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Editorial

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Mini review section – When antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-used by the public. Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

Current Trends section – Resistance to antibiotic treatment is becoming increasingly reported, thus making the management of superficial skin infections a major medical challenge. Antiseptics have broader spectrums of antimicrobial activity than antibiotics and a much lower risk of bacterial resistance selection. Antiseptics are therefore appropriate alternatives to antibiotics for the management of localized superficial skin infections. Povidone iodine has the broadest spectrum of antimicrobial activity of the available antiseptics and has a rapid and persistent microbicidal effect.

In Profile Scientist – Kiran Mazumdar-Shaw born on 23 March 1953 in Bangalore, Karnataka state, to Gujarati parents In 1984, Kiran began to develop a research and development team at Biocon, focusing on the discovery of novel enzymes and on development of novel techniques for solid substrate fermentation technology. Her work in the biotechnology sector has earned her numerous national awards, including the Padma Shri (1989) and the Padma Bhushan (2005) from the government of India. She was given the Economic Times Award for 'Businesswoman of the Year' in 2004.

Bug of the month – *Vibrio cholerae* is a species of Gram-negative, facultative anaerobe and comma-shaped bacteria. *V. cholerae* has an endemic or epidemic occurrence. In countries where the disease has been for the past three years and the cases confirmed are local (within the confines of the country) transmission is considered to be "endemic." Alternatively, an outbreak is declared when the occurrence of disease exceeds the normal occurrence for any given time or location. Epidemics can last several days or over a span of years. Additionally, countries that have an occurrence of an epidemic can also be endemic.

Did You Know? – Iron (Fe) deficiency has become one of the factors limiting plant quality and productivity around the world. IMA (IRONMAN), a family of small peptides, has been recently reported to play a positive role in the Fe deficiency response in Arabidopsis and rice (Oryza sativa). Two OsIMA genes were identified in rice.

Best Practices – Dialysis is a treatment for people whose kidneys are failing. When you have kidney failure, your kidneys don't filter blood the way they should. As a result, wastes and toxins build up in your bloodstream. Dialysis does the work of your kidneys, removing waste products and excess fluid from the blood. Renal patients have lowered immunity. That makes them more susceptible to infection, and it's much harder for them to recover from it. All this means that keeping a clean dialysis centre is very important.

Tickle yourself enjoying the jokes in our **Relax Mood section**.

Our JHS team is thankful to all our readers for their ever-increasing appreciation that has served as a reward & motivation for us. Looking forward for your continuous support.

SUPERBUGS AMOUNG US II

Antibiotic medications are used to kill bacteria, which can cause illness and disease. They have made a major contribution to human health. Many diseases that once killed people can now be treated effectively with antibiotics. However, some bacteria have become resistant to commonly used antibiotics.

Antibiotic resistant bacteria are bacteria that are not controlled or killed by antibiotics. They are able to survive and even multiply in the presence of an antibiotic. Most infection-causing bacteria can become resistant to at least some antibiotics. Bacteria that are resistant to many antibiotics are known as multi-resistant organisms (MRO).

Antibiotic resistance is a serious public health problem. It can be prevented by minimising unnecessary prescribing and overprescribing of antibiotics, correct use of prescribed antibiotics, and good hygiene and infection control.

Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective.

When antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-used by the public. Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

Main strains of super bug

- Vancomycin-resistant Enterococcus (VRE)
- Multidrug-resistant Acinetobacter
- Extended-spectrum beta-lactamases (ESBLs).

Vancomycin-resistant Enterococcus (VRE)

Enterococci are bacteria (germs) that are normally present in the human intestines and in the female genital tract, and are often found in the environment, like in soil and water. These bacteria can cause infections.

Enterococci bacteria are constantly finding new ways to avoid the effects of the antibiotics used to treat the infections they cause. Antibiotic resistance occurs when the germs no longer respond to the antibiotics designed to kill them. If these germs develop resistance to vancomycin, an antibiotic that is used to treat some drug-resistant infections, they become vancomycin-resistant enterococci (VRE).

Most VRE infections happen in people who are in the hospital. People who are infected often have a serious illness or weakened immune system.

You're more likely to become infected with VRE if you:

- were treated for a long period of time with vancomycin or other antibiotics, such as penicillin or gentamicin.
- have a serious illness such as kidney disease or a blood disorder
- spent time in the hospital, especially if you received antibiotics while you were there
- have a weakened immune system
- had surgery, such as to your abdomen or chest
- have a medical device that needs to stay in for a long time, such as a urinary catheter
- are 60 years or older, especially if you're in a nursing home or long-term care facility

Most VRE infections are transmitted in hospitals. The bacteria often spread when a doctor or other healthcare worker touches an infected person, surface, or medical equipment and then doesn't wash their hands properly before touching another patient. VRE does not spread through the air like the flu and some other bacterial infections.

It is diagnosed by taking a sample of blood, urine, pus, or other fluid from the infected area. The sample is sent to a lab to be tested for VRE.

VRE doesn't always need to be treated. If you have enterococci in your body but they're not causing an active infection, you don't need treatment.

Active VRE infections are treated with an antibiotic that's not vancomycin.

