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Communicable or transmissible (contagious) diseases have been around at least since biblical times. Mummified remains from ancient Egypt indicated the presence of smallpox in the early days of that empire, but recorded descriptions of viral illnesses didn’t come about until centuries later. Smallpox devastated populations in large parts of Europe, and the Europeans transmitted smallpox (and other diseases), largely eradicating Maya, Aztec, and Inca cultures, and had almost as devastating effect on Aboriginal groups in what is now Canada. In Europe, several hundred millions died as a result of smallpox before a vaccine was discovered by Edward Jenner in 1798. Still, during the twentieth century smallpox was thought to have been responsible for upward of 300 million deaths and, according to the World Health Organization, as recently as the 1960s the disease was contracted by more than 15 million people, leading to 2 million deaths. The bacterial disease bubonic plague (Black Death) also has a long history, having been recorded in Russia in the sixth century, subsequently reappearing on many occasions (Bos et al., 2011). An accurate figure of how many people died as a result of the Black Death aren’t certain, but estimates have ranged from 25 million up to 200 million within Western Europe and as high as 375 million world-wide. The Black Death only obtained its wicked status as a pandemic when two mutations developed. The first allowed the development of ‘pneumonic plague’, a respiratory condition that permitted spread through coughs and sneezes. The second was a mutation that allowed for the high incidence and killing potency of the bacteria (Zimbler et al., 2015). Puny little mutations allowed for a disease to become a pandemic. What other little surprises will occur in the bacterial genome that could lead to another pandemic?

(Continued)
Viruses and bacteria are horrible enemies who don’t seem to fight fairly, adopting all sorts of terrorist tactics. Viruses are able to mutate in order to avoid detection by vaccines, and every few years entirely new viruses pop up. Those that we’re most familiar with now are influenza (flu) outbreaks that occur each year. Most take a toll on humans, varying from year to year, and according to the Center for Disease Control (CDC) the number of people infected in the United States (comparable numbers occur on a per capita basis in Europe, the UK, Canada, and Australia) ranges from 5% to 20% of the population, leading to more than 200,000 hospitalizations and 3,000–49,000 deaths each year (Thompson et al., 2009), but there have been more severe outbreaks. The Spanish flu (swine flu) that raged from 1918 to 1920 affected 500 million people, and was responsible for the death of more than 50 million (perhaps even as high as 130 million), which eclipsed all the deaths of World War I that preceded the outbreak. This virus originated in pigs and mutated so that it could be passed to humans, and then was spread widely by home-bound soldiers following the end of the war. Most viruses tend to have much greater effects on the young and older people, whose immune systems might be somewhat less developed or more compromised. However, the Spanish flu was an equal opportunity killer, and actually preferentially affected young adults by setting off an over-reaction of the immune system and consequently a lethal cytokine storm (Simonsen et al., 1998).

By comparison to the Spanish flu, HIV/AIDS has had a relatively modest effect, infecting about 75 million people, and causing about 36 million deaths at a time when the population is far greater and travel is much simpler. Ebola, which is the most recent mass terrorist, has frightened people around the world because of its potential, even though its passage requires contact with infected tissues, and for the moment the number of infections is still relatively small. We’ve had scares of many epidemics and pandemics in recent years. Bird flu, SARS, West Nile Virus, and now there’s again the threat of MERS, and H5N1 as well as H7N9 lurking around the edges of our awareness. The recent version of the swine flu, H1N1, could be transmitted fairly readily, but we were lucky in that it wasn’t as lethal as other diseases, although approximately 60 million people contracted the illness, 275,000 people were hospitalized, and 12,500 deaths occurred (Shrestha et al., 2011).

There is a common belief that if we receive a vaccination, then we’ll be immune from a particular virus. However, vaccines aren’t always effective. Some vaccines protect people 90% of the time and thus many illnesses have been largely eradicated, but they can make a comeback when people stop enjoying the advantage of vaccination, as we’ve seen recently in relation to measles. Other vaccines are variable in their effectiveness, largely because the virus they’re meant to ward off keeps mutating. Although flu vaccines are generally effective in about 70% of people, the efficacy can drop to as low as 20%, as occurred in response to the 2014–2015 influenza outbreak. Mutations of the influenza variants are common, and it can be difficult to predict which will appear next; hence drug makers might not always get the right vaccine made, although there is some hope for a ‘universal vaccine’ eventually being made (Kanekiyo et al., 2013). It’s also difficult to predict which mutation will make the leap from animals to humans and lead to a vicious pandemic. Even if we are successful in preventing disease 99% of the time, these successes will be historical footnotes if we’re unsuccessful even once in being unable to deal with a novel and powerful virus.
IMMUNITY AND ILLNESS

Numerous factors related to our behaviors can influence immune system functioning and thus our ability to fend against challenges stemming from microorganisms. Chronic stressor experiences, an impoverished diet, or poor sleep might compromise our immune system’s ability to fight off viruses or deal with bacterial insults, thus increasing illness risk. Moreover, inflammatory processes have been linked to psychological disorders, such as depressive illness, and to the development of Alzheimer’s disease, and might account for the comorbidities reported between these disorders and others linked to inflammatory processes, including diabetes and heart disease. Still other illnesses may emerge owing to immune responses being turned on the self, culminating in an autoimmune disorder. In this chapter we’ll consider:

- the processes that are associated with several immune-related disorders
- how immune-related illnesses occur, including those that involve allergies, those that are infectious (occurring owing to microscopic germs, such as bacteria or viruses), and those that are contagious (spreading from person to person)
- what occurs when the immune system fails to attack pathogens, and what can occur when the immune system over-reacts
- illnesses that may come about when the immune system turns against the self
- how life experiences and behavioral factors may come to affect the development and progression of viral illnesses.

