

CHAPTER ONE: UNINTENDED CONSEQUENCES

Humans have suffered from communicable diseases since the dawn of history, but it is only in the last few generations that we have understood the science behind infections and been able to control spread of infectious disease. With understanding has also come the belated realisation that many human actions have had unintended consequences for communicable diseases. This chapter explores how changes in human society and behaviour have provided new opportunities for microbes to evolve and cause disease.

THE MICROBIAL PERSPECTIVE

Micro-organisms (microbes) exist, not to cause infection in humans, but simply for their own survival⁶. Indeed, bacteria existed on earth for three billion years before there were any plants or animals as potential hosts. A microbe can only survive within a human host if it can find a place to grow, compete effectively with other microbes and survive the person's immune defences. Only a few of the microbial and parasitic species around today can colonise humans and of these, only some cause human disease; the remainder colonise the skin, bowel, or respiratory tract as commensals that rarely cause harm⁷. The range of agents that can cause communicable disease is summarised in Table 1.1^{8,9}. Bacteria can grow in many situations, while viruses cannot multiply outside a living cell of another host organism. Parasites are heterogeneous and vary greatly in size; they typically have life cycles that are very complex.

How do bacteria and other microbes adapt to new hosts and new opportunities? Through random genetic change over generations, all living organisms are able to evolve and adapt. One generation for humans is perhaps 25 years, whereas a single generation for a microbe can be as short as 20-25 minutes. Microbes, with such rapid multiplication, thus can adapt very quickly. The natural forces that drive microbial evolution are selective; only the fittest microbes survive. If a new genetic mutation allows a microbe to better exploit its environment, the mutant has an advantage over sister microbes without that mutation. Thus any microbe that can grow more quickly, evade immune defences, hide in the host, be transmitted more effectively, or resist antibiotic treatment, will win the competition to survive.^{6,7,8}

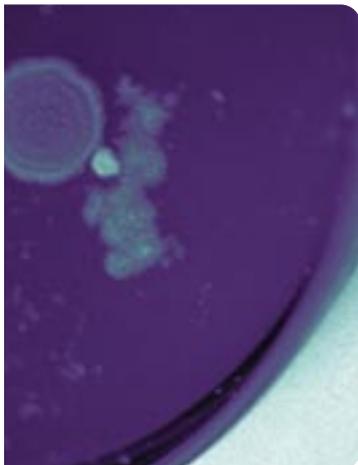




TABLE 1.1 AGENTS CAUSING COMMUNICABLE DISEASE

Type of agent	Size	Genetic material	Examples of disease
Prions	Protein molecule only a few nanometres* across	None- consists only of protein	Mad cow disease, Creutzfeldt-Jakob disease
Viruses	Ultramicroscopic (up to 200 nm*)	RNA or DNA	Common cold, influenza, cold sores, smallpox, polio, measles, AIDS, hepatitis C
Bacteria	Microscopic (about 1000 nm)	DNA	Tuberculosis, diphtheria, tetanus, pneumonia, wound infections
Fungi	Aggregates of microscopic cells	DNA	Thrush, ringworm, tinea
Parasites	Variable-from microscopic plasmodia of malaria to tapeworms up to 10 metres long	DNA	Malaria, tapeworms, hydatids, schistosomiasis (or other flukes)

* A nanometre (nm) is 10^{-9} metre (ie one billion nm to the metre)
 • For more details see Mims et al⁸ or Chin⁹

Changes in a host population such as overcrowding, changes in hygiene, medical practice including antibiotic use, intravenous drug use, or changing sexual networks, can act as selective forces. Such influences drive a microbe into a new evolutionary niche⁷ where it is possibly more transmissible or more virulent (dangerous) for humans.

Mutations that are advantageous in one microbe can also be transferred to other strains or species. For example, the genetic information (DNA) that allows a bacterium to resist an antibiotic can be transferred within and between bacterial species. For some bacterial species the transferred gene is in an infectious circle of DNA (a plasmid). For others, the transferred DNA is recombined into the bacterial chromosome⁸. Even though such transfer may only occur rarely, the receptive bacterium will spread widely in an environment, such as a hospital, where antibiotic resistance gives it a selective advantage¹⁰.

