Microbe of the month

Breaking The Chain of Infection

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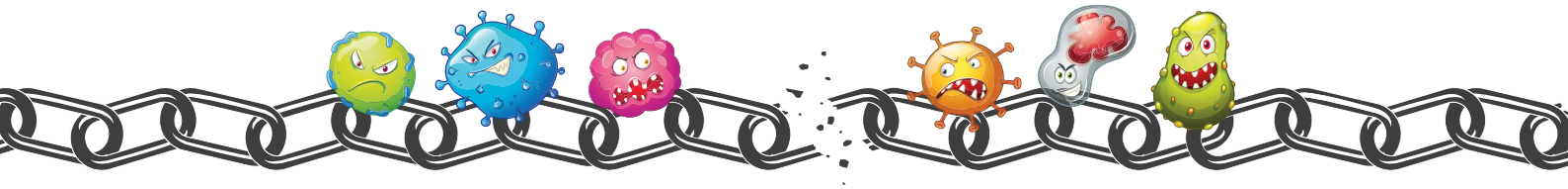


Featured this month:

ESCHERICHIA COLI (E. coli)

The good, the bad and the deadly!

15-minute read + QUIZ

Hello readers!

Microbe of the Month aims to provide a concise clinical resource to help you keep up to date about pathogens of importance, in an easy-to-read and understand format.

Each issue covers the aetiology (sources) and epidemiology of topical bacteria, viruses or fungi - their mode/s of transmission and the infections they cause, alerts on any Antimicrobial Resistance (AMR) capability they may have, and the relevant Infection Prevention and Control measures which should be routinely implemented for the safety of patients and healthcare personnel.

There is a quick quiz at the end of the newsletter to test your grasp of the content – please use this newsletter as a teaching tool in your workplace and start an 'infectious' dialogue about topical issues in infection control!

Escherichia coli (usually abbreviated as '*E. coli*') is a member of the **Enterobacterales** (previously termed *Enterobacteriaceae*) – a Gram-negative, non-spore forming, facultatively anaerobic (i.e., they can survive without oxygen if necessary), rod-shaped bacterium.

E. coli got its first name, *Escherichia*, from the German paediatrician **Theodor Escherich**, who was awarded a Nobel Prize for his discovery of the bacterium in 1885. [1,2]

Its second name, '*coli*', means "from the colon", which is the organism's natural habitat. Most *E. coli* live and grow harmlessly in the gastrointestinal tract of many animals, including humans (i.e., it is a commensal organism and part of our normal flora).

Most *E. coli* are not harmful to humans, and some are even beneficial. Many of us host a population of *E. coli* in our gut which aids digestion and protects us from other harmful microbes. Scientists have used strains of *E. coli* to study fundamental biological processes, contributing to many important scientific breakthroughs, and teaching generations of biology students the fundamentals of the scientific method. Other *E. coli* strains are utilised by researchers in the industry to produce important compounds we use every day. [1,2]

Key words: *commensal flora, pathogenic strain, Shiga toxin, extended spectrum beta-lactamase, bacteriophages, antimicrobial stewardship, infection control.*

THE GOOD - How *E. coli* has contributed to our understanding of biology [2]

The Nobel Prize is science's highest honour, and ***E. coli* has played a key role in many scientific discoveries which 'have conferred the greatest benefit to mankind'**.
Listed below are some of the Nobel-worthy discoveries to which *E. coli* has contributed:

1958	**Bacterial conjugation** (sex), and the ways bacteria share genes with one another.
1959	**DNA replication** – How life copies its genetic code.
1965	**Gene regulation** – How genes are turned on or off.
1968	**The genetic code** – The 'language' in which our DNA is written.
1969	**Viral replication** – How viruses reproduce inside cells.
1978	**Restriction enzymes** – Cellular 'scissors' that allow scientists to cut DNA.
1980	**Recombinant DNA** – The creation of the first genetically engineered DNA.
1989	The enzyme **RNA** is discovered.
1997	**ATP generation** – The energy molecule that powers life.
1999	**Signal sequences on proteins** – one of the ways in which cells organise themselves.
2008	**Green fluorescent protein** – A tag scientists use to track microbial cell components and biofilms.