ALLERGIES

What’s an allergy?

Allergic responses to environmental stimuli are exceedingly common, with about 30% of people reporting some type of allergy. People likely think of allergens such as pollen, dust mites, or animal fur (dander) as being most common, but there are a great many other environmental compounds that elicit allergic reactions. Certain medications (e.g., penicillin), plants (poison ivy, poison sumac, poison oak), and mold lead to strong allergic reactions, and substances such as latex (e.g., in surgical gloves) can elicit fairly strong reactions, including in patients undergoing medical treatments. As well, many foods (milk or milk products, wheat, soy, eggs, peanuts, fish, and shellfish) can elicit allergic reactions. Some individuals, incidentally, are also lactose intolerant owing to the absence of a particular digestive enzyme, but this is not the same as a milk allergy, and should be considered separately.

Immunoglobulin E

Although allergic reactions have been documented for millennia, it wasn’t until the early part of the twentieth century that it was discovered that they evolve as a result of individuals being
exposed to environmental antigens that had previously been encountered. When allergens appear on the body’s surface or in the eyes, mouth, nasal passage, throat, or gut, immune cells will act to eliminate them, and in doing so a memory of the antigen will be maintained by some cells. Having made contact with an allergen, a still stronger immune response will be elicited upon the allergen being encountered again some time later, taking the form of excessive Immunoglobulin E (IgE) activity (Gould & Ramadani, 2014). The IgE over-reaction triggers particular white blood cells, mast cells, and basophils, so that they release the hormone histamine, which causes secretions from mucus glands, coupled with nasal and/or bronchial congestion. These responses, however annoying, are typically manageable. But, in some instances, the reactions may be exceptionally marked, as seen among some individuals in response to insect (bee) stings, medications (e.g., penicillin), or particular foods (peanuts), leading to an anaphylactic reaction, characterized by itchy rash, throat swelling, and low blood pressure, and it can result in death. Anaphylactic reactions aren’t overly common, but estimates of their occurrence have ranged from 0.5% to 2.0%, with risk for such reactions being elevated in those with asthma, eczema, or allergic rhinitis (Simons & World Allergy Organization, 2010).

**Familial factors and stressors**

Allergic reactions may be linked to genetic influences given that allergies run in families, and identical twins tend to be more likely than non-identical twins to exhibit the same allergies (Galli, 2000). Beyond the genetic influence, the pathophysiological profile of those with allergies is in some ways similar to that which accompanies chronic stressors (Dave et al., 2011), and stressful events, especially those encountered early in life, may contribute to the development of allergies, including particular food allergies (Schreier & Wright, 2014). Predictably, the effects of stressors on allergic reactions are especially evident in the presence of a family history of certain types of allergic reaction (Yonas et al., 2012). Presumably, the increased allergic reaction associated with stressors stems from the immunological changes that are introduced, leading to an imbalance between those attributes of the immune system that activate and those that suppress immune functioning, so that the balance rests on the side of excessive immune functioning that promotes IgG release.

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**GENETIC, EPIGENETIC, AND PSYCHOLOGICAL FACTORS IN ALLERGY-RELATED ILLNESSES: THE CASE OF ASTHMA**

Illnesses associated with allergies, such as asthma – an inflammatory disease of airways stemming from genetic, epigenetic and environmental influences (Kabesch, 2014) – were at one time considered psychosomatic illnesses brought about principally by psychological factors, or a mix of psychological and medical problems. Asthma in children was referred to as ‘asthma nervosa’ because it was deemed to be a stress reaction that included neurological symptoms that stemmed from having a histrionic mother (when in doubt, blame mom). Another condition, atopic dermatitis, a form
of eczema characterized by a recurring, inflammatory skin condition, had been dubbed ‘neurodermatitis’, as it was considered to be a result of strong emotional responses. In fact, stressful events can instigate the occurrence of asthmatic episodes, and attempts were made to alter the coping methods that individuals used in an effort to diminish asthmatic reactions (Barton et al., 2003). Other approaches to diminish allergic reactions included relaxation therapy, biofeedback, or mental imagery to diminish anxiety (e.g., Lehrer et al., 2004). Psychotherapy or antidepressant medications were also reported to have positive effects among asthmatic patients who were depressed (Lehrer et al., 2002).

Stressors, including family conflict, negative life events, poor social support, and the presence of ruminative behaviors, might aggravate the symptoms of atopic dermatitis and increase asthma-related hospitalization (Schreier & Wright, 2014). Such effects might come about in combination with several genes related to asthma, and may be particularly amenable to epigenetic changes in response to environmental events (e.g., prenatal maternal smoking), and risk for asthma can be passed across generations (Harb & Renz, 2015).