Box 1.1 Natural selection

Studies of microbial evolution using genetic fingerprinting (DNA and RNA gene sequences) provide the most direct evidence for Charles Darwin's epoch-making idea of evolution by natural selection.

MICROBIAL TRANSMISSION AND DISEASE SEVERITY

The success of a microorganism's long-term survival is dependent on its ability to spread and survive rather than its capacity to cause severe disease. The common cold is a minor illness. The symptoms, sneezing and coughing, ensure that cold viruses are spread through droplets onto new hosts and into the air. Thus the viruses causing cold continue to infect many people without immobilising those affected.

In contrast, severe infections leave the patient bedridden, reducing the ability to spread the microbe to others. Smallpox is one example; if a patient is bedridden, only those who are closest can get the disease. Measles is another. If acquired in the home, measles tends to be more severe¹¹. If measles is acquired from outside the home it means a person with measles is well enough to be out and about and spreading disease. It is probably a milder form of disease that enables the spreader to be in contact with others. With a severe disease the person would be bed-ridden and only able to spread infection to those in their home. People at home may also get a larger dose of viruses because of their close contact. Paul Ewald has noted that ambulant patients with cholera may transmit bacteria that are less virulent and that the resultant selection pressures could help to explain the evolution of milder forms of the disease⁷.

CLIMATIC AND GEOGRAPHIC INFLUENCES

Smaller organisms are very sensitive to climatic conditions. Many microbes and parasites have adapted to warm and humid environments. A whole discipline of medicine is devoted to the diseases of the tropics caused by infective agents (malaria, yellow fever, schistosomiasis, dengue, flukes and worms etc), some of which are transmitted by 'vectors' such as mosquitoes, ticks and water-snails (see Box 1.2). Tropical diseases are endemic where parasites and vectors can survive year round in a climate that is warm and usually moist¹². Mosquito reproduction,

survival and biting rates are all influenced by temperature, rainfall and humidity. Furthermore, the infectious agents that actually cause tropical diseases, such as the malarial plasmodium or dengue fever virus, also grow more quickly as the temperature rises.

In temperate climates, outbreaks of food poisoning, caused by bacteria such as *Salmonella* and *Campylobacter*, are more frequent in summer than winter months⁹. Influenza tends to occur in the cooler months. Infections such as tuberculosis can occur year-round⁹, although air-borne transmission is inhibited by sunlight, which rapidly inactivates most bacteria and viruses.

Box 1.2 Flukes of nature¹²

Unlike the common use of the word fluke, the disease-causing flukes, seen in tropical countries, are anything but a 'fortuitous chance happening'. They are a type of worm that parasitises people. For example, Schistosomiasis is caused by one group of flukes, that settle in the liver, intestines, kidneys, lungs or brain. How do they get there? When an animal or person excretes the eggs of a fluke in their urine, faeces or sputum, the egg hatches in water and enters snails. After living in the snail, free-swimming forms of some flukes directly invade human skin. Others invade aquatic plants, fish or crabs that are then eaten by people. Once in the body the flukes travel through the skin and blood stream and mature into adult worms in the liver, intestine or kidney to send out their eggs and complete the complex life-cycle.

Flukes currently infect more than 200 million people in many tropical countries, causing many deaths and considerable disability.

EFFECTS OF SOCIAL CHANGE

HISTORIC EFFECTS OF SETTLEMENT

When humankind lived in small hunter-gatherer bands, there would often have been too few susceptible individuals to allow disease-causing microbes to survive long-term within the band. This is because affected individuals either became immune or died and did not spread the microbe to many others. Microbes that could survive long-term in such circumstances were those such as *E.coli* in the bowel which evolved as commensals, rarely causing harm⁷. With the rise of horticulture and agriculture and the domestication of animals in the last 10,000 years, the ecology of infectious disease changed. Most serious human infections of recent times, including influenza, tuberculosis, malaria and plague are of animal origin – what Diamond calls ‘the lethal gift of livestock’¹³. Tuberculosis, originally acquired from domesticated cattle, learnt to survive long-term within the human body and to spread from person to person.

