

The microbiological ages of man

Roger Finch

● The lot of man is characterized by nine months *in utero* followed by 'three-score years and ten'. Throughout this period there is the ever present challenge from endogenous micro-organisms making up the normal flora of the skin or mucous membranes, or from exogenous agents acquired through inhalation, droplet spread, ingestion, sexual contact or from behavioural activity such as intravenous drug use. Susceptibility to infectious diseases occurs despite an impressive array of defences which include an enveloping integument, fixed and circulating phagocytic cells, the ability to respond to infectious challenges with specific and non-specific antibodies, augmented by a sophisticated cellular immune system able to process and express a vast repertoire of microbe-inactivating molecules. However, inherited genetic defects, circumstances of birth, nutrition, geography, travel, occupation, animal exposure and social behaviour all impact on our vulnerability to infectious disease which may sometimes threaten survival. There are many parallels between Shakespeare's description of the seven ages of man and the microbiological challenges of life.

● Life *in utero*

The period from conception to delivery is relatively safe. However, maternal infections can have an adverse effect, despite the relatively short duration of pregnancy. Hepatitis A, B and E, and pneumococcal pneumonia are often more severe in pregnancy and may induce abortion or premature labour. Furthermore, the combined effects of a gravid uterus and elevated progesterone increase the risk of bacterial infection of the urinary tract which may ascend to involve the kidneys and sometimes spills over into the bloodstream.

The placenta provides an efficient protective barrier to many common infections. However, some micro-organisms can induce an active placentitis, thereby infecting the fetus, giving rise to diseases such as syphilis, cytomegalovirus (CMV), toxoplasmosis and rubella. Fetal death and congenital defects are well recognized complications of maternal syphilis and rubella, although influenced by the duration and timing of infection, respectively. Both diseases are routinely tested for as part of antenatal care in developed countries. Toxoplasmosis, rubella, CMV and herpes simplex in the pregnant woman can all result in minor to life-threatening infection in the newborn. Worldwide, the most important transmissible infection resulting from pregnancy is hepatitis B, which is particularly prevalent in developing countries. Infection acquired at birth results in a chronic carrier state in some 90% of newborns, compared with 10% when infection occurs in adult life. The legacy of chronic hepatitis B infection includes chronic liver disease, cirrhosis and liver cell cancer.

● Parturition

From the moment the maternal membranes rupture and delivery commences, the newborn child passes from the sterile environment of the womb to a world in which micro-organisms abound. Its skin and mucous membranes rapidly acquire a microbial flora, largely derived from its mother's birth canal and skin through contact and handling. This flora is largely harmless and offers some protection against potentially pathogenic organisms, but on occasions, virulent micro-organisms such as *Escherichia coli*, *Streptococcus agalactiae* and *Listeria monocytogenes* or herpes simplex virus may invade to produce generalized sepsis and meningitis. Mortality is still high despite prompt recognition and treatment, especially from *E. coli* meningitis.

Hospital delivery is the norm in many developed countries. It exposes the young to the potential for hospital-acquired infections at a stage when their immune defences are immature and passively acquired maternal IgG antibodies provide variable protection. Virulent pathogens, such as methicillin-resistant *Staphylococcus aureus*, multi-resistant *Enterobacteriaceae* and *Pseudomonas aeruginosa* are intermittently present in neonatal units and occasionally cause sporadic and epidemic illness, sometimes with fatal results.

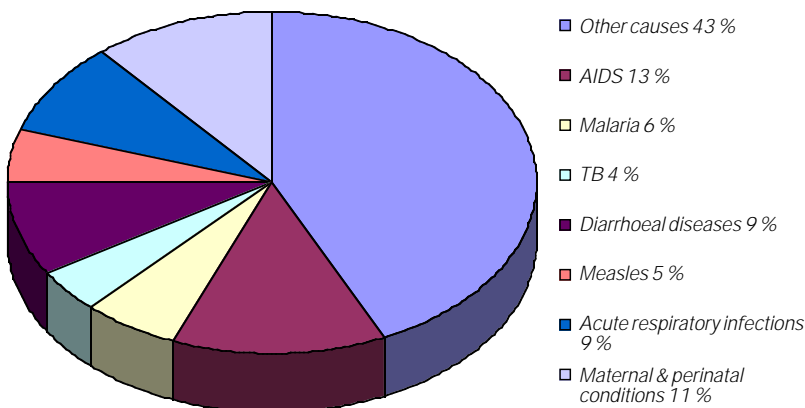
● Childhood

For the majority of the world's children, the tragedy of gastrointestinal infections and vaccine-preventable diseases continues to wreak a heavy toll. Fig. 1 highlights the causes of death in children and young adults in developing areas of the world. Poor nutrition, primitive or non-existent sanitation and the absence of a clean water supply are largely to blame. Measles carries mortality rates of up to 50% in some developing countries, while diphtheria has re-emerged in countries of the former Soviet Union with disastrous consequences.

