Infections Transmitted Via the Respiratory Route
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This lecture is one of a series looking at the routes of transmission by which infections are passed from one person to another. Understanding the route is key to understanding the diseases and combating them. These notes are not a direct transcript of the lecture but rather an indication of the main points covered.

The respiratory route has several advantages for the infection. Whilst it does require the person infecting to be relatively near the infected person, they do not need to be touching, to know one another or be in the same place at exactly the same time. A stranger in a crowded room can transmit to many others, leading to onward infections in multiple households. To achieve this, the infection has to remain viable outside the house long enough to infect.

Several major infections have evolved to take advantage of the respiratory route of transmission. These include the mycobacteria including tuberculosis; bacteria including pneumococcus, meningococcus and plague (also transmitted by the vector route); atypical bacteria such as Legionella; many viruses including measles, 'flu, COVID-19, smallpox.

Transmission via the respiratory route can take several forms. Much of the transmission for many diseases is via droplets. Sometimes these can land on objects which are touched by people's hands which then touch their face. These objects can remain infectious for some hours or longer. Direct mouth-to-mouth infection is also possible, for example parents kissing their children. Large and medium sized droplets travel quite small distances, often 1-2 m, before dropping to the ground or a surface. Coughs or sneezes may increase the range and will increase the number, but speaking, singing or breathing can also produce droplets. Aerosols, made up of much smaller droplets can be airborne for some period and travel longer distances, potentially infecting people further away and over an extended period for some infections.

Infections transmitted via the respiratory route can cause damage throughout the body. With some infections, the main damage is in the lungs, especially pneumonia. But for others, most of the damage is elsewhere including several causes of meningitis, sepsis, infections of the nerves and diseases of the heart. Medical staff broadly divide respiratory infections into upper and lower respiratory tract infections. Upper respiratory tract infections are of the nose, throat and upper airways. Many are trivial including coughs and colds. But they are also the route of entry for many serious infections. Lower respiratory tract infections are lung infections especially pneumonia. Many infections can be both, including COVID-19.

The body has multiple layers of **defence** against respiratory infections which include mucus. It is a physical barrier constantly being excreted and contains enzymes and antibodies. This includes mucus moving up from the lower lungs via the mucociliary escalator. Behind this are several other layers of immunological defence including the innate and adaptive immune system.

For an infection transmitted via the respiratory route we can use a number of **countermeasures which use the physical environment** to reduce the risk of transmission. Using outdoor spaces for meeting people significantly reduces the risk including through the rapid dilution aerosols, people being generally more geographically spaced out reducing the effect of droplets and ultraviolet light.

Ventilation can also be improved indoors, ranging from natural ventilation by opening windows through engineering in ventilation whilst keeping in heat. Ventilation can be engineered in through natural drafts, the effect of hotter air rising, and mechanical ventilation, +/- filters or ultraviolet light to remove or kill pathogens.

Personal behaviours can also help reduce the chances of passing on respiratory infections. Staying at home and isolating when unwell with a respiratory infection helps prevent spread to others. Maximising social time outdoors or with good ventilation, covering mouth and nose when coughing or sneezing, washing hands and disposing of tissues are all simple actions which help reduce transmission. In periods of high transmission, for example epidemics, facemasks can reduce the risk of transmitting via droplets and aerosols.

Poverty and deprivation play an important role in increasing the risk of respiratory infections. Reasons include poor housing, crowding, poorly ventilated working conditions, diet and malnutrition, access to vaccines and curative medical services. As poverty has decreased in many countries, some infections transmitted via the respiratory route have as well.

There is clear evidence that **smoking increases the risk of many respiratory infections**. These include tuberculosis, influenza and pneumococcal pneumonia. Smoking damages the lungs' defences and can lead to chronic obstructive airways disease, a very debilitating condition which leaves people vulnerable to repeated respiratory infections.

Some **occupations** also increase the risk of respiratory infections. Close contact occupations including healthcare workers, social care workers but also activities such as taxi drivers or front of house staff who meet many people at close quarters indoors increase risk of transmission. Some occupations damage the lungs' defences against infection, including mining and several occupations cause dust. Some occupations increase risk as specific infections, for example farming for fungal and zoonotic diseases.

Respiratory infections are often **seasonal,** particularly in the winter months. This is particularly likely where infections are in rough balance with population immunity. In winter, several changes occur which advantage the infection, including more time together indoors, windows shut, lower temperatures, changes in humidity and lower ultraviolet light.