Furthermore, the larger groups of people supported by horticulture or agriculture presented a sitting target for disease vectors such as mosquitoes, for organisms transmitted through human excreta or for organisms harboured by animals and pests such as rats^{13 14}. Human malaria appears to have evolved from malaria in birds and monkeys to become established in human populations in Africa^{7 13}.

Crop surpluses were traded. Grain attracted rats and trade helped to spread them around the civilised world. Rats were likely to be infected with plague and rat fleas helped to spread the plague from rat to rat, from rats to people and from person to person^{13 14 15}.

Box 1.3

Communicable diseases have been present throughout human history

Most communicable diseases are acquired from other humans:

- *by droplet infection or by direct contact,*
- *indirectly by (faecal) contamination of food and water supplies,*
- *via insect or animal vectors or needles that pierce the skin.*

Diseases of humans have often evolved from diseases of animals and some have:

- *been particularly dangerous when first transmitted to humans,*
- *evolved to spread from person to person.*

Human behaviours influence communicable disease transmission and evolution through:

- *changes in the natural environment,*
- *agricultural and animal husbandry practices,*
- *global distribution of food supplies,*
- *travel, trade and warfare,*
- *crowding in camps or cities, providing opportunities for cross infection or contamination of food or water supplies,*
- *poor hygiene*
- *sexual networks and lifestyle,*
- *intravenous drug use and other skin-piercing practices,*
- *medical practices (cross-infection, chemotherapy, transfusion, transplantation).*



As cities developed, crowding and poor hygiene allowed the spread of microbes causing 'crowd' diseases affecting the respiratory and gastrointestinal tracts. Diarrhoeal disease was an unintended consequence of drinking water being drawn from streams contaminated with faeces. Science eventually came to the rescue with John Snow's recognition in 1854 that cholera was spread through water supplies. Other 'crowd' diseases such as mumps, measles and chicken pox were able to thrive. City populations supported by agriculture were large enough to maintain ongoing transmission of many infectious diseases, with, from time to time, major epidemics^{15 16}.

TABLE 1.2 COMMUNICABLE DISEASE CONSEQUENCES OF SOCIAL CHANGE

Social changes	Consequences
Domestication of animals	Microbes from animals adapt to infect people, causing diseases such as tuberculosis and measles
Rise of agriculture providing food for larger population aggregated in cities	Diarrhoeal, respiratory and other infections spread more easily in crowded and unhygienic conditions
Food distribution systems to feed large populations	Widespread food-borne disease outbreaks
Hospitalisation	Cross-infection causing surgical infections and child-birth fever in historic times. Contemporary hospital infections with bacteria resistant to antibiotics
Unsterile needles for injection	Spread of blood borne disease in health care institutions and in illicit drug users
Changes in acceptance of sexual practices and networks; global travel; men who have sex with men; men living away from home for work	Global spread of HIV, with growing epidemics in Africa and Asia
Clearance of forests	Bats move to seek new homes and spread Nipah virus to pigs; virus spreads from pigs to humans ⁹
Feeding of bovine meat-and-bone-meal to cattle	BSE in cattle, variant CJD in humans ¹⁷

CONQUEST, TRADE AND TRAVEL

In recent millennia, the first contacts between two different civilisations have exposed one population to new infections from the other^{13 14 15}. This phenomenon led to the decimation of those historical populations which could not resist infections to which they had not previously been exposed. The Antonine smallpox plague in the 2nd century AD was introduced to Rome by the legions returning from Syria. Smallpox devastated much of the city and the empire to the west. It has been argued that this epidemic, as much as the aggression of the barbarian tribes, led to the decline and eventual fall of Rome. Similarly catastrophic was the Black Death or bubonic plague which arrived in Europe in the 14th century when Genoese merchants, fleeing from attack by Mongolians in the Black Sea, returned home with rats and their infected fleas on board their ships. Over the next generation bubonic plague killed one third of Europe's population.