Multidrug-resistant Acinetobacter

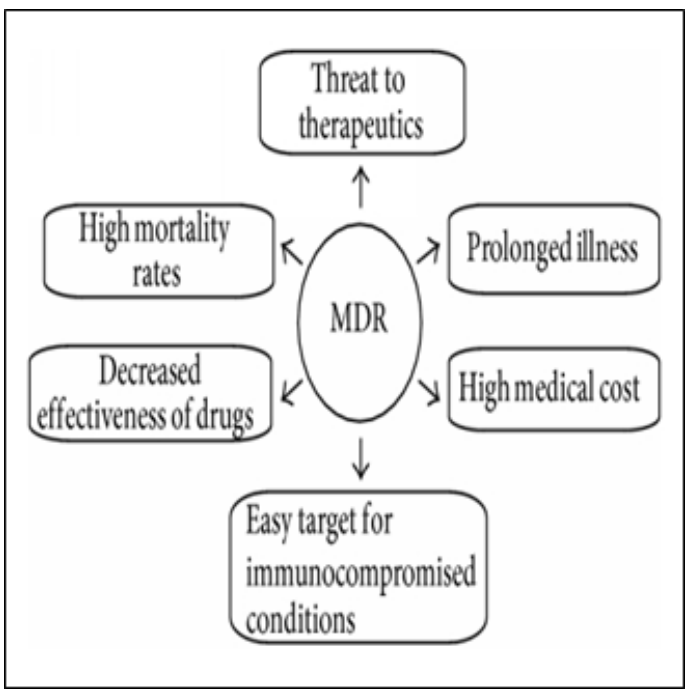
Acinetobacter is a group of bacteria (germs) commonly found in the environment, like in soil and water. While there are many types, the most common cause of infections is *Acinetobacter baumannii*, which accounts for most *Acinetobacter* infections in humans.

Acinetobacter baumannii can cause infections in the blood, urinary tract, and lungs (pneumonia), or in wounds in other parts of the body. It can also "colonize" or live in a patient without causing infections or symptoms, especially in respiratory secretions (sputum) or open wounds.

If they develop resistance to the group of antibiotics called carbapenems, they become carbapenem-resistant.

When resistant to multiple antibiotics, they're multidrug-resistant.

Carbapenem resistant *Acinetobacter* are usually multidrug-resistant (MDR).



Acinetobacter infections typically occur in people in healthcare settings. People most at risk include patients in hospitals, especially those who:

- are on breathing machines (ventilators)
- have devices such as catheters
- have open wounds from surgery
- are in intensive care units
- have prolonged hospital stays

Acinetobacter can live for long periods of time on environmental surfaces and shared equipment if they are not properly cleaned. The germs can spread from one person to another through contact with these contaminated surfaces or equipment or though person to person spread, often via contaminated hands.

Extended-spectrum beta-lactamases (ESBLs)

Enterobacterales can produce enzymes called extended-spectrum beta-lactamases (ESBLs). Extended-spectrum beta-lactamases (ESBLs) confer resistance to most beta-lactam antibiotics, including penicillin's, cephalosporins, and the monobactam aztreonam.

This resistance means that there are fewer antibiotic options available to treat ESBL-producing Enterobacterales infections. In many cases, even common infections, such as urinary tract infections, caused by ESBL-producing germs require more complex treatments. Instead of taking oral antibiotics at home, patients with these infections might require hospitalization and intravenous (IV) carbapenem antibiotics. Carbapenems are one of the few remaining antibiotics that can treat ESBL-producing germs, but resistance enzymes that destroy these antibiotics are on the rise, too.

These infections most commonly occur in people with exposure to healthcare, including those in hospitals and nursing homes. However, unlike many other resistant germs, ESBL-producing Enterobacterales can also cause infections in otherwise healthy people who have not recently been in healthcare settings. In healthy people, this often means urinary tract infections.

Possible medications used to treat ESBL infection include:

- carbapenems, which are useful against infections caused by *E. coli* or *Klebsiella pneumoniae* bacteria
- fosfomycin, which is effective against ESBL bacterial infections
- beta-lactamase inhibitors
- nonbeta-lactam antibiotics
- colistin, which is prescribed in rare cases when other medications have failed to stop the ESBL infection.

POVIDINE IODINE AND ITS RESISTANCE OVER TIME

Resistance to antibiotic treatment is becoming increasingly reported, thus making the management of superficial skin infections a major medical challenge. Antiseptics have broader spectrums of antimicrobial activity than antibiotics and a much lower risk of bacterial resistance selection. Antiseptics are therefore appropriate alternatives to antibiotics for the management of localized superficial skin infections. Povidone iodine has the broadest spectrum of antimicrobial activity of the available antiseptics and has a rapid and persistent microbicidal effect. It is active against Gram-positive and -negative bacteria, bacterial spores, fungi, protozoa, and several viruses, including H1N1 influenza virus (swine flu). It also has good skin tolerance and is only a weak allergen: it is rarely associated with immediate allergic reactions, which are more prevalent with chlorhexidine. It has also been shown to promote wound healing. Although additional data are needed from well-designed clinical trials, povidone iodine 10% can be considered as a first-choice antiseptic for the prevention and treatment of superficial skin infection.