**Microbiome involvement**

Increasingly more data have pointed to the microbiome’s contribution to allergies. Ordinarily, the mucosal membrane within the digestive system, together with various immune factors, limit the potential immunological effects of food antigens (they are, after all, foreign to the body), allowing tolerance for these to develop. However, problems can potentially arise owing to defects in this barrier system (Chahine & Bahna, 2010). Particular foods consumed during early life, including breast milk and solid foods that are subsequently introduced, can influence gut bacteria that lead to allergies and inflammatory illnesses (Calder et al., 2006). Indeed, the microbiome of individuals with allergies is distinguishable from those without allergies, possibly owing to diet, antibiotics, and other Western life-styles (Shreiner et al., 2008), and gut bacteria present early in life, say at 3 months of age, can predict food sensitization that appears by 1 year of age (Azad et al., 2015). The incidence of allergies has been increasing, making it likely that new external factors (possibly related to changing diets or increased use of antibiotics) are involved in disturbing balanced immune responses, and hence more frequent allergies (Belkaid & Hand, 2014).

**Treating allergies**

Allergic reactions can be precluded by staying away from allergens (e.g., not permitting kids access to peanuts), but some can’t be avoided, thus alternative approaches are needed. Allergen immunotherapy, which comprises administration of increasing levels of an allergen over an extended period, is used in an effort to desensitize reactions to the allergen. A variant of this approach was recently adopted in which young children (1 year of age) who were at risk for allergic reactions based on the presence of other immune-related conditions (e.g., eczema present) were fed peanuts several times a week until the age of 5. At that time the incidence of peanut allergy among children who had received peanuts previously was reduced by more than 80% (Du Toit et al., 2015).
If treatments to create tolerance to allergens aren’t effective, then several alternative treatments can be used to limit symptoms. Steroid hormones that reduce immune activity have served in this capacity, and medications such as antihistamines and decongestants reduce symptoms. In the case of strong anaphylactic reactions that can be life threatening, epinephrine injection is necessary should exposure occur. Those who show such reactions ought to carry an automatic injector with them (e.g., an Epipen®), but I’d guess that a few people might not have it with them just when it’s needed.

**CAN THINGS BE TOO CLEAN?**

We hear it all the time; having kids in day care exposes them to all sorts of bacteria so that their immune systems are strengthened. The hygiene hypothesis holds that early experiences that are too sterile can result in immune tolerance to foreign substances not developing, and hence exaggerated responses (allergies) will develop to some substances that are ordinarily harmless. This view was advanced to account for the progressive growth of asthma in the last few decades (Strachan, 2000), and has been applied to other immune-related illnesses, such as multiple sclerosis (Okada et al., 2010), inflammatory bowel disease, as well as the process by which immune factors might come to promote depressive disorders (Raison et al., 2010). In fact, it has been shown that growing up in a microbially rich environment (e.g., farms) was accompanied by diminished occurrence of inflammatory bowel disorder during adulthood (Timm et al., 2014). In essence, that maxim about ‘cleanliness is next to godliness’ could be a little over the top, and obsessive cleanliness might be more damaging than helpful.

**INFECTIOUS DISEASES**

Our immune system has to deal with many viruses and bacteria, fungi, multicellular parasites, protozoa, as well as prions that cause illness (prions are misfolded proteins that lead to pathogenic proteins that cause Bovine spongiform encephalopathy, more commonly known as mad cow disease, in cattle and other livestock, and Creutzfeldt-Jakob disease, which occurs in humans). The goal of these microorganisms is their own survival, and if we are the means to that end, then they just do what they have to do. Many of these agents have developed means to multiply in great numbers and to escape from our ways of combating them. Under the right conditions bacteria can double their number every 30 minutes, but they need particular environments to flourish, including the right temperature and pH, and they need water, oxygen, and a source of energy. Some bacteria, like streptococcus, can be self-sufficient, being able to persist for some time on various external objects, such as door handles, as well as on toys and cribs, and thus can represent a fairly persistent threat.
Table 10.1  Routes of infection

Transmissible (communicable) illnesses are those that can be transmitted from one human to another or from one animal species to another member of the same species, or can be transmitted across species. These pathogenic organisms can be transmitted through several different routes.

- **Airborne transmission** – when individuals breathe, cough, or sneeze, infected droplets are placed in the air (particular dust particles can also have these droplets attached), and if these can remain suspended for long periods, another person can inhale them, leading to illnesses.
- **Droplet contact** – coughing or sneezing on another person.
- **Contact transmission (direct)** – when a disease agent is transmitted directly from an infected individual to someone else through direct physical contact, such as touching an infected person, including sexual contact.
- **Contact transmission (indirect)** – infection transmitted indirectly, for example carrying an infection on unwashed hands, depositing these on a surface, which is then touched by another person. Contact illnesses include ringworm, smallpox, scabies, scarlet fever, and impetigo.
- **Vehicle transmission** – disease agents that can be transmitted through water, ice, food, serum, plasma, or other biological products. Many diseases are passed in this manner, including cholera, dysentery, diphtheria, scarlet fever, tuberculosis, typhoid fever, and viral hepatitis.
- **Transplacental transmission (vertical disease transmission)** – diseases can be passed from a pregnant mother to her fetus, e.g., HIV, syphilis, rubella, measles, toxoplasmosis.
- **Fecal–oral transmission** – usually develops when a person doesn’t take basic hygienic precautions (e.g., failing to wash their hands following a bathroom stop) so that fecal bacteria contaminate door handles, counter tops, food or water sources, thereby being passed on to others.
- **Vector transmission** – when transmission occurs indirectly through another organism, such as a mosquito, or through an intermediate host, as in the case of tapeworm being passed on through improperly cooked pork.
- **Zoonotic diseases** – infectious diseases that are transmitted from animals to humans.