The arrival of 'European' microbes in the New World was equally devastating. How was it possible for Cortez and his 600 Spaniards to defeat the mighty Aztec Empire in 1520? The answer was probably smallpox. Most of the Spaniards were immune from previous

exposure, but the smallpox they introduced killed half the Aztec population, including the emperor. A similar fate awaited the Incas in Peru a few years later. In North America in the 15th and early 16th centuries, large Native American populations living in major settlements had inhabited the Mississippi Valley. By the late 17th century those communities had virtually disappeared, wiped out by 'European' microbes to which they had never previously been exposed. These organisms had spread overland following the arrival of Columbus in the Americas in 1492 and the subsequent arrival of European settlers on the East Coast.

In Australia from the late 18th century, the previously unexposed Aboriginal population was even more vulnerable because of disruption of social structures and food supplies. Smallpox, typhus, typhoid, measles and whooping cough all wrought havoc^{18 19}. A smallpox epidemic occurred soon after the First Fleet arrived in Port Jackson in 1788. Although the origin of the outbreak was never identified, the infection could have come from 'variolous matter' brought by ship's surgeons. This was eight years before Jenner's discovery that 'cowpox matter' could protect against smallpox. In 1831, Indigenous people in the Liverpool range of NSW were

affected by a virulent smallpox outbreak that was controlled by vaccination. The pattern was to be repeated in subsequent generations.

In modern times, increased world travel has provided many opportunities for diseases such as HIV, influenza^{1 10 15} and SARS²⁰ to spread quickly from country to country. Indeed, with fast travel many people previously exposed to an infection can arrive in another country before they have themselves developed symptoms, making it difficult to stop the entry of a new disease at the border. International travel has also spread antibiotic resistant bacteria causing health-care associated infections to hospitals across the world²¹. Resistant staphylococcal strains from UK hospitals are indistinguishable from those in eastern Australia. The consequences of our globalisation and travel are clear.

With increasing travel and tourism and with many students from tropical countries studying in Australia, malaria and other vector borne diseases are increasingly diagnosed in Australian hospitals. In northern Australia, with a permissive climate and vectors, there is the further risk that tropical diseases such as malaria and dengue could become permanently re-established²².

HUMAN INFLUENCES ON MICROBIAL HABITATS

Many human activities have provided new environments and opportunities for harmful microbes. For example, many outbreaks of deadly Legionnaires disease have been recognised since humans first began to install water-cooled air-conditioning systems. The causal microbe, *Legionella*, previously restricted to its natural aquatic environments, could thrive in this new ecological niche. When dispersed in aerosol form from the air-conditioner, the microbe could be inhaled to cause severe pneumonia or death in vulnerable people. The first recognised outbreak affected a group of elderly US veterans attending an American Legion reunion in Minnesota in 1957⁹. Australia has not been spared from this disease. For example, there was a large outbreak at the Melbourne Aquarium in 2001²³.

The clearance of forests to build an international airport in Malaysia in the 1990s led to a devastating outbreak of Nipah virus, carried by forest bats fleeing to agricultural lands. The bat virus, relatively harmless to them, spread to pigs and from them to humans, with deadly effect. The epidemics were stopped only after millions of pigs were slaughtered in 1998-9⁹.

Large dams, irrigation schemes, land reclamation, road construction and population resettlement programmes – notwithstanding their other economic and social benefits – have sometimes helped to spread diseases such as malaria, dengue fever, schistosomiasis and trypanosomiasis.^{5,9} In the Sudan, for example, schistosomiasis appeared within several years of the start of a large irrigated cotton project⁵. Today, there are concerns that the China's Three Gorges Dam project could promote local transmission of schistosomiasis and malaria.

REFUGEE CAMPS, SLUMS AND SHANTY TOWNS

Disease spreads readily in crowded conditions; close contact facilitates the spread of microbes spreading via respiratory secretions and faeces. If water supplies are poor and sewerage inadequate, hygiene suffers and infections become rife. This explains higher rates of infection in shanty towns, slums and in refugee camps where crowding is extreme and services inadequate²⁴.

