



27TH MARCH 2019

INFECTIONS OF THE ABDOMINAL ORGANS

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Infections of the gut and other abdominal organs are some of the most important in history and today. Over the course of history, they have killed many millions and the origins of much of public health, sanitation and epidemiology are bound up with these infections. This includes many great figures of public health including John Snow, Florence Nightingale, Edwin Chadwick and Joseph Bazalgette. We are currently seeing a major shift in importance of different infections globally and this is set to continue over the next few decades. Infections of the gut, liver, spleen and urinary tract system have different causes and outcomes. This talk will consider each of these in turn including progress that has been made against them.

The gut is central to our defence against infections and needs to be. Every day in typical high-income diet we eat and drink more than 200,000 microbes most of which are harmless. In low income settings a greater number of these are dangerous. As the gut is constantly under assault it has many layers of defence including smell, taste, stomach acids, physical barriers and multiple layers of the immune system. One in nine deaths in children worldwide are caused by diarrhoea. Bacteria cause dangerous gut infections by several mechanisms. These include toxins, direct invasion, inflammation of the gut wall and damaging the ability the gut to absorb.

The classic example of a toxin mediated gut infection causing diarrhoea is cholera. Its toxin leads to a massive release of water from the gut. People die of rapid dehydration. It is mainly transmitted where water has been contaminated by human faeces. Arguably cholera is one of the reasons that the epidemiology of infectious diseases was first understood; John Snow in around 1854 showed how it was transmitted by contaminated water in a London epidemic. Famously he mapped cases onto a pump in Broad Street and theatrically removed the water handle. From that time, it became clear that the key to preventing cholera deaths is providing safe water, sewerage and more recently oral rehydration. Currently cholera epidemics still occur, mainly associated with war, disaster and chaos. It still affects an estimated 3 to 5 million people worldwide. Current major outbreaks include Yemen (due to war) and Mozambique (due to flooding).

The bacteria *E. coli* can also produce a toxin which has some similarities although it is usually much milder than cholera. It causes probably more than 50% of travellers' diarrhoea. As sanitation and plentiful water for handwashing is spreading through the world the probability is this will decrease in importance. Some ingested bacterial toxins can cause diarrhoea and vomiting even if the bacteria is not present. Staphylococcus, the bacteria normally found on the skin can produce a toxin which if someone contaminates foods can cause an explosive short-lived diarrhoea.

Bacterial infections which invade or inflame the gut lining can also cause what is commonly called food poisoning. Examples include Campylobacter and Shigella. Shigella is a mainly human to human transmitted infection whilst campylobacter primarily comes from poultry, particularly when undercooked. Salmonella food poisoning presents rather differently and for this, animals are the main reservoir. There was a major epidemic of salmonella associated with eggs in the UK. Poultry vaccination contributed to this epidemic largely ending.

Typhoid and paratyphoid infections, also known as enteric fevers, are wholly human diseases. They are passed person-to-person faeco-orally and associated with lack of water and sanitation. They invade the body and cause systemic illness. Once good sanitation is in place they tend to disappear. Antibiotic resistant typhoid is an increasing problem. There is now a significant spread of drug-resistant *Salmonella typhi* around the world. For most



of these diseases the long-term solution is handwashing with soap and readily available toilets, ideally with good sewerage.

Viral infections can also lead to significant diarrhoeal disease. Rotavirus is the most common severe diarrhoea in infants and young children, by age 5 most children have been infected globally. Good sanitation and hygiene can help, but the key to controlling it in higher income countries has been rotavirus oral vaccine. It has led to a substantial drop in cases in the UK and elsewhere and is now being deployed widely in Africa and Asia. As a result of improving sanitation and vaccination, deaths from diarrhoea and enteric fevers are rapidly falling almost everywhere. Currently around 8.6 global deaths in children under five are due to diarrhoea but this is declined more than 30% since 2000.

Whilst the greatest burden of diarrhoeal diseases is in children, outbreaks of viral disease can cause seasonal local outbreaks in adults and the most important of these is norovirus. This is very easy to catch and causes around 20% of diarrhoea in high-income countries. Rather like flu norovirus strains globally change over time. There is no vaccine on the horizon for this infection.

Several parasites can also cause diarrhoea. The commonest of these is the single celled parasite giardia. Up to 260 million people are infected worldwide and over 4000 cases a year occur in the UK. Although it is carried by some animals, humans are the main risk. Here it damages the absorption of the upper part of the gut leading to bulky offensive stools. It is easy to treat although there is some drug resistance. Another single cell organism, an amoeba, generally affects the lower part of the gut and can cause dysentery (bloody diarrhoea).

The gut is also home to a large number of worm species. Two important ones, passed on by the faecal oral route, are *Ascaris* (roundworm) and *Trichuris* (whipworm). There are also worms which are spread to the environment by open defecation and get into the body by penetrating the skin when people walk barefoot or lie on beaches. All of these worms caught from the environment are infections of poverty and when sanitation and plentiful water are available largely disappear.