Medical countermeasures against infections transmitted by the respiratory route include drugs such as antibiotics and antivirals, and vaccines. We have vaccines for some, but not all, infections via the respiratory route. Some prevent infection occurring at all whilst others are more effective at preventing severe disease.

Some diseases of importance transmitted via the respiratory route.

Historically, **tuberculosis** was common everywhere, killing people in all walks of life including in the UK. It is still a leading cause of death worldwide. It is mainly spread by droplets via the respiratory route. If untreated, people can be chronically infected and infectious over many years. Malnourished and immunosuppressed people are most at risk. When the NHS was established, TB was a major cause of mortality, but it has dropped sharply over the succeeding decades. This is due to a combination of improved living conditions, reduced poverty and proper treatment. The first effective drugs were introduced in 1946 (streptomycin). We now have highly effective treatments for the great majority of cases. The key to preventing spread of pulmonary TB is early diagnosis followed by six months of multidrug treatment. While spread is respiratory, TB is not just a disease of the lung. TB meningitis of the brain generalised (miliary), TB around the heart, TB of the spine and bones, TB of the kidneys and glands and of the lymph nodes all occur. Whilst treatment is central to control, tuberculosis vaccination with BCG helps prevent severe disease although it has limited impact on transmission. Over the coming decades there are several opportunities and one major threat with TB. Opportunities include reductions in global poverty, improve diagnosis and treatment and treatment and prevention of HIV. The major threat is multidrug resistant TB which is already widespread.

Leprosy, one of the most feared and stigmatised diseases, was another mycobacterium historically of great importance. Transmission is thought to be through droplets from the nose and mouth. This requires close prolonged contact. Leprosy destroys nerves, can lead to blindness and multiple disabilities. It can now be treated with affected multidrug treatment and BCG is a fairly effective vaccine against it. Leprosy is now much rarer than it was historically.

Diphtheria used to be a major cause of death especially in children. It is mainly transmitted by droplets. The infection is in the throat, but the damage is caused by toxins from the bacteria. They can be local effects with massive swelling compressing the throat, but the toxins can also cause heart block stopping the heart working effectively, and nerve damage. Improved living conditions, antibiotics and a highly effective vaccine have led to a substantial reduction in this serious infection.

Another bacterial throat infection which can cause systemic effects is streptococcal sore throat leading to **rheumatic fever**. Spread by droplets this can cause joint pains, neurological effects and, probably most

importantly, permanent heart valve damage that can cause a child lifelong problems. The damage is not caused by the infection itself but by the immunological response to it. Once very common, appropriate use of antibiotics among other things have led to this being much rarer.

Several forms of **bacterial meningitis** are transmitted via the respiratory route. These include meningococcus (A, B, C, W, X, Y). It can cause rapid meningitis or septicaemia with very high mortality if untreated. We now have effective vaccines against all important forms of meningococcus. The dominant form depends on geography. In Africa, meningococcus A epidemics used to be very large but have been almost entirely gone since the introduction of vaccines although cases still occur. In the UK, meningococcus B and C have been dominant but are now substantially reduced due to vaccination.

In children under 4, the most common form of meningitis was the bacteria *Haemophilus influenzae* b (Hib). This is passed on by droplets through coughing or sneezing. One in 20 children with this meningitis died and one in five were left with serious neurological disability. The Hib vaccine has reduced incidence by more than 90%.

Measles, spread by coughs and sneezes, is often underestimated. It is highly infectious and up to 90% of immune-naïve children near an infected person will catch it. It can remain in the air for up to 2 hours. In epidemics where there is poor nutrition, especially reduced Vitamin A, mortality of 5 to 10% can be reported. Although mortality is significantly lower in high-income settings, measles can still kill children or cause permanent neurological damage from encephalitis (brain inflammation). For that reason, vaccination has been a major step forward to reduce mortality and disability in children and the measles vaccine is usually effective lifelong.

Along with vaccine against measles, the MMR vaccine provides protection against mumps and rubella, two other infections spread by the respiratory route**. Mumps** used to cause one in four cases of viral meningitis in children prior to MMR. **Rubella**, passed on by droplets, can cause a significant risk for miscarriage, stillbirth and faecal abnormalities if women catch it in early pregnancy.

Pneumonia, caused by bacteria, viruses or occasionally fungi, is very common with up to 450 million cases a year globally. Historically, it has killed people throughout their lives but now that we have effective antibiotics deaths tend to occur in the very young, the very old, those living in less wealthy countries with limited access to treatment and the immunosuppressed. In many settings, it is the most common cause of mortality, especially in children, and remains a leading cause of mortality in the UK, mainly amongst older adults.