Refugees dislocated by war, as in Rwanda, can bring numerous infectious agents of diverse origin. In overcrowded conditions everyone can be exposed, usually to multiple agents. Undiagnosed or poorly treated dysentery, tuberculosis, hepatitis A and parasitic diseases can spread readily. Health workers struggle to prevent deaths from acute respiratory infections, diarrhoea, measles, malaria or other conditions. Malnutrition facilitates infection leading to a vicious cycle of decreased appetite, wasting and worse malnutrition in young children. With war, or political and social instability from other causes, many refugees are not vaccinated. Outbreaks in refugee camps can potentially lead to outbreaks of measles and rubella or other vaccine-preventable diseases beyond the refugee community. War can drive a cycle of deprivation, leading to further unrest and conflict, with many ongoing consequences for communicable disease.

Box 1.4 Eastern Zaire, 1994

Death rates when migration is forced are usually high. The exodus of almost one million Rwandan refugees into eastern Zaire in 1994 resulted in death rates more than 30 times greater than rates prior to the conflict. Severe cholera and dysentery epidemics were seen in the first month after the influx.

RISKS FOR CHILDREN AND OLDER PEOPLE

Crowded conditions are not limited to developing countries or to disadvantaged minorities in developed countries. The needs of families have led to group care arrangements for children and for some older persons in countries such as Australia; the resultant contact and crowding can spread communicable disease. Children in child care settings are particularly prone to communicable disease because of immature immunity, close contact with each other and limited personal hygiene. Australian research²⁵ has shown how such children can be better protected from communicable diseases by implementation of the Australian guidelines: 'Staying Healthy in Child Care'²⁶.

Elderly people are also vulnerable to infectious diseases as their immunity declines with age. This disease burden can be reduced by improved vaccination coverage, particularly for influenza and pneumococcal pneumonia, by effective and prudent use of antibiotics in primary care, by enhanced surveillance and by improved infection control in aged care institutions²⁷.

INTENSIVE PRODUCTION OF FOOD

New and 'efficient' methods of production of livestock and poultry have also had unforeseen consequences. Chickens reared in intensive conditions have feed that is supplemented with antibiotics to promote growth and to treat and prevent disease. Unfortunately such antibiotic use has favoured the survival of bacteria that are resistant

to antibiotics. Bacteria in chickens that are resistant to antibiotics can spread directly to people and cause infections that are hard to treat. Furthermore the genes for antimicrobial resistance can also spread to other bacteria that infect humans.

The feeding of meat-and-bone-meal as a protein supplement to cattle to promote growth has had even more disastrous consequences¹⁷. The outbreak of 'mad cow disease' (Bovine Spongiform Encephalopathy

Box 1.5 Cannibalism, Kuru and CJD

In the 1950s, a fatal nervous disease (kuru) was recognised amongst the Fore people in the Eastern Highlands of New Guinea. The epidemic of kuru was shown to have spread by ritual cannibalism of those who had previously died from the disease. In the 40 years after cannibalism ceased, the epidemic has subsided.

Kuru has been shown to resemble Creutzfeldt-Jacob Disease (CJD), a rare but fatal disease of older people. Both diseases could be transmitted to animals by affected brain tissue. Unfortunately, before the risk was recognised, CJD was also inadvertently transmitted to patients receiving hormones or grafts made from infected tissues.

Kuru, CJD, BSE and variant-CJD are all now known as Transmissible Spongiform Encephalopathies (TSEs). The infective agents are prion proteins.



A boy with Kuru in 1966 - probably infected as a toddler in the late 1950s. His hand is trembling - an early sign of the disease.



or BSE) first recognised in UK in 1986¹⁷, was caused by the feeding of meat-and-bone-meal prepared from cattle carcasses back to cattle. In the light of the kuru story (see Box 1.5 and²⁸), this cycle of 'bovine cannibalism' might have been anticipated to cause trouble. Health authorities in the UK reassured the public and the world, well into the 1990s, that BSE was unlikely to 'jump species' and affect people. They were proven wrong when a new fatal human disease, variant-CJD, with 'spongiform' changes in the brain similar to those of BSE

infection and kuru, was recognised in 1996. By 2003, some 130 cases of variant-CJD had been diagnosed in UK, predominantly in younger people thought to have eaten BSE-contaminated beef at the height of the BSE epidemic²⁹.