The emergence of antibiotic resistant strains of bacteria, including VRE and methicillin-resistant *Staphylococcus aureus* (MRSA), has become a significant issue for healthcare facilities throughout the world. Indeed, studies have shown that approximately 42% of *S. aureus* isolates in Europe and Japan harbour genes that enable resistance to quaternary ammonium compounds and chlorhexidine, with chlorhexidine overuse thought to be a factor in emerging resistance in some strains of Gram-negative bacteria. The prevalence of methicillin resistance harboured by strains of *S. aureus* capable of causing bloodstream infection between 1990 and the early 2000s in the UK rose significantly from 2 to >40%, with mean overall rates of bacteraemia involving MRSA ranging from 0.10 to 0.19 per 1000 occupied beds. The overuse of antibiotics is thought to be a contributing factor towards rising antibiotic resistance, and is now being discouraged in favour of the wider usage of antiseptics, to which it is more difficult for bacteria to develop resistance.

While evidence of cross-resistance to antiseptics and antibiotics has been documented for many agents, in over a century of use, no significant acquired resistance or cross-resistance has been reported for iodine when used for specific indications. This striking lack of resistance is thought to be due to the diverse mechanisms through which iodine simultaneously exerts its effects.

In a hallmark study, the development of bacterial resistance to iodine was investigated by serial passage of two strains of *Pseudomonas aeruginosa*, two strains of *Escherichia coli*, two strains of *Klebsiella aerogenes*, and one strain of *Serratia marcescens* in the presence of sub-optimal concentrations of iodine that were insufficient to cause cell death. The investigators found that, after 20 passages, no detectable change was observed in the minimal inhibitory concentration of iodine needed, nor the time taken until cell death occurred between the parent strain and the passaged subcultures when exposed to efficacious concentrations of iodine. The PVP-I formulation containing up to 1% available iodine was able to kill all strains tested in under 5 min, with most cells being destroyed within 30 s. While dilute concentrations were noted to take in excess of 10 min to achieve an effect, even these iodine dilutions were successful in killing all strains upon prolonged exposure.

Kiran Mazumdar-Shaw

Kiran Mazumdar-Shaw was born on 23 March 1953 in Bangalore, Karnataka state, to Gujarati parents. She was educated at Bangalore's Bishop Cotton Girl's High School, graduating in 1968. She then attended Mount Carmel College, Bangalore, a women's college offering pre-university courses as an affiliate of Bangalore University. She studied biology and zoology, graduating from Bangalore University with a bachelor's degree in zoology in 1973. Mazumdar hoped to go to medical school, but was not able to obtain a scholarship.

Mazumdar went to Ballarat College, Melbourne University in Australia to study malting and brewing. In 1974, she was the only woman enrolled in the brewing course and topped in her class. She earned the degree as master brewer in 1975.

She worked as a trainee brewer in Carlton and United Breweries, Melbourne and as a trainee maltster at Barrett Brothers and Burston, Australia. She also worked for some time as a technical consultant at Jupiter Breweries Limited, Calcutta and as a technical manager at Standard Maltings Corporation, Baroda between 1975 and 1977.

After a brief period as a trainee manager at Biocon Biochemicals Limited, of Cork, Ireland, to learn more about the business, Kiran Mazumdar Shaw returned to India. She started Biocon India in 1978 in the garage of her rented house in Bengaluru with a seed capital of Rs. 10,000. Although it was a joint venture, Indian laws restricted foreign ownership to only 30% of the company, which meant that 70% of the company belonged to Kiran Mazumdar Shaw.

The company's initial projects were the extraction of papain (an enzyme from papaya used to tenderize meat) and isinglass (obtained from tropical catfish and used to clarify beer). Within a year of its inception, Biocon India was able to manufacture enzymes and export them to the U.S. and Europe, the first Indian company to do so. At the end of her first year, Mazumdar used her earnings to buy a 20-acre property with plans to expand in the future.

Mazumdar spearheaded Biocon's evolution from an industrial enzymes manufacturing company to a fully integrated bio-pharmaceutical company with a well-balanced business portfolio of products and a research focus on diabetes, oncology and auto-immune diseases. She also established two subsidiaries: Syngene (1994) which provides early research and development support services on a contract basis and Clinigene (2000) which focuses on clinical research trials and the development of both generic and new medicines. Clinigene was later merged with Syngene. Syngene was listed on BSE/NSE in 2015 and has a current market cap of ₹23,000 crores.

In 1984, Kiran began to develop a research and development team at Biocon, focusing on the discovery of novel enzymes and on development of novel techniques for solid substrate fermentation technology. The company's first major expansion came in 1987, when Narayanan Vaghul of ICICI Ventures supported creation of a venture capital fund of US$250,000. This money enabled Biocon to expand its research and development efforts. They built a new plant featuring proprietary solid substrate fermentation technology based on a semi-automated tray culture process, inspired by Japanese techniques. In 1989, Biocon became the first Indian biotech company to receive U.S. funding for proprietary technologies.

In 1990, Mazumdar incorporated Biocon Biopharmaceuticals Private Limited (BBLP) to manufacture and market a select range of biotherapeutics in a joint venture with the Cuban Center of Molecular Immunology.

Biocon Biochemicals of Ireland was acquired from Leslie Auchincloss by Unilever in 1989. The partnership with Unilever helped Biocon to establish global best practices and quality systems. In 1997, Unilever sold its specialty chemicals division, including Biocon, to Imperial Chemical Industries (ICI). In 1998, Kiran Mazumdar's fiancée, Scotsman John Shaw, personally raised $2 million to purchase the outstanding Biocon shares from ICI. The couple married in 1998, whereupon she became known as Kiran Mazumdar-Shaw. John Shaw left his position as chairman at Madura Coats to join Biocon. He became Biocon's vice chairman in 2001.