**Bacterial infection and antibiotic use**

Bacteria can promote a range of illnesses, such as food poisoning and gastritis, upper respiratory tract infections, pneumonia, skin infections, urinary tract infections, and sinusitis. Some illnesses come about owing to a specific bacterium, whereas others can be provoked by a number of different bacteria. For instance, bacterial meningitis, which affects about 4,500 in the US and 3,200 people each year in the UK (with a 10% death rate) can arise owing to infection by streptococcus pneumonia, neisseria meningitidis, or several other bacteria. Having antibiotic agents to fight bacteria has been among the most important weapon in our arsenal to protect human health, and history tells us about the horrid consequences of not having agents that are effective in this capacity.
How antibiotic resistance develops

Unfortunately, the increasing use of antibiotics has been met by increased resistance to their effects (antimicrobial resistance), leading to ever more serious challenges in the treatment of many infectious diseases, lengthier recovery times from infection, and a greater probability of death (Maragakis, 2010). Bacteria are fairly clever little marauders, who develop their resistance through a process much like natural selection. Those hardy bacteria that aren’t destroyed by the antibiotic will give rise to similarly resistant clones, and over successive generations they will be unaffected by agents attempting to destroy them. In fact, when a threat is present, as in the case of antibiotics being around, they mutate more quickly, possibly in an effort to escape the challenge (Al Mamun et al., 2012). But, they also have another skill set that makes them still more capable. Specifically, they can go dormant in the presence of an antibiotic so that they’re less likely to be attacked, and with repeated antibiotic attacks they ‘learn’ to stay dormant for periods that match the antibiotic’s actions, and then come out of this state when the antibiotics actions have dissipated (Fridman et al., 2014). If this craftiness weren’t enough, it also seems that bacteria act as a team, coordinating their actions so that maximal toxic effects can be provoked, probably owing to messaging from some external source (quorum sensing), such as the liquid in which they rest (Ng & Bassler, 2009). Communication not only occurs within a bacterial species, but across species, so that a variety of bacteria can get into squabbles with us. Should a set of bacteria find themselves without their teammates, they begin to mutate at a greater rate, and can grow as a group rather than floating about in isolation (Krašovec et al., 2014). This is a very adaptive response on the part of the bacteria, as finding itself alone might mean that it has lost allies to some agent acting against them, and the mutations may enhance the odds of survival of that bacterial species.

Resistance to the broad-spectrum antibiotic ciprofloxacin (Cip) has been found in some forms of common bacteria, creating havoc in relation to our well-being. This is not unique to bacteria, but also occurs in relation to parasites, such as lice, which have become progressively more resilient to lice-killing chemicals (Durand et al., 2012), and it is believed that treating mosquito netting may have inadvertently increased the risk for malaria owing to insecticide-resilient mosquitoes (Norris et al., 2015). Ranchers and farmers who load up their livestock with antibiotics that humans eventually ingest may be a major contributor to antibiotic resistance, although this issue is still being debated in some quarters.

Beating antibacterial resistance

Health Canada has indicated that since 2002, there has been an enormous increase of last-line (last resort) antibiotic use and that 5% of people will likely be affected by antibiotic-resistant bacteria. It’s not a Canadian problem alone, as the World Health Organization has considered the issue a global emergency. Owing to the relatively rapid appearance of bacterial-resistant infections it essential for new and better antibiotic treatments to be developed. But, even if these come down the pipeline, will the same type of resistance occur again? Behavior of patients and doctors needs to change in order to prevent this. People need to be educated so that they don’t ask for or obtain antibiotics every time they’re ill, especially when the illness is viral, for which antibiotics aren’t effective. Moreover, well-intentioned doctors need to be re-educated as they occasionally do mess up. More than two-thirds of bronchitis patients in the US received antibiotics, even though bronchitis is most often of viral origin (Barnett & Linder,
Likewise, 60% of physicians prescribed antibiotics for sore throats, despite just 10% of cases being related to strep bacteria. Incidentally, doctors also had an affinity for prescribing newer broad-spectrum meds (newer must be better), even when these weren’t the best medication. In light of these problems, medical agencies have been making efforts to have doctors act more responsibly and take on greater stewardship in relation to their patients’ medications.

MULTIPLE COSTS OF ANTIMICROBIAL RESISTANCE

Hospital-acquired infections have been a problem for some time, and the CDC estimated that within the US, bacteria and other microorganisms are responsible for about 1.7 million hospital-associated infections and 100,000 deaths annually, with staphylococcus aureus (S. aureus) being best known. *Staph infection* is the most frequent cause of post-surgical wound infection, endocarditis (inflammation of the inner layer of the heart), bacteria in the blood (bacteremia), sepsis and whole body infection, as well as toxic shock syndrome, meningitis, and pneumonia. Although these infections could be treated with antibiotics, such as methicillin, a bacterial strain has developed, termed methicillin-resistant Staphylococcus aureus (MRSA), that has ceased responding to this agent (Chambers, 2001). Infection by S. aureus within hospitals has increased progressively over the years, doubling between 2000 and 2010 (Jarvis et al., 2012), but thankfully, owing to improved health practices, infection rates have been declining. As it turns out, however, it became progressively more common for community-acquired infection to be found in individual homes (Kassakian & Mermel, 2014) and in foods such as meat and poultry.