CHANGING FOOD TRENDS

All foods, but particularly those that are moist, or contain meat or seafood, can nourish bacteria if they become contaminated; dangerous bacteria multiply rapidly in a warm environment. Prevention of food-borne disease is straightforward in principle. Adequate cooking kills most microbes, but does not fully inactivate the prions that transmit TSE. Preservatives, drying and refrigeration inhibit bacterial growth³⁰.

Yet some members of our younger generations have forgotten the food hygiene principles from the past. Furthermore, new food trends, demands for fast foods and for foods without preservatives have radically changed food supply chains and introduced new risks.

Food-borne diseases have re-emerged with a high profile in the last few years. Outbreaks affect public confidence in health authorities, yet the tried and tested methods of the past are losing acceptance. The promotion of 'health' and 'natural' foods creates pressure to remove the preservatives (eg salt, nitrite, sugar or others) from food that were originally introduced to reduce microbial growth. Preservative-free food products, at clear risk of microbial contamination, can cause large outbreaks, even across international borders³⁰.

Box 1.6 New trends in food

Recent changes in food supply include:

- natural/health foods without preservatives,
- 'take-aways' or 'fast food',
- 'cook-chill' (pre-cooked and cold-stored),
- 'sous vide' (vacuum packaged products which consumers cook in their plastic pouches),
- large processing plants and
- international traffic in fresh foods.

Box 1.7 'Preservative Free'

Outbreaks of gastro-enteritis or food-poisoning from bacterial contamination of preservative-free "dips" and other foods have been reported internationally.



SUCCESSSES & LIMITATIONS OF MEDICAL SCIENCE

In 1796, Jenner had shown that vaccination with pus from cowpox, a mild disease, could protect against subsequent infection with deadly smallpox. By the 20th century, his insight had spawned the science of immunology, leading to vaccines against whooping cough, tetanus, polio and other deadly diseases^{14 15}.

Infection control principles date back to the work of Oliver Wendell Holmes in USA, James Simpson in Britain and Ignatz Semmelweis



A younger [Gus Nossal](#), at the time of succeeding Frank Macfarlane Burnet as Director of the Walter and Eliza Hall Institute in Melbourne. The success of Australia's research in immunology and vaccine development owes a great deal to his leadership and personal contributions.

in Vienna. Long before the responsible microbe (*Streptococcus pyogenes*) had been identified, they showed in the 1840s that doctors who did not wash their hands spread deadly 'childbirth fever' to women in obstetric hospitals. Yet it was not until the 1890s, following the acceptance of 'germ theory' and the work of Joseph Lister, that infection control measures were routinely introduced into obstetric and surgical practice¹⁴.

Box 1.8

'It may seem a strange principle to enunciate as the very first requirement of a hospital that it should do the sick no harm.'
(Florence Nightingale, 1863)

Penicillin was discovered accidentally when a mould, blown through Alexander Fleming's laboratory window in 1928, produced an antibiotic that killed bacteria growing on a culture plate. By the 1950s, antibiotics such as penicillin had made most bacterial diseases treatable and therefore much less threatening¹⁴.

Box 1.9 Penicillin history¹⁵

*The mould, *Penicillium notatum*, killed staphylococcal bacteria and led Fleming to identify the antibiotic properties of penicillin.*

An Australian, Howard Florey, working in Oxford, proved the value of penicillin and ensured its place in history in the early 1940s. Fleming, Florey and Chain later won the Nobel Prize for their work on penicillin.

Fleming was also one of the first to recognise that antimicrobial resistance would be a problem. Only recently has the magnitude of the problem and Fleming's prescience, become widely understood

With vaccines, infection control and antibiotics, we thought we had won the war with communicable disease. More than 30 years ago, the then US Surgeon General stated that 'the time has come to close the book on infectious diseases'. Hindsight is a great teacher and the last three decades have taught us that there will be no closing of books on infectious disease, now or ever.

Nevertheless, we have learnt much since the 19th century. The concepts underlying public health prevention, antisepsis, asepsis, immunisation and treatment have evolved from vague ideas into the powerful technologies of today (see Appendices 1 to 3). In the overall march of health, an important lesson is that preventive strategies are still more effective than curative approaches.