Mazumdar-Shaw's belief in "affordable innovation" has always been a driving philosophy behind Biocon's expansion. Inspired by the need for affordable drugs in less-wealthy countries, she has looked for opportunities to develop cost-effective techniques and low-cost alternatives. She has also proposed that drug companies be cost-sensitive in marketing to developing countries, so that people can afford the drugs they need, particularly chronic therapies.

Mazumdar-Shaw noticed the market potential for statins (cholesterol fighting drugs) early on. When the patent of the cholesterol-lowering drug lovastatin expired in 2001, Biocon got involved in its development. Biocon continues to expand into new areas. Yeast expression platforms offer a desirable alternative to mammalian cell cultures for the genetic manipulation of cells for use in a variety of drug treatments. Unicellular methylotrophic yeasts such as Pichia pastoris are used in the production of vaccines, antibody fragments, hormones, cytokines, matrix proteins, and biosimilars.

Biocon's major areas of research now include cancer, diabetes, and other auto-immune diseases such as rheumatoid arthritis and psoriasis. Because of the high percentage of people in India who chew betel or tobacco, India accounts for eighty-six per cent of oral cancer in the world, known locally as "cancer cheek". Diabetes is prevalent, and people who do not wear shoes are at risk to have a minor scrape or injury develop into gangrene, or "diabetes foot". Biocon is also working on drugs to treat psoriasis, a skin pigment disease.

Bio-pharmaceuticals developed by the company include Pichia-

derived recombinant human insulin and insulin analogs for diabetes, an anti-EGFR monoclonal antibody for head and neck cancer, and a biologic for psoriasis. Biocon is Asia's largest insulin producer, and has the largest perfusion-based antibody production facilities.

In 2004, Mazumdar-Shaw started a corporate social responsibility wing at Biocon, the Biocon Foundation. The Foundation focuses on health, education and infrastructure, especially in rural areas of Karnataka which lack healthcare facilities.

Mazumdar-Shaw dislikes the term "philanthropy", believing that it often provides temporary fixes rather than addressing the root cause or the underlying situation. She prefers the term "compassionate capitalist", believing that properly applied business models can provide an ongoing foundation for sustainable social progress. Mazumdar once said, "Innovation and commerce are as powerful tools for creating social progress as they are for driving technological advancement. When they are put to use for social progress, the implementation is a lot cheaper, a lot more people benefit, and the effect is more lasting." In 2015, she joined The Giving Pledge, promising that at least half of her wealth will be dedicated to philanthropy.

Rural areas in India are estimated to have only one doctor for every two thousand people, it is estimated that 70 million people do not have the money to pay for a doctor's visit or for medicine. The Biocon Foundation is involved in numerous health and education outreach programs to benefit the economically weaker sections of Indian society.

With Devi Shetty of Narayana Hrudayalaya Hospital, Mazumdar-Shaw has supported the development of Arogya Raksha Yojana (Disease Protection Program/Health Help). Through this program Biocon Foundation establishes clinics to offer clinical care, generic medicines and basic tests for those who cannot afford them. As of 2010, seven clinics each served a population of 50,000 patients living within a radius of 10 km, treating in total more than 3,00,000 people per year. Clinics organize regular general health checks in remote villages by bringing in physicians and doctors from network hospitals. To improve early detection of cancer, they have trained young women as community health workers, using smartphones to send photographs of suspicious lesions to oncologists at the cancer center. Public health campaigns such as "Queen of Heart" educate people about specific health issues and promote early detection of problems such as cardiovascular diseases.

The clinics operate based on a model of micro-financed health insurance. Biocon provides low-cost drugs, making a negligible profit on a unit basis, but an overall profit on volume due to the participation of large numbers of people. Clinics also use a "subsidised convenience" pricing plan, under which more wealthy patrons pay full price in return for the convenience of scheduling their visits and procedures at desirable times, while poorer patients can obtain cheap or even free services by choosing less desirable times. Doctors and researchers look for opportunities to use cutting-edge technology in ways that will drive down costs and ensure quality of service.

Mazumdar Shaw Medical Foundation is a non-profit organization and has two arms to support its cause, which are Mazumdar Shaw Center for Translational Research and Mazumdar Shaw Cancer outreach program.

She funded a multi-year research program by creating the Biocon Cell for Innovation Management with Prasad kaipa at the Indian School of Business in 2009.

Mazumdar-Shaw speaks about the importance of improving India's infrastructure, emphasizing the need to address issues such as efficient governance, job creation, and food, water, and health insecurity.

Biocon, Infosys and other companies have had a significant impact on Bengaluru. These companies attract many scientists who would otherwise go overseas. Once a "pensioner's paradise", Bangalore is now called "the best urban working environment in India".Biocon Park, built in 2005, is a ninety-acre campus with five thousand employees. Outside the developed city, however, infrastructure is still poor.

As of 2010, Mazumdar-Shaw was named among TIME magazine's 100 most influential people in the world. She is on the 2011 *Financial Times*' top 50 women in business list. As of 2014, she was listed as the 92nd most powerful woman in the world by Forbes. In 2015, she had risen to 85th in the Forbes ranking. She was voted global Indian of the year by Pharma Leaders Magazine in 2012.