In the past, **insulin** was harvested from pigs (or even sharks); but by inserting the human gene for insulin into *E. coli* bacteria, human insulin can now be produced inexpensively in large quantities. Another good example of a commercial product produced by *E. coli* is rennin. Used in cheese production, **rennin** was previously harvested from the stomachs of calves – now it is mostly manufactured from special strains of *E. coli*. [2]

With the recent cholera outbreak in South Africa uppermost in our minds, *E. coli* bacteria are used as an everyday marker to determine food and water safety. Because *E. coli* is excreted in faeces, diagnostic tests have been designed to detect all types of *E. coli* (harmless and pathogenic strains) to alert regulators to the possibility of contamination before food or water are consumed. [2]

Fast Fact!

E. coli is usually a harmless commensal in the large intestine, where it assists with digestion and nutrient absorption as well as the production of vitamin K, which is essential for blood clotting. [1,3]

THE BAD - Pathogenesis and virulence of *E. coli* [1,2,3]

There are many different types of *E. coli*, and these are referred to as ***strains***. Importantly, different strains of *E. coli* can mix with each other to produce new strains with a combination of traits. Scientists sort *E. coli* into different strains according to the specific markers they carry on their cell surfaces.

Commensal strains

"Harmless" commensal *E. coli*

Intestinal pathogenic strains (IPEC)

EPEC — enteropathogenic *E. coli*

EHEC — enterohemorrhagic *E. coli*

EIEC — enteroinvasive *E. coli*

ETEC — enterotoxogenic *E. coli*

Causing diarrhea

Extraintestinal pathogenic strains (ExPEC)

NMEC — meningitis *E. coli*, causing newborn meningitis (NBM)

UPEC — uropathogenic *E. coli*, causing UTI and pyelonephritis

SEPEC — sepsis associated *E. coli*

Figure 1. **The different strains of *Escherichia coli* and the infections they cause.** [2]

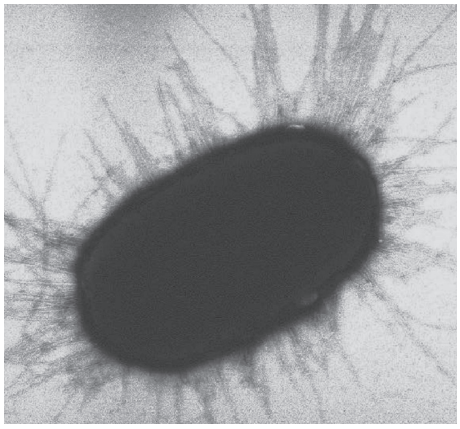
Special **virulence characteristics** (which enhance their capacity to cause disease) have been identified in *E. coli* bacteria which help them to overcome host defences and invade tissue:

- **Fimbriae**: These tiny hair-like projections help with adherence of the bacteria to the lining of the jejunum and ileum, and the epithelium of the urinary tract in diarrhoeal and urinary tract infections respectively.

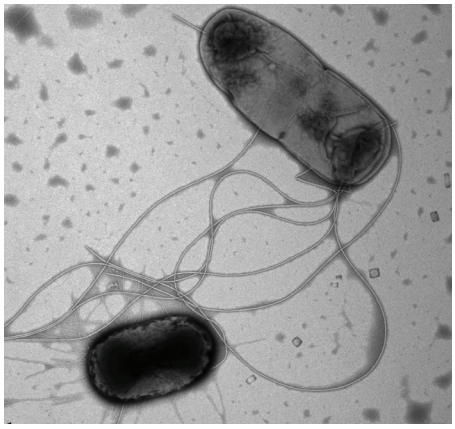
- **Cell capsule**: A special polysaccharide coats the cell, interfering with immune detection and phagocytosis by leukocytes, playing a major role in systemic infections.

- **Endotoxins** (lipopolysaccharide): These are released upon bacterial lysis (death) and are responsible for the features of Gram-negative sepsis such as fever, hypotension and disseminated intravascular coagulation (DIC).

- **Exotoxins** (e.g., Shiga toxin): These virulent proteins act on the cells of the jejunum and ileum to cause profuse watery diarrhoea.



Scanning electron microscopy image of *E. coli*. Note the tiny hair-like projections (fimbriae) **which are used for irreversible adhesion to tissue.**



Electron micrograph of the H30 pandemic strain of *E. coli* (usually a urinary tract pathogen, but may also cause blood stream and other infections).

