetic elements, which is a major driving force of S. aureus evolution. Resistance is conferred by the mecA gene, which codes for an altered penicillin-binding protein (PBP2a or PBP2') that has a lower affinity for binding β-lactams (penicillins, cephalosporins, and carbapenems). This allows for resistance to all β-lactam antibiotics, and obviates their clinical use during MRSA infections. Studies have explained that this mobile genetic element has been acquired by different lineages in separate gene transfer events, indicating that there is not a common ancestor of differing MRSA strains. Aminoglycoside antibiotics, such as kanamycin, gentamicin, streptomycin, were once effective against staphylococcal infections until strains evolved mechanisms to inhibit the aminoglycosides' action, which occurs via protonated amine and/or hydroxyl interactions with the ribosomal RNA of the bacterial 30S ribosomal subunit. Three main mechanisms of aminoglycoside resistance mechanisms are currently and widely accepted: aminoglycoside modifying enzymes, ribosomal mutations, and active efflux of the drug out of the bacteria. Aminoglycoside-modifying enzymes inactivate the aminoglycoside by covalently attaching either a phosphate, nucleotide, or acetyl moiety to either the amine or the alcohol key functional group (or both groups) of the antibiotic. This changes the charge or sterically hinders the antibiotic, decreasing its ribosomal binding affinity. In S. aureus, the best-characterized aminoglycoside-modifying enzyme is aminoglycoside adenylyltransferase 4' IA (ANT(4')IA). This enzyme has been solved by X-ray crystallography. The enzyme is able to attach an adenyl moiety to the 4' hydroxyl group of many aminoglycosides, including kamamycin and gentamicin. Glycopeptide resistance is mediated by acquisition of the vanA gene. Today, S. aureus has become resistant to many commonly used antibiotics. In the UK, only 2% of all *S.*

aureus isolates are sensitive to penicillin, with a similar picture in the rest of the world. The β-lactamase-resistant penicillins (methicillin, oxacillin, cloxacillin, and flucloxacillin) were developed to treat penicillin-resistant S. aureus, and are still used as first-line treatment. Methicillin was the first antibiotic in this class to be used (it was introduced in 1959), but, only two years later, the first case of methicillinresistant Staphylococcus aureus (MRSA) was reported in England. Despite this, MRSA generally remained an uncommon finding, even in hospital settings, until the 1990s, when the MRSA prevalence in hospitals exploded, and it is now endemic. MRSA infections in both the hospital and community setting are commonly treated with non-β-lactam antibiotics, such as clindamycin (a lincosamine) and co-trimoxazole (also commonly known as trimethoprim/sulfamethoxazole). Resistance to these antibiotics has also led to the use of new, broad-spectrum anti-Gram-positive antibiotics, such as linezolid, because of its availability as an oral drug. First-line treatment for serious invasive infections due to MRSA is currently glycopeptide antibiotics (vancomycin and teicoplanin). A number of problems with these antibiotics occur, such as the need for intravenous administration (no oral preparation is available), toxicity, and the need to monitor drug levels regularly by blood tests. Also, glycopeptide antibiotics do not penetrate very well into infected tissues (this is a particular concern with infections of the brain and meninges and in endocarditis). Glycopeptides must not be used to treat methicillin-sensitive S. aureus (MSSA), as outcomes are inferior. Because of the high level of resistance to penicillins and because of the potential for MRSA to develop resistance to vancomycin, the U.S. Centers for Disease Control and Prevention has published guidelines for the appropriate use of vancomycin. In situations where the incidence of MRSA infections is known to be high, the attending physician may choose to use a glycopeptide antibiotic until the identity of the infecting organism is known. After the infection is confirmed to be due to a methicillin-susceptible strain of S. aureus, treatment can be changed to flucloxacillin or even penicillin, as appropriate. Vancomycin-resistant S. aureus (VRSA) is a strain of S. aureus that has become resistant to the glycopeptides. The first case of vancomycin-intermediate S. aureus (VISA) was reported in Japan in 1996; but the first case of S. aureus truly resistant to glycopeptide antibiotics was only reported in 2002.[99] Three cases of VRSA infection had been reported in the United States as of 2005.[100] At least in part the antimicrobial resistance in s.aureus can be explained by its ability to adapt. Multiple two component signal transduction pathways helps S. aureus to express genes that are required to survive under antimicrobial stress.

CONTROL

Spread of *S. aureus* (including MRSA) generally is through human-to-human contact, although recently some veterinarians have discovered the infection can be spread through pets with environmental contamination thought to play a relatively unimportant part. Emphasis on basic hand washing techniques are, therefore, effective in preventing its transmission. The use of disposable aprons and gloves by staff reduces skin-to-skin contact, so further reduces the risk of transmission. Recently, myriad cases of *S. aureus* have been reported in hospitals across America. Transmission of the pathogen is facilitated in medical settings where healthcare worker hygiene is insufficient. *S. aureus*

is an incredibly hardy bacterium, as was shown in a study where it survived on polyester for just under three months; polyester is the main material used in hospital privacy curtains. The bacteria are transported on the hands of healthcare workers, who may pick them up from a seemingly healthy patient carrying a benign or commensal strain of S. aureus, and then pass it on to the next patient being treated. Introduction of the bacteria into the bloodstream can lead to various complications, including endocarditis, meningitis, and, if it is widespread, sepsis. Ethanol has proven to be an effective topical sanitizer against MRSA. Quaternary ammonium can be used in conjunction with ethanol to increase the duration of the sanitizing action. The prevention of nosocomial infections involves routine and terminal cleaning. Nonflammable alcohol vapor in CO 2 NAV-CO2 systems have an advantage, as they do not attack metals or plastics used in medical environments, and do not contribute to antibacterial resistance. An important and previously unrecognized means of community-associated MRSA colonization and transmission is during sexual contact. *S. aureus* is killed in one minute at 78 °C and in ten minutes at 64 °C but is resistant to freezing. Certain strains of *S. aureus* have been described as being resistant to chlorine disinfection As of 2015, no approved vaccine exists against *S. aureus*. To date, none of these candidates provides protection against a *S. aureus* infection.