Mazumdar-Shaw is the recipient of several international awards including the Othmer Gold Medal (2014) for outstanding contributions to the progress of science and chemistry, the Nikkei Asia Prize (2009) for regional growth, the 'Veuve Clicquot Initiative For Economic Development For Asia' Award (2007), Ernst & Young Entrepreneur of the Year Award for Life Sciences & Healthcare (2002), and 'Technology Pioneer' recognition by World Economic Forum (2002). In May 2015 Federation University Australia (formerly the University of Ballarat) named a road in its Mt Helen campus as Mazumdar Drive. Kiran and Shaw attended the opening ceremony. She was elected as a member of the United States National Academy of Engineering (NAE) in 2019 for the development of affordable biopharmaceuticals and the biotechnology industry in India. She is the first Indian woman to get this honor. In January 2020, Kiran became the fourth Indian citizen to be honoured with Australia's highest civilian honour.

Her work in the biotechnology sector has earned her numerous national awards, including the Padma Shri (1989) and the Padma Bhushan (2005) from the government of India. She was given the Economic Times Award for 'Businesswoman of the Year' in 2004. At the Pharma leaders Pharmaceutical Leadership Summit she was named "Global Indian Woman of the Year" (2012); she also received the Express Pharmaceutical Leadership Summit Award for "Dynamic Entrepreneur" in 2009. The Indian Merchants' Chamber Diamond Jubilee Endowment Trust's Eminent Businessperson of the Year Award was presented to Kiran Mazumdar-Shaw in 2006 by the Governor of Maharashtra, S. M. Krishna. She has also received the Indian Chamber of Commerce Lifetime Achievement Award (2005), the 'Corporate Leadership Award' by the American India Foundation (2005). and the Karnataka Rajyotsava Award (2002).

Mazumdar-Shaw received an honorary doctorate from her alma mater, Ballarat University in 2004, in recognition of her contributions to biotechnology. She has been awarded honorary doctorates from the University of Abertay, Dundee, UK (2007), the University of Glasgow, UK (2008), Heriot-Watt University, Edinburgh, UK (2008) and University College Cork, Ireland (2012). She received an honorary doctorate from Davangere University, India, at its first convocation, July 2013, in recognition of her contribution in the field of biotechnology.

Jokes

After finishing our Chinese food, my husband and I cracked open our fortune cookies.

Mine read, *"Be quiet for a little while."*

His read, *"Talk while you have a chance."*

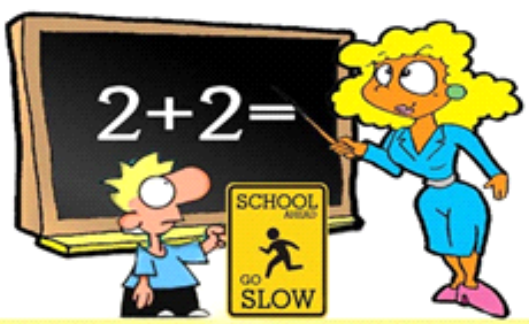
What do you call a sleeping bull?

A bulldozer.

Teacher : why are you sleeping in the class ?? >.<
Student : Your voice is so sweet that is why Im sleeping :P
Teacher : Then why others are not sleeping ? :0
Student : they aren't listenin to you mam :D ♥

A ham sandwich walks into a bar and orders a beer,

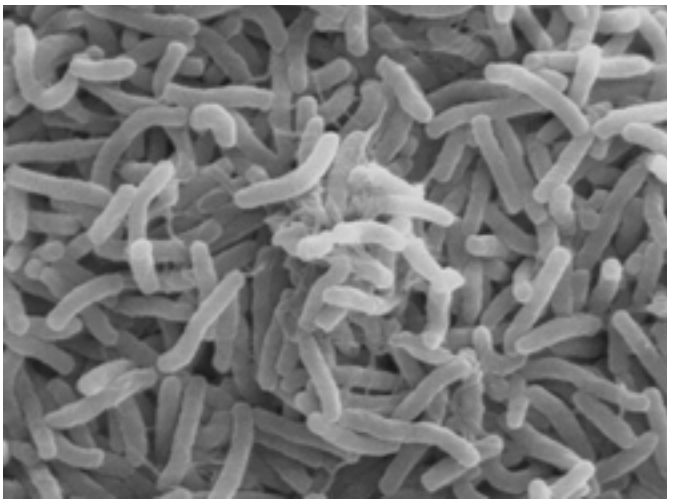
bartender says "sorry, we don't serve food here."



Teacher: Why are you Late Today?
Student: Because of sign down the road.
Teacher: What does a sign have to do with your being late?
Student: The sign said, "School Ahead, Go Slow!"

A lady calls Santa for repairing doorbell,
Santa doesn't turn up for 4 days.
Lady calls again, Santa replies, I'm coming daily since 4 days, I am coming here and pressing the bells for 4 days

Vibrio cholerae



Vibrio cholerae is a species of Gram-negative, facultative anaerobe and comma-shaped bacteria.The bacteria naturally live in brackish or saltwater where they attach themselves easily to the chitin-containing shells of crabs, shrimps, and other shellfish. Some strains of *V. cholerae* are pathogenic to humans and cause a deadly disease cholera, which can be derived from the consumption of undercooked or raw marine life species.

