GRESHAM COLLEGE

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THE CHANGING IMPACTS OF INFECTIONS

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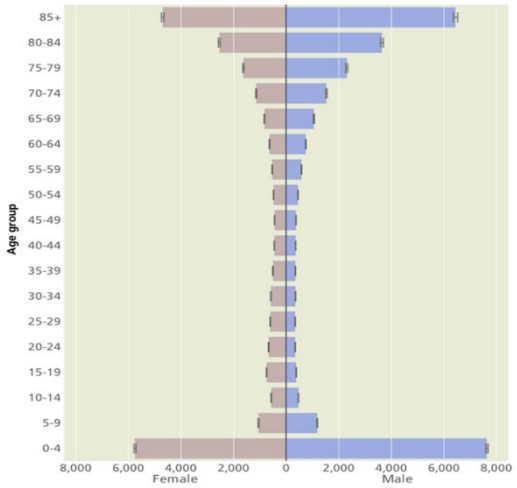


The probability of acquiring infections, and their effect, varies throughout our life course. Some of this is due to behavioural changes and changes in the environment as we grow older, some due to biological differences as we go through life events. The majority of infections are most dangerous in the very young and very old, but not all. The same infection may be trivial one age but potentially serious at another or will present very differently in children and adults. Infections have been declining as a cause of mortality globally, mainly due to rapid reductions in mortality in children. This improvement in child mortality will continue for some time, but it is likely that infections will then begin to increase again as a cause of mortality as the global population ages. Figure 1 shows hospital admissions from infections by age per 100,000 for the UK.

The risk of infection starts on the **first day of birth**. Infections in the birth canal can be passed on to the baby causing early-onset infections. The most important of these is Group B streptococcus (GBS) which causes over 50% of serious infections. Group B streptococcus is very common. In the UK it is carried by between 20 and 40% of women and normally does no harm and just 1/1750 babies develop early-onset GBS which can cause severe disease, especially sepsis, pneumonia or meningitis. Most babies with GBS make a full recovery with antibiotics but just over 5% die and 7% have long-term disability. There is a live controversy about whether to screen for GBS. Different countries do different things essentially because the evidence is very mixed. Screening, and then treating with antibiotics will prevent a small number of these tragic cases but will lead to massive use of antibiotics in pregnancy which have significant downsides. This debate will only be settled with proper trials.

There is also the risk of mixing blood between the mother and child at the time of birth, which had been kept separate by the placenta, and this is a risk for transmitting bloodborne viruses like HIV and Hepatitis B. In the early HIV epidemic up to 45% of children were infected, mostly (around 65%) during the birth process although transmission via breastmilk and during pregnancy also occur. In high-income settings transmission is now less than 1% mainly due to the effective use of antiretrovirals (anti-HIV drugs) in pregnancy.

From **72 hours after birth** the serious neonatal infections change. In high-income settings this is strongly associated with prematurity, low birth weight and ventilation. Breastmilk is protective. Most common bacteria at this stage originate from the skin, especially staphylococcus. This may be drug resistant in intensive care units.

Neonatal tetanus was one of the commonest causes of neonatal deaths everywhere and tended to come on about **7 days** after birth. Infection occurs with unsafe birthing practices has over 80% mortality. It is almost entirely preventable with immunisation of mothers and good midwifery. There has been around a 95% reduction since the 1980s.

New-borns are very vulnerable to infection, but this is reduced by maternal protection. There is placental transfer of antibodies in the last three months of pregnancy to what the mother is immune to whether by infection or

vaccination. This is supplemented by breastmilk; breastmilk just after birth is very rich in antibodies. Protection fades within around two months for most infections but last longer for measles mumps and rubella which is why MMR vaccines can be started later.

In the period **1 to 59 months** infections which start to become important including pneumonia, diarrhoea, measles and in areas there is transmission malaria. HIV can also play a role. The one month to 5 years period is also when our major countermeasures to infection: sanitation, nutrition and vaccination have the greatest impact. For diarrhoeal disease sanitation and more recently the rotavirus vaccine has led to substantial reductions. Measles, pneumococcal disease, whooping cough, diphtheria and also meningococcus, Hib and other causes of meningitis are largely vaccine preventable. Other major infections which used to kill children in the UK, and still kill children globally are shadows of their former selves. These include cholera, typhoid, TB, rheumatic fever and polio.

The transition to **school** occurs at an age where the greatest risk from life-threatening infection for most children has passed. This is not to say that children do not get many infections, an a few older children may get major infections, but the biggest risk is in the early months. School is one of the best places to catch whatever is going, and the immune system learns a lot whether or not the child does. Because schools are such a good way of transmitting particular respiratory infections closing schools in epidemics such as influenza can reduce the peak effect of the epidemic.

The transition to **adulthood** leads to a number of behavioural changes which expose people to a new set of infections. Certain infections are optimised to be passed on sexually and they will occur, if at all, after sexual debut. They therefore tend to be diseases of young adults. Numerically most are common but no more than a nuisance like genital warts, or unpleasant but seldom dangerous including herpes simplex and gonorrhoea. A few however can be life-threatening including HIV, syphilis and cancer-causing papilloma viruses. In the lifetimes of most of the audience the major sexual pandemic was HIV, 35 million deaths to date. The development of highly effective antiretroviral drugs has led to a substantial fall in deaths from HIV. In high-income settings there is now clear evidence that once treatment makes the virus undetectable, the risk of transmission is effectively zero. Historically the previous dangerous sexual pandemic was syphilis, which arrived in Europe around 1495, spread rapidly and was frequently fatal at that stage. This remained common including in the UK until the advent of penicillin.