The occurrence of MRSA within the community, estimated to be about 12% in the US, has been linked to recent antibiotic use, people sharing contaminated items, the presence of active skin diseases or injuries, poor hygiene, and crowded living conditions. As with many illnesses, some individuals are more likely to develop S. aureus infections, including diabetics who use insulin, individuals undergoing chemotherapy, and those with HIV/AIDS or with a weakened immune system stemming from other factors. Vulnerability to infection is also elevated among individuals with burns, cuts, or lesions on the skin, as well as patients who undergo breathing intubation, or who have urinary or dialysis catheters inserted, as well as people who have medical implants such as hip replacements. Stressful experiences, presumably because of the effects on immune functioning, can also influence vulnerability to S. Aureus infection, especially in vulnerable populations such as older people (Bailey et al., 2003). Among children who have experienced trauma, hospital-associated infection could be predicted on the basis of a low and persistent immune response (Muszynski et al., 2014). MRSA also seems to thrive among smokers, and aspects of cigarette smoke may somehow protect MRSA from factors that would otherwise destroy these bacteria (McEachern et al., 2015). Evidently, the only thing that cigarette smoke doesn’t harm is some things that are otherwise bad for our health.

It’s not just S. aureus that has developed resistance to antibiotics. Tuberculosis has been infecting people for centuries, and was a leading cause of death in Europe in the eighteenth and nineteenth...
centuries, but couldn’t be treated effectively until the introduction of streptomycin in the mid-twentieth century. Tuberculosis is still around, affecting about 9 million people in 2013, and led to about 1.5 million deaths primarily in Asia and sub-Saharan Africa. This infection seems to get relatively little attention, even though a drug-resistant form of it has been spreading (World Heath Organization, 2014b). Likewise, an antibiotic-resistant form of typhoid has been spreading throughout Asia (Wong et al., 2015). This bacterial strain, dubbed H58, initially appeared several decades ago, but only recently has it become the dominant form of these bacteria. Given that typhoid affects about 30 million people each year, high levels of global surveillance will be necessary.

It so happens that yet another bacterial infection has turned up in Western countries, which seems to be treatment resistant. The usual treatment of Shigella had been ciprofloxacin, but the CDC (2015c), in their Morbidity and Mortality Weekly Report (MMWR), announced that this agent can’t be counted on to treat this illness much longer. More than 500,000 people are affected by Shigella within the US on a yearly basis through the ‘the fecal–oral’ route. What this means is that some infected person went to the washroom, and then with disregard to basic health issues didn’t bother washing their hands before exiting. They deposited their bacteria on the washroom door knob, or shook hands with you, and you may well have touched your mouth afterward. Alternatively, perhaps that person offered you half of their sandwich, which you accepted, and you thus became an unwitting consumer of poo-bacteria. Because Shigella is as infectious as it is, causing illness after ingestion of only a dozen or so bacteria, you became a victim of this chain, causing symptoms such as fever and even bloody diarrhea. You might get better on your own, or it might require antibiotics. But if Shigella is resistant to treatment, then you’ll be sicker longer, and thus more likely to spread the bacteria to others. The messages here are fairly clear. Don’t over-use antibiotics and wash your hands after visiting the ‘washroom’. For what it’s worth, I’ve neurotically taken to using paper towels to grab the door handle when I exit washrooms.

There have been numerous attempts to curb resistant bacteria and, as already indicated, some advances have been made by adopting simple procedures, such as hand-washing and having physicians alter their practices in doling out antibiotics. It has also been suggested that by alternating doses of antibiotics, and those that are used in successive infections, the appearance of resistance can be diminished (Fuentes-Hernandez et al., 2015). Another approach has entailed genetically altering resistant bacteria to make them more sensitive to antibiotics (Yosef et al., 2015).

**Viral infection**

Viruses, unlike most bacteria, can only multiply inside living cells, and they can be transmitted to other organisms in a variety of ways, as described earlier. Components of a virus (virions) attach to and penetrate a host cell, and then the virus incorporates itself into the genome of this cell. Thereafter, replication of the virus occurs within the host’s DNA or RNA. After sufficient replication, the virus can force itself through the host cell’s membrane or the host cell disintegrates, but either way the virus may infect other nearby cells (Dimmock et al., 2007). Viruses have been
considered not to be a life form because of their inability to reproduce on their own. Instead, they have been thought of as ‘organisms at the edge of life’ as they possess genes and can change through natural selection, which is dictated by environmental demands (Rybicki, 1990). The most common viruses that affect humans are depicted in Figure 10.1.

The extent to which a virus spreads through a population depends on how readily it can be passed on from one person to another, the route by which it’s transmitted, how readily it can penetrate the host’s tissues and attach itself to cells, its ability to inhibit the host’s immune defenses and to obtain nutrition from the host, and how quickly the virus kills the host. If a virus causes death of the host too rapidly, then the opportunity for the virus to be transmitted is diminished, although passage from one person to the next, as in the case of Ebola, may come about even if the host is dead. If the host doesn’t die immediately, then the opportunity for viral
transmission is increased, depending on the viral load being carried and whether the virus can avoid detection. Some viruses, like influenza, have further dirty tricks they use to cause illness. With the assistance of particular proteins (neuraminidase) they have the ability to counter the attack of natural killer cells, increasing the likelihood of the host becoming ill. As it happens, in this instance, treatments have been developed to deal with the wicked skills that viruses possess. Inhibitors of neuraminidase can be used to make natural killer cells more effective, and thus diminish flu symptoms. Antibodies have also been developed that bind to proteins that otherwise hinder natural killer cell activity, thereby allowing them to do their job more effectively (Bar-On et al., 2014).