V. cholerae was first described by Félix-Archimède Pouchet in 1849 as protozoa. Filippo Pacini correctly identified it as a bacterium and from him, the scientific name is adopted. The bacterium as the cause of cholera was discovered by Robert Koch in 1884. Sambhu Nath De isolated the cholera toxin and demonstrated the toxin as the cause of cholera in 1959.

The bacterium has a flagellum at one pole and several pili throughout its cell surface. It undergoes respiratory and fermentative metabolism. Two serogroups called O1 and O139 are responsible for cholera outbreaks. Infection is mainly through drinking contaminated water, therefore is linked to sanitation and hygiene. When ingested, it invades the intestinal mucosa can cause diarrhea and vomiting in a host within several hours to 2–3 days of ingestion. Oral rehydration solution and antibiotics such as fluoroquinolones and tetracyclines are the common treatment methods.

V. cholerae is a highly motile, comma shaped, gram-negative rod. The active movement of *V. cholerae* inspired the genus name because "vibrio" in Latin means "to quiver". Except for v.cholerae and v.mimicus, all other vibrio species are halophilic. Initial isolates are slightly curved, whereas they can appear as straight rods upon laboratory culturing. The bacterium has a flagellum at one cell pole as well as pili. It tolerates alkaline media that kill most intestinal commensals, but they are sensitive to acid. It is a facultative anaerobe, and can undergo respiratory and fermentative metabolism. It measures 0.3 µm in diameter and 1.3 µm in length with average swimming velocity of around 75.4 µm/sec.

V. cholerae pathogenicity genes code for proteins directly or indirectly involved in the virulence of the bacteria. To adapt the host intestinal environment and to avoid being attacked by bile acids and antimicrobial peptides, *V. cholera* uses its outer membrane vesicles (OMVs). Upon entry, the bacteria shed its OMVs, containing all the membrane modifications that make it vulnerable for the host attack.

V.cholerae can cause syndromes ranging from asymptomatic to cholera gravis. In endemic areas, 75% of cases are asymptomatic, 20% are mild to moderate, and 2-5% are severe forms such as cholera gravis. Symptoms include abrupt onset of watery diarrhea (a grey and cloudy liquid), occasional vomiting, and abdominal cramps. Dehydration ensues, with symptoms and signs such as thirst, dry mucous membranes, decreased skin turgor, sunken eyes, hypotension, weak or absent radial pulse, tachycardia, tachypnea, hoarse voice, oliguria, cramps, kidney failure, seizures, somnolence, coma, and death.Death due to dehydration can occur in a few hours to days in untreated children. The disease is also particularly dangerous for pregnant women and their fetuses during late pregnancy, as it may cause premature labor and fetal death.

V. cholerae infects the intestine and causes diarrhea, the hallmark symptom of cholera. Infection can be spread by eating contaminated food or drinking contaminated water. It also can spread through skin contact with contaminated human feces. Not all infection indicates symptoms, only about 1 in 10 people develop diarrhea. The major symptoms include watery diarrhea, vomiting, rapid heart rate, loss of skin elasticity, low blood pressure, thirst, and muscle cramps. This illness can get serious as it can progress to kidney failure and possible coma. If diagnosed, it can be treated using medications.

V. cholerae has an endemic or epidemic occurrence. In countries where the disease has been for the past three years and the cases confirmed are local (within the confines of the country) transmission is considered to be "endemic." Alternatively, an outbreak is declared when the occurrence of disease exceeds the normal occurrence for any given time or location. Epidemics can last several days or over a span of years. Additionally, countries that have an occurrence of an epidemic can also be endemic. The longest standing *V. chloerae* epidemic was recorded in Yemen. Yemen had two outbreaks, the first occurred between September 2016 and April 2017, and the second began later in April 2017 and

recently was considered to be resolved in 2019. The epidemic in Yemen took over 2,500 lives and impacted over 1 million people of Yemen. More outbreaks have occurred in Africa, the Americas, and Haiti.

The basic, overall treatment for Cholera is re-hydration, to replace the fluids that have been lost. Those with mild dehydration can be treated orally with an oral rehydration solution (ORS). When patients are severely dehydrated and unable to take in the proper amount of ORS, IV fluid treatment is generally pursued. Antibiotics are used in some cases, typically fluoroquinolones and tetracyclines.

When visiting areas with epidemic cholera, the following precautions should be observed: drink and use bottled water; frequently wash hands with soap and safe water; use chemical toilets or bury feces if no restroom is available; do not defecate in any body of water and cook food thoroughly. Supplying proper, safe water is important. A precaution to take is to properly sanitize. Hand hygiene is an essential in areas where soap and water is not available. When there is no sanitation available for hand washing, scrub hands with ash or sand and rinse with clean water. A single dose vaccine is available for those traveling to an area where cholera is common.

There is a *V. cholerae* vaccine available to prevent disease spread. The vaccine is known as the, "oral cholera vaccine" (OCV). There are three types of OCV available for prevention: Dukoral®, Shanchol™, and Euvichol-Plus®. All three OCVs require two doses to be fully effective. Countries who are endemic or have an epidemic status are eligible to receive the vaccine based on several criteria: Risk of cholera, Severity of cholera, WASH conditions and capacity to improve, Healthcare conditions and capacity to improve, Capacity to implement OCV campaigns, Capacity to conduct M&E activities, Commitment at national and local level Since May the start of the OCV program to May 2018 over 25 million vaccines have been distributed to countries who meet the above criteria.