In women, **pregnancy** significantly increases the risks of some infections which can harm the mother, the baby or both. Around 10% of maternal deaths globally are due to infection. Poor medical or midwifery practice is the most common cause, although it is now much rarer than it used to be. Several infections are more severe in pregnancy; for others pregnant women are more susceptible. Diseases which tend to be more severe in pregnant women include influenza, Hepatitis E, Herpes simplex and malaria. Pregnancy also makes women more susceptible to infections including listeria, malaria and HIV.

The placenta is a specific target of a few infections and globally the most important is malaria. The placenta is however usually a very good barrier between many infections in the mother and the baby. Rubella is an example of one of the infections that can cross the placenta and harm the baby in utero causing eye, hearing and congenital abnormalities. Other important infections are chickenpox, toxoplasmosis and CMV. Recently the most dramatic new example of a virus capable of causing congenital abnormalities was Zika. For most the risk is greatest in the first two trimesters.

The **world of work** can also be associated with particular infections. Major groups of workers have higher incidence of infection for different reasons. These include agriculture, industrial workers in certain industries and healthcare workers. Those dealing with crops are for example at risk of fungal infections of the lung. Farmers, vets, abattoir workers and dairy workers can be exposed to zoonotic diseases from animals. An example of industry leading to increased risk of infections is that miners, who can have their lungs badly damaged by silica dust, have increased risks of tuberculosis and pneumonia. Healthcare workers are at significantly increased risk in particular of diseases that can be passed on by the respiratory or touch routes. These include influenza, TB, SARS and Ebola.

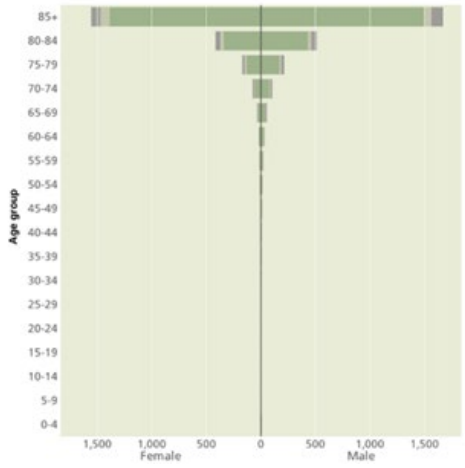
Childhood diseases in adults can be more severe than in children and examples include chickenpox, mumps, Hepatitis A and Epstein-Barr virus. Chickenpox in children is unpleasant but rarely serious but in adults can cause a dangerous pneumonia; adults are at a significantly higher risk of death although the rates are still very low. Additionally, shingles is a common presentation of the same virus in adults but not children. Mumps is generally mild in children although rare serious complications can occur. After puberty complications are more common and in particular in men, testicular inflammation (orchitis) is very common and can lead to sub-fertility. Hepatitis A generally has no symptoms in children but can cause jaundice and usually temporary liver damage in more than 70% of adults. Epstein-Barr virus is a very common infection which in childhood is usually trivial but those first encounters in adults can have significant symptoms of glandular fever and in some cases prolonged fatigue.

Infections can change their presentation during epidemics; an example was the 1918 influenza pandemic which had a significant peak of mortality in young adults although normally it is the very young and very old who are likely to die from it.

Certain infections behave completely differently depending on age. A good example of this is the major parasitic infection malaria. The same falciparum malaria parasite in very young children causes anaemia predominantly, in older children cerebral malaria, acidosis and bacterial coinfection and in adults' cerebral malaria, renal failure and lung injury. Malaria also illustrates the fact that the reason many children die of infections globally is because of poverty rather than biology. The great majority of malaria deaths in the world are in children, but in high income countries like the UK there are almost no deaths in children and the major risk group is older adults.

The remarkable reduction in infections in young children leading to mortality has contributed very substantially to the dramatic fall in child mortality globally. This will never go back again and is one of the great public health achievements.

In high-income settings, mortality from infections is heavily skewed towards **older ages** (Figure 2, UK data per 100,000), and this is the direction of travel for every country in the world. As the population ages, these infections of old age are bound to increase. There is a very strong age effect, particularly in those over 80 within increase susceptibility to, and deaths from, urinary tract infections, pneumonia and sepsis. We do have vaccinations for some of these infections most notably pneumococcal pneumonia but the impact of vaccine on disease in the elderly is often not as pronounced as in young children. This is not to say that there are not some major advances in vaccine specifically for older people, and example recently is a significant improvement in the shingles vaccine.



The direct effects of mortality from infection are quite significant, but there are also indirect effects. What has become increasingly clear is that there is a significant link between various forms of infection and cardiovascular events and deaths, including myocardial infarction (heart attack) and stroke. Infections can also cause the alarming phenomenon of delirium in older adults.

One area which has a long way to go is a proper exploration of whether infections are sometimes causal, contributory or irrelevant for people with dementia. We know that certain infections can cause dementia; historically syphilis and more recently HIV did so. There is still no conclusive proof one way or the other on whether currently other infections contribute to some cases of Alzheimer's or dementia with Lewy bodies. Current theories of infections which may accelerate dementia include some of the herpesviruses and *P. gingivalis*. It would probably be good if there was a causal link because we have been highly successful at preventing or treating the great majority of infections.

The probability of acquiring and being harmed by infections varies throughout our life. Most infections are most dangerous in the young, the old and those who are pregnant. We have made remarkable strides forward against infections of infancy and childhood. We made steady but much slower progress against infections of older adults. Infections are declining as a proportion of mortality globally, and this will continue for some time but over time it will increase again as the population globally ages. Richer countries like the UK are at the forefront of this switch. Much less interest has gone into infections in the older population than in children and younger adults; this is going to have to be a priority for the coming decades.