**THERE’S SOMETHING ABOUT MARY**

Some individuals are ‘superspreaders’, seemingly infecting more than their share of people by passing on bacteria or viruses. It may be that there’s something about their immune response that makes them so capable of infecting others, or they may be especially social and thus come into contact with more people than do others, or have occupations that permit them to do so. In the early 1900s, Mary Mallon, much better known as Typhoid Mary, was a cook who seemed to be a virtuoso in spreading typhoid (which comes from the bacteria salmonella), even though she never actually showed symptoms of the illness. She is credited with infecting about 50 people, eight of whom died. Poor Mary has been villainized, as she should have – not just because she spread the disease, but because she refused to alter her behaviors when suspicions arose that she was the ‘spreader’, and she even put herself in places (e.g., as a hospital cook) where she could do particular damage (Ram, 2014). She was eventually isolated, but she did become a bit of a celebrity thanks to the newspapers encouraging sympathy for her. The 80–20 rule (also known as the Pareto principle) may apply to viral spread in that 80% of an infectious disease is transmitted by 20% of the people. We can only hope that the potential spreaders choose to be vaccinated.

**Zoonotic diseases**

Viruses and bacteria can be transmitted to humans through a ‘vector’, such as mosquitoes or ticks (malaria, Lyme’s disease, West Nile virus, dengue fever, and yellow fever), birds, pigs, or rodents and even through dogs (as in the case of rabies) and monkeys (Simian immunodeficiency virus might have been transferred to humans which then could have mutated into HIV). Over the past two decades the frequency of emerging vector-borne zoonotic diseases has been increasing (Kilpatrick & Randolph, 2012), but typically these viruses don’t make the leap to being transmitted between humans. However, if a virus mutates in some way so that it can be transmitted between humans, the outcomes can be horrendous, as we’ve seen in the case of HIV/AIDS, as well as in the recent Ebola epidemic.
The best way to deal with any illness is prevention, and in the case of viral illnesses, this entails being vaccinated against them. Having encountered a foreign pathogen, T and B cells will have a memory of it so that if it is subsequently encountered again, our strong secondary immune response will sharply reduce the odds of the illness developing. Vaccines that we currently use are based on this very principle, being made up of dead, inactivated, or weakened viral particles, or products that are derived from them. The vaccine won’t cause us to become ill (contrary to some of the rumors spread by anti-vaxxers), but because the dead or weakened virus will be recognized as being foreign, an immune response will be mounted, and information about this virus will be retained by immune cells. Thus, when a potentially harmful virus is later encountered, it will be eliminated by the strong immune response that occurs. It’s thanks to mass vaccinations that diseases such as polio have been almost eradicated and measles, mumps, and rubella, which also caused many deaths, have been diminished (Lane, 2006).

In the case of many illnesses (e.g., measles, polio), the effectiveness of vaccines is impressive, although their effectiveness may vary somewhat across people, and may decline with age. In other instances, such as flu vaccines, their effectiveness is far more variable. Just as we keep looking for better ways to detect and destroy viruses, they make considerable efforts to avoid being detected or find ways in which the agents that we use to destroy them will not have the desired effects. One way viruses do this is through mutations so that they’ll be less likely to be recognized. As influenza viruses come in a set number of formats, we can anticipate what they might look like, and thus have a head start in making supplies of vaccine. Yet, even with the best information available, vaccine producers may be fooled, and thus the effectiveness of the vaccine will be diminished. In other instances the vaccine might be an effective one, but some individuals might simply be ‘nonresponders’ to certain vaccines in that they don’t produce sufficient antibodies to fight future infection (Osterholm et al., 2012).

The ability of a virus to affect whole populations or to turn into a pandemic is influenced by the extent to which the virus can be spread. Some viruses are effective in this capacity (e.g., when one infected person spreads it to 12 others), whereas others spread poorly and die off (1 person infects 0.5 others). When enough people in a population are vaccinated, even fairly potent viruses may have difficulty spreading, and the group as a whole will be protected (herd immunity). Ironically, this herd immunity also protects the children of parents who refuse to have their children vaccinated, which reinforces their noncompliance. However, like teeter-totters, this relationship moves up and down. When enough people within a population decide not to be vaccinated (or not have their children vaccinated), the ‘tipping point’ may be reached so that the herd immunity effect is no longer present, and the viral illness will spread, affecting those who hadn’t been vaccinated as well as those who are vaccine nonresponders. In the case of measles, which is easily spread, the tipping point is around 92%, and in some places vaccination rates have dropped below this level, so we can pretty much forget about herd immunity working (Continued)
much count on measles reappearing. While we’re on the topic of measles, don’t be misled into thinking that this is just one of those childhood illnesses that children get through. It’s not a benign disease and can be very serious, leading to many hospitalizations and deaths. Moreover, following measles infection, the immune system may be altered for as long as 2–3 years so that the risk for other illnesses is increased (Mina et al., 2015). As well, among young children in whom the immune system is not fully developed the measles virus can hide in the body, even for years, and may come to infect the brain. The so-called subacute sclerosing panencephalitis (SSPE) will then manifest in the infected person years afterward as mood swings, behavioral problems, convulsions, coma and, inevitably, by death.