MAGIC BULLETS

It is hard now for people to recall the world before antibiotics, when many people died from infections. In 1941, Florey and Chain purified penicillin and showed its dramatic effects against pus-forming bacteria such as streptococci. Deaths from infected war wounds were greatly reduced following large-scale manufacture and use of penicillin in the latter years of World War 2. In civilian use, penicillin led to striking reductions in death or disability from childbirth fever, scarlet fever, syphilis, meningitis, pneumonia, osteomyelitis and many other infections. Since 1945, penicillin is estimated to have saved at least 50 million lives. Treatment of tuberculosis with streptomycin, isoniazid and para-amino-salicylic acid and other anti-microbials was similarly successful¹⁵.

Box 1.10 Selective advantage and antibiotic resistance^{7 10}

Although genes for antibiotic resistance have existed for aeons, the human use of antibiotics has given the genes for resistance, through the microbes that carry them, a great evolutionary advantage. When sensitive bacteria are inhibited by antibiotics, resistant bacteria thrive and take over the living space.

Antibiotic resistance is more likely to emerge if the antibiotic dose is low or interrupted, as bacteria with partial resistance can survive to accumulate new mutations or new genes for increased resistance.





We were confident for many years that we could easily deal with resistance to antibiotics because there was always another antibiotic in reserve. We have been proven wrong (see Appendix 4). Since the 1940s, antibiotics have been applied uncritically to the treatment of many minor conditions rather than being reserved for serious and life-threatening bacterial infections. They have also been used, unwisely, for viral infections for which they are not effective. Harmless bacteria in the skin and the bowel, as well as bacteria that can cause disease, were thus needlessly exposed to antibiotics. Genes conferring resistance to antimicrobial agents have thus spread quickly.

Doctors had acquired the habit of prescribing antibiotics and found it difficult to change. In 1974, Lockwood described a syndrome of compulsive antibiotic prescribing (CAP) and suggested formation of Antibiotics Anonymous to deal with the problem³². Although light in heart, the message was blunt. Yet we took little heed.

The problem of antibiotic resistance has been compounded, since the 1950s, by the widespread use of antibiotics in intensive animal production. Antibiotics were added to stock feed to treat and to promote rapid growth of chickens, pigs and other animals housed under intensive conditions. Such agricultural uses selected for resistant bacteria in animal populations and increased the risk that such a bacterium could spread into human populations, or that a resistance gene could spread into bacteria able to infect people.

Overuse of antibiotics in medicine and agriculture has thus spread bacteria carrying genes for antibiotic resistance³³. If a resistant bacterium causes disease, it can now be difficult to find an antibiotic that will be effective. Recently one of our last line antibiotics, vancomycin, became ineffective against some strains of 'golden staph' (*Staphylococcus aureus*). The staphylococcus acquired the resistance gene (called *vanA*) from a bowel microbe (*Enterococcus*)³⁴. The problem of antibiotic resistance has now attracted international attention. Australian responses to antimicrobial resistance are summarised in Chapter 3.

Antiviral drugs are now available to combat infections caused by viruses such as influenza, herpes, HIV and hepatitis B and C⁹. The lessons from overuse of antibiotics will guide their future use. It is already known that HIV mutates very quickly and that resistance to antiviral agents can emerge quickly.

MEDICAL AND SURGICAL ADVANCES ALSO GENERATE RISKS

We have seen great strides in medical and surgical management of disease. Patients with debilitating joint disease, or organ failure, can be treated by surgical replacement of a joint or by transplantation of a new organ such as a liver. However all medical and surgical procedures can have unintended consequences. The mere fact of bringing vulnerable people close together in a hospital increases the risk that infection will spread from one to another. Since the time of Semmelweis we have known that hospital staff can carry such infections from patient to patient. Subsequent generations have shown how difficult it can be to achieve full compliance with hand-washing and other infection-control procedures in the complex environment of a busy hospital³⁵.



Health-care associated infections are increasingly common because of the vulnerability of sick patients, because complex surgical treatments open up many portals of entry for infection, because of the accumulation of antibiotic resistant bacteria in hospital and because of cross-infection risks. Such infections of patients cause significant illness and death, at considerable economic cost³⁵. Many are preventable through effective infection control interventions (see Chapter 3).