Breastfeeding protects against diarrhoeal diseases, largely through the presence of secretory IgA in maternal colostrum. The decline in breastfeeding in developing countries as a result of commercial pressures promoting

Throughout our lives, microbes pose a threat to our health and well-being. Roger Finch charts the microbiological ages of man.

BELOW:
Fig. 1. Deaths in developing countries. Two out of three deaths among children and young adults in Africa and Southeast Asia are due to seven causes (ages 0–44)
SOURCE: WORLD HEALTH ORGANIZATION/CDS



baby foods or from personal preference, has been highlighted by the WHO, UNESCO and other child welfare agencies.

Multiple upper respiratory tract viral infections are common in early childhood. In the West they are increasingly spread by attendance at day-care centres, nurseries and kindergartens as more parents select these facilities for reasons of personal choice, education and employment. Occasionally, more serious infections, such as meningococcal sepsis, may arise.

Antibiotics are frequently prescribed in early childhood and this has recently been highlighted as an area for more prudent use, since most childhood infections are viral in nature. Antibiotic resistance among community and hospital pathogens is increasing. Of considerable concern is the global prevalence of penicillin-resistant pneumococci which are an important cause of bacterial middle ear infection. Pre-school children experience, on average, an attack of acute otitis media every year. In the USA, there are increasing reports of failure to respond to conventional oral antibiotics, such as amoxycillin and erythromycin. Hospital admission and the use of injectable cephalosporins is now necessary to cure some children.

● Adolescence and young adulthood

The infectious hazards of the years between childhood and adulthood often have life-long consequences. Sexually transmitted diseases, such as syphilis and gonorrhoea, are readily treated if recognized and diagnosed promptly. On the other hand, *Chlamydia trachomatis*, now the commonest sexually transmitted infection, has a legacy of infertility as a result of complicating pelvic inflammatory disease. Genital virus infections, such as herpes simplex, can recur throughout life, while the link between papillomavirus as a cause of genital warts and cervical carcinoma is becoming clearer. The emergence of HIV and AIDS in 1981 has led to the global pandemic which has the greatest impact on persons of reproductive age. Safe sex contributes to its control, but is clearly not the solution to containing this disease which continues to claim the lives of millions. Likewise, despite an ever impressive array of anti-retroviral therapies, drug management provides only temporary interruption in the progression to death.

The escalating use of prohibited drugs largely affects the young. The use of intravenous drugs is the major source of the newly recognized hepatitis C virus, which like hepatitis B, frequently causes chronic hepatitis, sometimes leading to cirrhosis, failure and cancer of the liver.

● Maturity and old age

International travel is booming. This may be occupational, but is increasingly recreational in nature.

The reality of the global village has resulted in an increase in travel-associated infectious disease. Malaria, schistosomiasis, tuberculosis, rickettsioses, salmonellosis and, less commonly, more exotic conditions, including Leishmaniasis and ectoparasitic diseases, such as jiggers (*Tunga penetrans*), are a sample of the recent problems dealt with in the infectious disease clinics and ward in Nottingham.

Malignant disease becomes increasingly common through adult life to old age. Current therapeutic approaches include oncolytics, radiotherapy and immunosuppressives. The latter, especially corticosteroids, are used to control a wide variety of other conditions, including those with an autoimmune basis. Similar approaches are adopted to prevent rejection in organ transplantation recipients. The therapeutic benefits unfortunately bring in their wake a repertoire of potential infectious complications across the whole range of micro-organisms, including viruses, bacteria, fungi and protozoa. Some reflect past infection with reactivation complicating the state of immunosuppression. These include varicella-zoster and cytomegalovirus, *Mycobacterium tuberculosis*, *Candida* spp., *Pneumocystis carinii* and occasionally *Strongyloides stercoralis* infections. Other challenges originate from the normal flora and hospital environment. A successful bone marrow transplant can still be frustrated by severe and life-threatening infectious complications. This has resulted in a variety of management strategies, such as isolation care, anti-bacterial chemoprophylaxis, and granulocyte and macrophage colony stimulating factors, all complemented by strict hygiene measures.

Survival into old age and the involution of the immune system and other defence mechanisms leads to increasing vulnerability to infectious disease. These mainly affect the respiratory tract, so that pneumonia is a frequent complication of other diseases, such as stroke, influenza and post-operative states. Pneumonia has been described as 'Captain of the men of death'. It can sometimes be viewed as nature's way of relieving suffering from more serious underlying afflictions, as man enters his final state '*sans teeth, sans eyes, sans taste, sans everything*'.

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