The effectiveness of vaccines has been enormously successful in preventing many diseases, and this very success may have bred some of the current vaccine hesitancy that has become more common. People brought up in vaccinated societies who haven’t seen the horrendous impact of viruses such as measles and polio have become blasé in their attitudes.

There are many reasons why individuals might choose not to be vaccinated for common illnesses, such as influenza. Some of these have already been mentioned, such as mistrust of media and government agencies with respect to recommendations that have been made. A qualitative meta-analysis suggested that to a considerable extent individual behaviors in relation to vaccination are linked to personal experiences, such as those provided in Table 10.2 (Nowak et al., 2015).

Table 10.2  To be vaccinated or not

Factors driving choice to receive flu vaccination
- belief that individual is flu susceptible
- belief that the vaccine is effective and that being vaccinated matters
- being an older person or having an existent chronic health condition
- having had a recommendation come from a physician
- having previously experienced a bad flu or a similar illness
- having encountered active vaccination promotion indicating that it makes a difference
- easy access to vaccination

Factors driving choice to not receive flu vaccination
- belief, often based on personal experiences, that flu is a ‘manageable illness’
- belief that the recommendations for vaccination don’t apply to them
- belief that flu vaccines are ineffective
- hesitation based on belief that they could get the flu from the vaccine
- belief (or rationalization) that other measures are more effective
- having had some sort of negative personal experience with the vaccine
Neglected tropical diseases

We’re all now somewhat familiar with Ebola virus, but far fewer have ever heard of hookworm, schistosomiasis, lymphatic filariasis, ascariasis, or onchocerciasis, which are a few of the ‘neglected tropical diseases’ that appear primarily in Africa, Asia, and South and Central America. There are a fair number of such illnesses, stemming from protozoa, bacteria, viruses, and worms, but the World Health Organization has 17 that are most frequent, some of which are on the way to being eradicated, but there is still some distance to cover. These diseases affect more than a billion people a year, including almost half the school-aged children in sub-Saharan Africa, and a number are affected by more than one infection (Hotez & Kamath, 2009). Some of these illnesses are very treatable and inexpensive (as little as 20 cents per day in the case of schistosomiasis); others are more costly and beyond affordability for most people.

The economic and social impact of these diseases (think of responses to leprosy, which is one of these diseases) has been enormous, but they’ve been largely ignored. This might have occurred because of the double whammy of occurring primarily in the poorest parts of the poorest continent of the world, coupled with attention to these conditions being supplanted by HIV/AIDS, malaria, and tuberculosis. Several corporations have donated millions of dollars to deal with these conditions, as have private–public partnerships, such as the ‘Global Health Innovative Technology Fund’. It is surprising, though, that the total investments in eradicating these diseases has been so limited, particularly as these emerging infections may eventually come to affect those in the West.

SEXUALLY TRANSMITTED INFECTION

Some pathogens are endemic to our society, meaning that they don’t simply appear and then disappear, but instead are constantly present, as in the case of many sexually transmitted diseases (STDs). Some of these are more infectious than others, and some produce obvious symptoms, whereas others don’t. As a result, their transmission rates differ, as does their appearance within the population. There are several STDs that are of a viral nature, including hepatitis B, Herpes simplex virus 2 (HSV-2), HIV, and Human Papillomavirus (HPV), or they may be bacterial (chlamydia, gonorrhea, syphilis, bacterial vaginosis), fungal (candidiasis), protozoal (trichomoniasis), or a result of parasites (crabs, lice, scabies).

STDs are frequent throughout the world, and in Western countries they had been increasing with changes in sexual behaviors as well as the availability of oral contraceptives. This was compounded by increased travel, which allowed the greater spread of diseases, and by the increase of drug-resistant bacteria, as in the case of those that had previously responded to penicillin. Some STDs can be treated through antibiotics (chlamydia and gonorrhea) and penicillin was the preferred treatment of syphilis, although resistant bacteria have become more common in relation to syphilis, and a resistant strain of gonorrhea (H041) has appeared that is considered a superbug (Shimuta et al., 2013). In the case of some STDs, such as hepatitis B and HPV, vaccines have been developed, although a backlash has occurred as some parents refuse to have their kids vaccinated against HPV. Still other STDs are incurable (HIV, herpes), although the length and severity of herpes outbreaks can be reduced by antivirals (e.g., Zovirax, Famvir, and Valtrex). At the moment, abstention or use of condoms, rather than cure, is the key to dealing with these illnesses.
LIFE-STYLE FACTORS IN RELATION TO IMMUNE FUNCTIONING AND WELL-BEING

The ability of our immune system to contend with a variety of insults may be influenced by genetic factors, life-style – including what we eat, our sleep, exercise, as well as by stressor experiences, and thus each of these variables may influence the emergence of illnesses. Because so many of these variables affect one another, it is difficult to dissociate the influence of any single factor from others that are concurrently present.

Diet and immunity

Considerable attention has been devoted to analyses of the processes by which eating and energy metabolism can affect immune functioning, as well as the influence of various foods and specific diets. Aside from its role in digestive processes, the gastrointestinal (GI) tract serves as a barrier to limit potential adverse effects stemming from the foods that we eat. This is no easy task, as it means that the GI tract must differentiate between those substances that are good for us and those that aren’t. In part, this is accomplished by the presence of an appreciable portion of our immune system’s cells being present within the gut. As well, the epithelial cells of the GI tract, together with protective mucous, diminish the passage of damaging molecules into the body while allowing passage of beneficial substances. For effective immune system functioning, several essential vitamins and minerals (e.g., zinc, selenium, iron, copper, and folic acid) need to be present, which are largely obtained from the foods we eat. Likewise, essential fatty acids and mono-unsaturated fats are required for effective functioning of immune-related processes and for the maintenance of microbial balances.