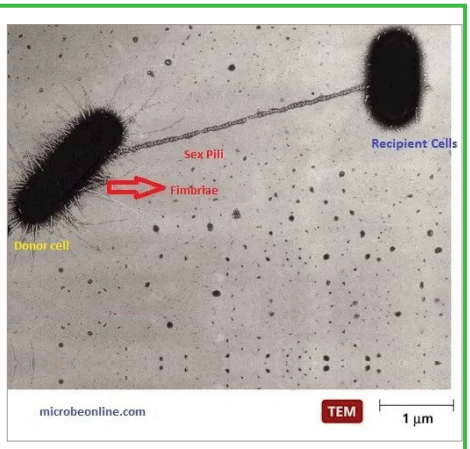


Image depicting the process of bacterial 'conjugation'. The extension of 'sex pili' act as a conduit for the transfer of resistance genes between bacterial cells.

THE DEADLY - Spectrum of infections caused by *E. coli* [3]

01 Complicated urinary tract infection (UTI):

- Because *E. coli* is a bowel commensal, it gains access to the urinary tract either via the perineum (in females) or contamination of urinary catheters / instrumentation during breaches in aseptic technique.
- The urinary tract is the most common site of *E. coli* infection, and more than 90% of all uncomplicated UTIs are caused by **uropathogenic strains** of *E. coli* (the recurrence rate after a first *E. coli* UTI is 44% over 12 months).
- Individuals with multiple prior episodes of urinary tract infection, multiple courses of antibiotic therapy, urinary tract obstruction, or infection developing after urinary instrumentation or catheterisation tend to develop urinary infections caused by antibiotic-resistant strains of *E. coli*.
- Signs and symptoms are usually sudden in onset, and include dysuria, increased frequency / passing small volumes of cloudy urine, urgency, suprapubic pain, back pain, concentrated appearance, and haematuria. (Note: These symptoms may not be present if the patient has an indwelling catheter.)
- **Confusion, hypotension and pyrexia may be a sign of bacteraemia and impending sepsis.**
- **Failure to treat a complicated urinary tract infection, or a delay in treatment, can result in sepsis and SIRS (systemic inflammatory response syndrome), which carries a mortality rate of up to 50%.**

02 Acute bacterial meningitis:

- Most cases of neonatal meningitis are caused by *E. coli* and Group *B Streptococcal* infections. Pregnant women are at a higher risk of colonisation with the K1 capsular antigen strain of *E. coli*, and this strain is commonly observed in neonatal sepsis with a mortality rate of 8%.
- Most infant survivors have subsequent neurologic or developmental abnormalities, especially those with a low birth weight and a positive cerebrospinal fluid (CSF) culture.
- *E. coli* meningitis is rare in adults, but may occur as a healthcare-associated infection (HAI) following neurosurgical trauma or procedures involving the CNS.

03 Pneumonia:

- *E. coli* respiratory tract infections are uncommon and are almost always associated with an *E. coli* UTI.
- However, *E. coli* bronchopneumonia may also be community-acquired in patients who have underlying diseases, such as diabetes mellitus, alcoholism and emphysema.
- Healthcare-associated *E. coli* pneumonia may also result from micro-aspiration of upper airway secretions in critically ill and ventilated patients. (Note: *E. coli* bacteraemia may precede pneumonia – usually from another focus of *E. coli* infection in the urinary or gastrointestinal tract/s.)

04 Intra-abdominal infections:

- These usually result from a bowel perforation (e.g., the appendix, a diverticulum or disrupted colonic anastomosis) or are associated with an intra-abdominal abscess, cholecystitis or ascending cholangitis. Patients with diabetes mellitus are also at high risk of liver abscesses.