One species that has found a way around improvements in sanitation and hygiene is pinworm or threadworm. This lays eggs perennially that are very itchy. Infected children scratch themselves and can then pass them on by touching their own, their friends and their family's mouths.

There are a large number of worms that can be transmitted by eating uncooked or undercooked meats. Many exotic dishes, particularly but not limited to Southeast Asia, can lead to transmission. In terms of numbers the most important are beef and pork tapeworm. The cycle is that human faeces is eaten by a cow or pig directly or indirectly. This contains eggs which lead to cysts in the meat. If the meat is eaten uncooked it causes tapeworm in humans.

After the gut the second organ to consider is the liver. The most well-known infections of the liver are hepatitis. Viral hepatitis A and E are passed on faeco-orally. They cause inflammation of the liver and often jaundice. Most people make a full recovery from Hepatitis A. Because it is a disease of limited sanitation it is rare in high-income settings except in high-risk groups and there is a highly effective vaccine. Hepatitis E is rarer and more dangerous, with around 1% mortality and is particularly dangerous to pregnant women.

Hepatitis B and C are blood-borne and sexually transmitted viruses. Hepatitis B is very common and easy to catch. In many parts of the world there is vertical transmission mother to child, and then horizontal transmission between children with most infected before five years old. There can also be sexual and blood-borne transmission in adults. Hepatitis B can cause cirrhosis and liver cancer. There is a highly effective vaccine. Hepatitis C is much harder to catch, and the great majority is acquired in adults mainly from unsafe medical practice and intravenous drug use. There is no vaccine. Over the last 10 years several highly effective oral drugs have been deployed. Hepatitis B and C combined cause a substantial proportion of liver cancers.

Several other infections can cause hepatitis. This is however mainly self-limiting and seldom the major cause of illness. Viruses include HIV, EBV and influenza. Bacteria include brucellosis from unpasteurised milk products and disseminated tuberculosis.



Whilst hepatitis causes generalised inflammation of the whole liver, several infections can cause localised problems. Abscesses can occur in the liver as other organs. These are usually from gut bacteria. They can suggest other gut damage and usually occur in older people. Treatment is to drain the pus and give antibiotics as for other abscesses. In areas with more limited sanitation amoebic liver abscesses can occur often in much younger patients. A parasitic infection which can look like an abscess is hydatid disease from the dog sheep cycle.

A number of specialist flukes have a natural home in the liver; some of them are specifically human diseases and others are animal diseases with humans accidentally infected. All of them pass through a snail cycle. Important ones include the Asian liver flukes which are caught by eating undercooked fish. They can cause liver and bile duct cancer. Some forms of schistosomiasis, caught by swimming in infected waters, can also cause fibrosis of the liver, although this is much less of a problem than it was historically. Some large flukes, many from sheep and cattle can be caught from eating or chewing plants.

The spleen is a significant part of our defence against infection and in particular protecting against encapsulated bacteria including pneumococcus and meningococcus. It also plays a role in removing malaria parasites from the blood and protect against the red tickborne blood parasite babesia.

The spleen can also be hiding place for infections. Two important ones are the bacterial infection melioidosis which causes spleen micro abscesses, and a parasitic infection leishmaniasis that is passed on by sand-flies. Whilst most of the infections highlighted above are decreasing in importance, infections of the urinary tract and kidneys are set to increase. Their importance varies by age. Children can get urinary tract infections, and after the age of about three months girls are more prone to this than boys due to their shorter urethras. They are caused by infection with gut bacteria, in particular *E. coli*.

In younger adults, who will occasionally get bladder infections the aim is to prevent or treat kidney infection (pyelonephritis). Less than 3% of cystitis or bacteria progress to pyelonephritis. They are usually relatively easily treated if there is no obstruction from kidney stones or other anatomical features. Among young healthy women specific clones of *E. coli* cause >90% of cases. The main future threat is antibiotic resistance.

The major change in urinary tract infections comes as the population grows older. Urinary infections are the commonest bacterial infections in those over 65 - over 10 years around 20% will have at least one infection. There is an increased risk of this converting to sepsis as we grow older, and higher probability of sepsis leading to mortality as we age. Urinary tract infections are also associated with delirium. There is evidence of an increase over time. Urinary tract infections present a dilemma to GPs and other doctors; overtreatment with antibiotics is associated with drug resistance but treatment delay is associated with increased sepsis and mortality.

Overall there has been a generational transformation in infections of the abdominal organs, and this is continuing. The diarrhoeal diseases of limited sanitation and water, which dominated medicine, are going as the world develops. Most parasitic diseases of the gut and liver are also on the way out. Hepatitis has remained a serious issue, but we now have tools to tackle it. Infectious diseases of ageing rather than of poverty will become increasingly important. There is therefore a global shift from infectious diseases of the gut, liver and spleen to those of the urinary tract.