New Strategy for Iron Fortification in Rice

Iron (Fe) deficiency has become one of the factors limiting plant quality and productivity around the world. IMA (IRONMAN), a family of small peptides, has been recently reported to play a positive role in the Fe deficiency response in Arabidopsis and rice (Oryza sativa). Two OsIMA genes were identified in rice. However, it was still unclear how OsIMA1 and OsIMA2 activate the Fe deficiency response in rice.

In a study published in the *Journal of Experimental Botany*, researchers from the Xishuangbanna Tropical Botanical Garden (XTBG) of the Chinese Academy of Sciences showed that IMA positively regulates Fe homeostasis by interacting with OsHRZs (Haemerythrin Motif-Containing Really Interesting New Gene and Zinc-Finger Proteins), and an artificial IMA peptide derived from OsPRI1 is useful for Fe biofortification in rice.

To verify whether OsIMA1 and OsIMA2 interact with OsHRZ1 and OsHRZ2, the researchers carried out yeast-two-hybrid assays. OsIMA1 and OsIMA2 play positive roles in Fe homeostasis since their overexpression promotes the expression of Fe deficiency inducible genes (Kobayashi et al., 2021). It was reported that Arabidopsis IMAs physically interact with the C-terminal region of BTS (Li et al., 2021) which is an ortholog of OsHRZ1 (Kobayashi et al., 2013). OsHRZ2 is a paralog of OsHRZ1 in rice. To verify whether OsIMA1 and OsIMA2 interact with OsHRZ1 and OsHRZ2, we carried out yeast-two-hybrid assays. OsIMA1 and OsIMA2 were fused with the GAL4 DNA binding domain (BD) in the pGBKT7 vector as the baits, and the C-terminal regions of OsHRZ1 and OsHRZ2 with the GAL4 activation domain (AD) in the pGADT7 vector as the preys. As shown in the growth of yeast, both OsIMA1 and OsIMA2 interact with the C-terminal regions of OsHRZ1 and OsHRZ2 (Figure 1A). OsHRZ1 protein localizes in the nucleus, and OsHRZ2 in both the nucleus and cytoplasm (Kobayashi et al., 2013). To investigate the subcellular localization of OsIMA1 and OsIMA2, mCherry was tagged to the N-end of OsIMA1 and OsIMA2 respectively and expressed in tobacco leaves. As shown in Figure 1B, both OsIMA1 and OsIMA2 were present in the nucleus and cytoplasm. To further confirm the location where the protein interactions occur, we employed the tripartite split-GFP system monitoring the localization of protein complex. The GFP10 fragment was fused with OsIMA proteins in their N-end (GFP10-OsIMAs) and the GFP11 with OsHRZs in their C-end (OsHRZs-GFP11). When GFP10-OsIMA1/2 and OsHRZ1-GFP11 were transiently co-expressed with GFP1-9 in tobacco leaves, the GFP signal was only visible in the nucleus of transformed cells. By contrast, when GFP10-OsIMA1/2 and OsHRZ2-GFP11 were transiently co-expressed with GFP1-9, the GFP signal was visible in both the nucleus and cytoplasm. Taken together, our data suggest that OsIMAs physically interact with OsHRZs in plant cells. The IMAs feature a conserved C-terminal region. We wanted to know whether the C-terminal region is responsible for their interactions with OsHRZs. We performed yeast-two-hybrid assays. OsIMA peptides were divided into two parts, the N-terminal region and the C-terminal 17-amino acid region, and respectively fused to the BD in the pGBK-T7 vector as baits. Yeast growth assays indicated that their C-terminal regions, but not the N-terminal regions, interact with OsHRZs (Figure 2B). The last amino acid A of Arabidopsis IMAs is crucial for their interactions with BTS (Li et al., 2021). The last amino acid of OsIMAs is also A. We asked whether the same case occurs in rice. We generated the full-length OsIMAs with their last amino acid changed from A to V, and fused them with the BD as baits. Yeast growth indicated that the mutation of last amino acid A disrupted the interactions between OsIMAs and OsHRZs .These data suggest that the C-terminal regions of OsIMAs contribute to their interactions with OsHRZs, and the last amino acid A is necessary. To further investigate how OsIMAs regulate the Fe deficiency response, the researchers generated OsIMA1 overexpressing transgenic plants (OsIMAox) in which the OsIMA1 gene was driven by the maize ubiquitin promoter. They found that OsIMA1ox plants mimic the hrz1-2 mutant plants and OsHRZ1 and OsHRZ2 promote the degradation of OsIMAs. The C-terminal region of OsPRIs is required for the interactions with OsHRZ1 and OsHRZ2.They developed an artificial small peptide, aIMA, which possesses the ability to interact with OsHRZs and can be degraded by OsHRZs. Indeed, the increased Fe accumulation and normal fertility were achieved in the transgenic plants overexpressing aIMA peptides. Unlike the strong increase of Fe concentration in the OsIMAox plants, the moderate Fe increase was detected in the aIMAox plants. Moreover, the aIMA overexpressing rice plants 36 accumulate more Fe without reduction of fertility. This work establishes the link 37 between OsIMAs and OsHRZs.

"The artificial IMA strategy can apply to other plant species beyond rice. Our exploration of an artificial IMA peptide provides a new strategy for Fe fortification in crops," said Liang Gang of XTBG.