05 Wound infection:

- Chronic wounds soon become colonised with strains of *E. coli* (transferred from the gut by unwashed hands, house pets or contaminated surfaces in the environment), and are therefore prone to infection if cleansing, debridement and excess exudate levels are not managed proactively.
- **The use of dressing products which control local wound bioburden through hydrophobic attraction and the irreversible binding of surface microbes** (e.g., DACC dressings) **is a safe and useful measure for promoting antimicrobial stewardship (AMS), preventing the premature or unnecessary use of topical antiseptics in heavily colonised but healing wounds.**
- For wounds which are clinically infected (or have an unacceptably high risk of infection with potentially devastating consequences), the use of topical antimicrobial antiseptics such as PHMB, chlorhexidine, povidone iodine, medicinal Manuka honey or silver are all suitable options, in conjunction with wound cleansing and appropriate debridement methods to minimise the formation of biofilm or slough, which hinder the action of locally-applied antimicrobial agents.
- Dressings for moderate to highly exuding wounds should have proven fluid handling capacity (including under compression therapy) and ideally, the ability to sequestrate (contain or isolate) microorganisms and harmful proteases away from the wound bed, hindering the cyclical inflammatory process which delays healing.

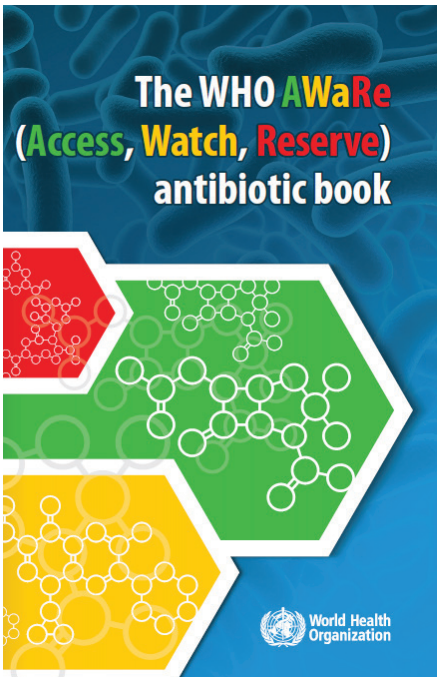
06 Enteric infections:

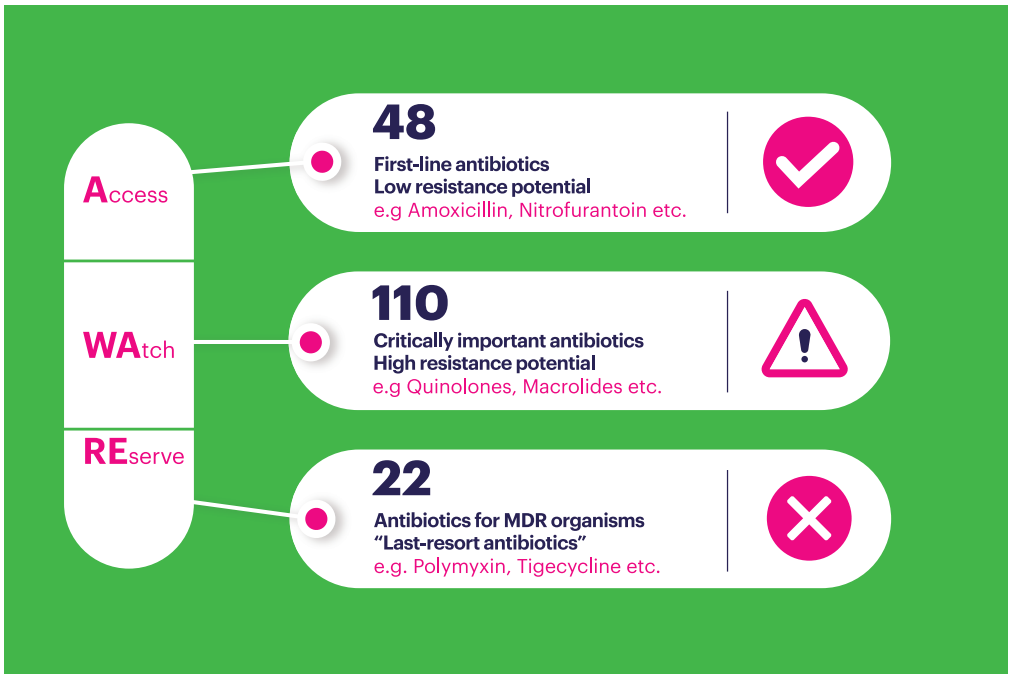
- *E. coli* O157:H7 is one of the most virulent strains which causes food poisoning after the ingestion of contaminated ground beef, unpasteurised milk or contaminated water.
- The 'Shiga' toxin produced by this strain may cause stomach cramps, vomiting, acute dehydration, fever, bloody diarrhoea and kidney failure, and has been responsible for numerous outbreaks worldwide.
- Note: antibiotics are not routinely recommended for patients with suspected *E. coli* O157 diarrhoeal infections, and most cases resolve within 3 days with supportive management.