In developing countries, with less well-resourced health systems, there are additional risks. Outbreaks of exotic infections such as Ebola have been seen in African hospitals. In some countries, the re-use of needles and syringes, or the use of unsterile blood equipment has transmitted HIV, hepatitis C or other infections to patients in hospital or outpatient clinics.

Hospital staff are also at increased risk of infection in developed countries. HIV or hepatitis B and C can be spread through accidental (needle-stick) injuries involving needles previously used for infected patients. Most infectious diseases, but notably tuberculosis and SARS, can also spread from infected patients to health staff caring for them.

Box 1.11 Hospitals spread Ebola and SARS

In Africa, hospitals amplified two outbreaks of Ebola, a disease caused by a virus spreading through re-use of syringes and needles in 1976 and through poor hygiene in 1995. Seventy-six medical staff were infected in the first weeks of the 1995 outbreak. Following improved hygiene, barrier nursing and patient isolation only one other worker became infected¹⁹.

Hospitals in developed countries are also at risk as seen with the rapid spread of SARS to health care workers in Singapore and Toronto²⁰.

BENEFITS AND RISKS OF RESEARCH

The sciences of microbiology, epidemiology and immunology have already provided impressive tools for communicable disease treatment and control. Genetic engineering of microbes has provided even more possibilities for improved diagnosis, new vaccines, rational drug design and for other advances. Indeed, in the world of the future, Australia is very well situated to exploit new technology for public benefit. NHMRC³⁶ and other research agencies already support talented Australian medical researchers, with a proud record of achievement in communicable diseases and immunology (see also Chapter 4 and Appendices 2 & 3). The Department of Education, Science and Technology, through the Australian Research Council, the Commonwealth Cooperative Research Centre Program and the CSIRO, has also supported Australian research expertise of relevance for communicable diseases.

However some research can also have unintended consequences. For example, genetic manipulation of the mouse-pox virus recently created a new virus able to kill mice that were immune to the original mouse-pox virus³⁷. This example underlines why Australia has a rigorous and transparent risk assessment process for all genetically modified organisms. Humankind has opened Pandora's Box of genetic science and technology.

In realising the future benefits of research, Australia must also plan to minimise the risks. Fortunately, regulatory procedures are already in place³⁸. Scientists, alert to the possibility of such unforeseen consequences, are already working on solutions. Nevertheless, the public has a right to be informed of the issues and to be reassured that the precautions are adequate and that the net benefit of such research will continue to advance the public good.

CONCLUSIONS

Communicable disease control has hitherto been successful through the public health reforms to create healthy environments, through infection control and through scientific discovery of vaccines, antibiotics and other treatments. Improved public administration and education, clean water supplies and sanitation, improved nutrition and personal hygiene, better housing and working conditions led to dramatic reductions in death and disease in the generations born after 1850, with increased survival of infants and children, increased life expectancy and improved quality of life. Science and public health have made many advances.

Nevertheless, changes in human society have also given rise to many new problems in communicable diseases. For each unintended consequence of our actions, we have sought to find a solution. Sometimes the solutions themselves have led to other risks. For example, in response to our introduction of antibiotics, microbes have adapted with genes that resist their effects.

Box 1.12 The Red Queen Principle

In any evolutionary system, continuing development is needed just to maintain fitness relative to any competitor. This principle, from L. van Valen in 1973³⁹, is named from the observation to Alice in Lewis Carroll's "Through the Looking Glass". As the Red Queen said: "in this place it takes all the running you can do to keep in the same place."

This race between us and the microbial world, as epitomised by the "Red Queen"³⁹, is likely to be never-ending. Microbes will always be able to evolve quickly to exploit the gaps in our armoury and in our defences against them.

Life can never be risk free and our medical scientists and public health professionals must be prepared and supported to keep abreast of the microbial challenges that will arise in future years and generations. Furthermore, with the burgeoning of new scientific knowledge comes the additional responsibility of keeping our society informed about the known benefits and risks of new

treatments and interventions. Along with the balance of benefit and risk that we can see now, we need to also consider unintended consequences that may be unforeseen and even unimaginable. The lesson from history is clear. Any action we take, regardless of whether we see it as health-related, can have an impact on communicable disease.



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