The most common bacterial cause is pneumococcal pneumonia. **Pneumococcus** is carried in the throats of many adults and over half of preschool children and is transmitted by droplets and secretions. It can cause a significant lobar pneumonia which has to be treated with antibiotics. Pneumococcus can also cause meningitis and sepsis particularly in young children and those over 65 years old. There is very high mortality for untreated pneumococcal meningitis and survivors often have significant disability. There is now routine immunisation for the 13 most common strains in infants and vaccination for over 65s. This has led to a significant reduction in invasive pneumococcal disease and some reduction in pneumococcal pneumonia although cases are still common.

As a result of better living conditions, better treatment and vaccination, global under five deaths due to pneumonia have decreased significantly even in lower income settings over the last two decades.

Viral pneumonia makes up a large portion of the pneumonia, but a much smaller proportion of pneumonia deaths pre COVID-19. In children, the most important is respiratory syncytial virus (RSV) for which we currently do not have vaccines.

Influenza is important both in children and in older adults. There have been significant spikes in global seasonal influenza every winter up to 2020/21 when the social distancing necessary for tackling COVID-19 reduced influenza rates to very low levels. Whilst influenza spikes usually occur at roughly the same time of year every year over late autumn and winter, both the number of people infected and the number of people dying can vary significantly from one year to the next. In some years the influenza is more virulent than others, or infects more people, or less well matched to the seasonal 'flu vaccine for that year.

By contrast, the 1918 **influenza pandemic** probably killed between 50 and 100 million people globally (estimates vary but all include very high numbers). The speed and scale of the pandemic had a massive impact. In addition to the very young and very old who are usually at most risk of dying from seasonal influenza, young adults were also at risk.

The final major respiratory infection to consider is the newest: **COVID-19**. I have covered the early stages of this (although some of the science has moved on), and vaccines against the disease, in previous lectures but a few points from recent events are worth highlighting. This coronavirus has only been with us for just over two years at the time of this lecture. It spread very rapidly by the respiratory route first in China and then around the world. There were previous coronaviruses affecting humans (and many human ones), including the four human coronaviruses which cause colds and sore throats; these are often common and rarely serious. At the other end of severity, two previous coronaviruses transmitted by the respiratory route have jumped from other species: MERS-CoV from dromedaries in the Arabian Peninsula with a 35% case fatality rate and SARS with around 11 to 15% case fatality rate but with small numbers infected to date.

As the UK has gone through each successive wave of COVID-19, the medical countermeasures against it have improved. In the first wave there were very limited diagnostic tests, no treatment, no vaccine and no population immunity. We therefore were entirely dependent on social measures in which the whole population substantially reduced their social and work interactions to reduce transmission. Without this, the size of the wave, the impact on the NHS and disease mortality would have been much higher. In the alpha wave we had good and widely available diagnostic tests, better hospital treatment but only early vaccine rollout and no antivirals. We therefore remained heavily dependent on social measures. By the delta wave, vaccines had been rolled out so there was high population immunity. Despite that, and delta being at least as severe as previous variants, there was a more limited need for social measures because most of the reduction in hospitalisation and mortality was achieved by vaccination and other medical countermeasures.

In the omicron wave, the vaccine plus the booster, some antivirals, and a less severe variant (but still with significant hospitalisation) have required many fewer social measures than would have been needed in previous waves of a similar size. The total number of hospital cases has already been substantial in the omicron wave, with pressure on the NHS which would have been significantly higher without social actions taken by the population, but mortality has been much lower in a country with very high vaccination rates and a less severe variant. Until / unless we get a significant vaccine escape variant (a real and persisting risk), medical countermeasures rather than societal actions should be able to take the great majority of the weight for most of the year although we can expect further surges especially in winter and COVID-19 is here to stay.

Infections transmitted via the respiratory route can, as COVID-19 has demonstrated, spread extremely rapidly. Although they are transmitted via the respiratory route, they can have significant health impacts on many parts of the body far from the respiratory tract. Medical countermeasures including drugs, vaccines and diagnostics have been highly effective at tackling many established infections by this route and substantially reducing mortality. Simple social measures which everyone can do as part of their ordinary lives, and ventilation particularly in public buildings, can help reduce transmission of these infections. Infections transmitted via the respiratory route will however remain a major cause of hospitalisation and mortality for the foreseeable future, even though modern medicine is producing very effective tools for tackling many of them.