E. COLI AND ANTIMICROBIAL STEWARDSHIP (AMS) [2]

***E. coli* is genetically promiscuous.** It exchanges genes with other strains of *E. coli* and even unrelated species of bacteria, which can result in a non-harmful *E. coli* strain becoming pathogenic or antibiotic resistant. Moreover, **the replication** ('doubling') **time of *Escherichia coli* bacteria is only 20 minutes!**

- The most common way that *E. coli* bacteria exchange genes is by infection with special viruses that target bacteria, called **bacteriophages** (or 'phages'). Bacteriophages replicate by injecting their genes into *E. coli*, 'hijacking' the bacterium's internal machinery – effectively taking over the bacterium. Once this occurs, the infected bacteria disintegrate, releasing millions of viral copies which go on to infect other bacteria.
- Antimicrobial resistance (AMR) genes are also transferred from one bacterium to another by **conjugation**, the bacterial equivalent of sex. To begin the process, one bacterium extends a 'bridge' called a 'sex pilus' to another bacterium, establishing a physical connection between the two bacteria. Once this link is established, genes on DNA structures called plasmids are transferred from one bacterium to the other. Conjugation is a common way for antimicrobial resistance (AMR) to be spread amongst many different bacteria.





The WHO AWaRe system groups the hundreds of different antibiotics used globally into three simple categories – '**Access, Watch and Reserve**' – based on their clinical importance and the risk of their use promoting resistance. Clear guidance is provided on the choice of antibiotic, formulation, dose and duration for essential antibiotics for hospitals and primary healthcare settings, including guidance on when not to use antibiotics. [4]

THE BOTTOM LINE... [2,3,4]

- *E. coli* is spread via the '**contact route**', which may be directly via unwashed hands, or indirectly through contact with contaminated surfaces, invasive catheters and shared patient equipment in the hospital setting.

- Given the wide spectrum of infections caused by this pathogen, hand hygiene, aseptic technique and scrupulous attention to personal hygiene after using the toilet is critical for the prevention and transmission of infection.

- Avoid unnecessary urinary catheterisation and implement catheter-associated **UTI (CAUTI) infection prevention bundles**.

- Urinary catheters and drainage bags should be treated as a 'closed system'; bladder instillations and washouts should not be used to prevent urinary infection. Remove urinary catheters as soon as they are no longer required.

- **Patients colonised or infected with an antibiotic-resistant or pathogenic strain of *E. coli* should be isolated from other patients, and strict contact precautions implemented.**

  - Handle used and soiled linen carefully and dispose of healthcare risk waste correctly.
  - Supervise cleaning practices, using a sodium hypochlorite-based detergent cleaner (incl. colour-coded cloths, mops and buckets). Frequently touched surfaces should be disinfected at least twice daily.
  - Limit transport of these patients and always inform receiving departments / hospitals of the patient's multi-drug-resistant (MDR) status.

- Always obtain cultures before antibiotic therapy is commenced; **use antibiotic guidelines** and start antibiotics promptly where clinically indicated.

- Without the implementation of **antibiotic stewardship measures** for last-line, potentially life-saving antibiotics, we will likely rapidly lose their efficacy, with few to no treatment options in the near-future.

Supply the correct answer!

Question 1. *Escherichia coli* (*E. coli*) is a member of the _____ family of bacteria.

Question 2. *E. coli* has played an important role in scientific discoveries – including the production of _____ for Type 1 diabetics.

Question 3. Tiny hair-like projections called _____ help with adherence of *E. coli* bacteria to tissue and the lining of the bladder and small intestine.

Question 4. The _____ _____ produced by the strain O157:H7 of *E. coli* causes stomach cramps, vomiting, bloody diarrhoea and kidney failure, and has been responsible for numerous outbreaks worldwide.

Question 5. Antibiotic resistance genes are transferred via 'sex pili' between bacteria on structures called _____.

ANSWERS: 1. Enterobacterales **2.** Insulin **3.** Fimbriae **4.** Shiga toxin **5.** Plasmids

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