Best practices in dialysis unit disinfection

Dialysis is a treatment for people whose kidneys are failing. When you have kidney failure, your kidneys don't filter blood the way they should. As a result, wastes and toxins build up in your bloodstream. Dialysis does the work of your kidneys, removing waste products and excess fluid from the blood.

Renal patients have lowered immunity. That makes them more susceptible to infection, and it's much harder for them to recover from it. All this means that keeping a clean dialysis centre is very important.

Preparation for Disinfection of the Dialysis Station

- Gather necessary supplies including:
  - Personal protective equipment (PPE): eye goggles, gown and clean gloves.
  - Properly diluted hospital disinfectant and wipes/cloths (separate wipe(s)/cloth(s) per machine).
  - Biohazard disposal container(s)
- Perform hand hygiene.
- Don gown, eye goggles and clean gloves.
- Disconnect and takedown used blood tubing and dialyzer from the dialysis machine.
- Discard tubing and dialyzers in a leak-proof container (container is brought to the dialyzer station or is placed as near to the station).
- Check that there is no visible soil or blood on surfaces.
- If drain bag is still hanging, remove bag and empty in the soiled utility area.
- Ensure that the patient has left the dialysis station.
  - Patients should not be removed from the station until they have completed treatment and are clinically stable.
  - If a patient cannot be moved safely, delay routine disinfection of the dialysis station.
  - If patients are moved to a separate seating area prior to removing cannulation needles or while trying to achieve hemostasis, disinfect the chairs and armrests in those areas in between patients.
- Discard all single-use supplies. Move any reusable supplies (e.g., clamps) to an area where they will be cleaned and disinfected before being stored or returned to a dialysis station. This may occur before or after the patient has left the station.
- Remove gloves and perform hand hygiene.

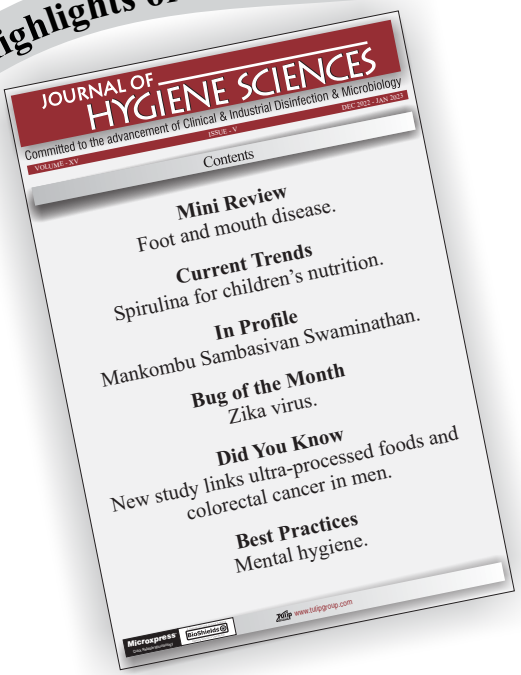
Routine Disinfection of the Dialysis Station

- Perform hand hygiene and don clean gloves.
- Using a wiping motion (with friction), disinfect all surfaces in the dialysis station in contact with the patient and/or staff. e.g., dialysis chair or bed; tray tables; blood pressure cuffs; countertops; keyboard, etc.
- Clean dialysis machine from top to bottom.
  - If visible contaminant on the machine, wipe off using an absorbent material.
  - Clean the machine using wipes/cloths with a disinfectant that is acceptable to the machine manufacturer and the renal program/infection control.
  - Remove excess fluid from the wipes/cloth(s) prior to using to clean machine
  - Clean the top of the machine.
  - If the machine has a door(s), clean the front first, then the insides of the doors.
  - Clean all components of the main interface (screen) and the back of the machine unless recommended otherwise by the manufacturer
  - Clean exposed surfaces of dialysate, concentrate, and bicarb connectors.
  - Clean each side of machine.
  - Clean the area between the main interface (screen) and brakes, including the shelf
  - Clean the brakes.
- Ensure surfaces are visibly wet with disinfectant but not dripping. Allow surfaces to air-dry. Air-drying is recommended to allow for sufficient contact time with the disinfectant.
- Remove gloves, eye goggles and gown.
- Perform hand hygiene.

Preparation for Disinfection of the Dialysis Station

- Gather necessary supplies including:
  - Personal protective equipment (PPE): eye goggles, gown and clean gloves.
  - Disinfectant wipes.
  - Disinfectant concentrate (accelerated hydrogen peroxide).
  - Measuring cup.
  - 1-4L water (depending on number of items).
  - 1-4L container (clean).
  - Drying rack or clean absorbent cloths.
- Perform hand hygiene.
- Don gown, eye goggles and clean gloves.
- Discard solutions if containers are not empty.
- Prepare fresh solutions daily.
- Fill clean container with 1-4L of water.
- Add 25 mL of accelerated hydrogen peroxide per 1L of water (100mL of concentrate for 4L of water).
- Collect dirty small items in soiled utility room until ready to disinfect.
- Wipe any soiled items with approved disinfectant wipes.
- Soak small items in solution for 5 minutes.
- Allow small items to air dry in drying rack or on clean absorbent cloth.
- Discard solutions at end of day.

Highlights of the coming issue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