As we’ve seen, many systems act in opposition to one another in an effort to maintain biological equilibrium. One mechanism may be present to get things started and another to get things stopped; one system may operate in an inhibitory capacity to regulate the excitatory effects of a second system. Similarly, the presence of reactive oxygen species (by-products of cellular metabolism) and other free radicals is needed at sites of inflammation in order to facilitate the death of cells that aren’t healthy. At the same time, antioxidant processes are needed to diminish the reactive oxygen species once they’ve done their job so that they don’t create damage to healthy cells. Once again, the ingestion of particular foods (e.g., red beans, blueberries, raspberries, cranberries, artichokes) facilitates antioxidant production, thereby limiting cellular damage.

Microbiota

Gut bacteria contribute to efficient immune functioning, and the alliance between the microbiome and the immune system is fundamental in the elicitation of responses to pathogens and in maintaining tolerance to innocuous antigens so that unnecessary immune activation does not occur (Belkaid & Hand, 2014). Likewise, gut bacteria can have pronounced effects on brain functioning and thus can affect psychological well-being (Ochoa-Repáraz et al., 2011). However, over-use of antibiotics and dietary changes may have favored microbial changes that have neither the diversity nor the resilience necessary for effective and balanced immune responses to be engendered (Belkaid & Hand, 2014), thereby affecting illness vulnerability. These core
microbial communities, and hence well-being, might also come to be indirectly affected by variations of socioeconomic status, cultural traditions, and increased urbanization, any of which influence diets. The repercussions of these changes may be particularly pronounced in young children given their sensitivity to foods (Jain & Walker, 2015) and may have particularly marked consequences on brain functioning among preterm infants (Sherman et al., 2015), and infants treated with antibiotics may be at increased risk of developing adult diseases (Vangay et al., 2015). It is especially interesting that a stressor in the form of repeatedly separating mouse pups from their mom during the first 3 postnatal weeks later exhibited altered gut microbiota, altered levels of the neurotransmitter acetylcholine, and displayed increased signs of anxiety and depression. When mice received the stressor treatment in germ-free conditions the microbiota and hormone changes were still apparent, but the elevated anxiety was absent. When mice were, however, colonized with bacteria from control mice, the anxiety was again apparent. Thus, it seems as if both host characteristics and microbial contributions are necessary for the adverse effects of early-life stress in the formation of psychological disturbances (De Palma et al., 2015). Beyond these effects, it also appears that gut microbes contribute to the programming and subsequent responsivity of stress systems, including those involving neuronal, hormonal, metabolic, and immune mechanisms, ultimately affecting the regulation of mood and cognitive processes (Moloney et al., 2014).

**Exercise and immunity**

Given all that’s been said about the importance of exercise in maintaining well-being and in diminishing the impact of life stressors (Fleshner et al., 2009), it comes as no surprise that a proper exercise regimen enhances immune functioning (e.g., augmenting NK cell functioning) (McFarlin et al., 2005), and perhaps limits the immune system’s decline with advancing age (*immunosenescence*). Although the available data are inconsistent in several respects, it largely appeared based on animal studies that moderate intensity exercise enhances immune functioning, and thus beneficial health effects may be accrued (Pedersen & Hoffman-Goetz, 2000).

Among humans who exercised on a regular basis (habitual-exercisers) life span was shown to have increased, and the time during which they remained healthy (*health span*) was lengthened relative to individuals who typically didn’t exercise. Ordinarily a sedentary life-style may lead to increased visceral fat, and the cytokine release from *adipokines* (cytokines released from fat cells) may favor the development of illnesses. Thus, by limiting visceral fat, exercise might serve to prevent the development of these illnesses (Pedersen, 2009). This doesn’t imply that more exercise is necessarily better. Unlike the positive effects of moderate exercise, excessive exercise that leads to fatigue has produced lymphocyte loss and increased illness symptoms brought on by an influenza virus (Hoffman-Goetz & Quadrilatero, 2003). Similarly, among people who engage in ‘extreme exercise’, which is often the behavior of high-performance athletes, immune functioning may be both impaired and accompanied by increased incidence of virally-related conditions, such as herpes virus and reactivation of Epstein-Barr virus (Walsh et al., 2011), as well as a marked increase of upper respiratory infection (Edwards et al., 2008). The health disturbances were attributed to disturbed natural killer cell functioning and reduced immunoglobulin within mucosal secretory (nasal and salivary) glands, allowing infectious molecules the opportunity to invade.
Figure 10.2  Life span and health span vary with age among individuals who maintain generally sedentary life-styles (nonexercisers), those who participate in regular exercise to enhance their health and well-being (habitual exercisers), and those who participate in extreme exercise. Whereas habitual exercisers may experience longer life and an extended health span, among extreme exercisers diminished immune functioning and poorer control in relation to viral infections may occur, and hence they will experience reductions of life span and health span. These findings raise several questions, including how being brought up with particular life-styles will affect life span and health span, and whether exercise regimens at various ages influences health disturbances that might be provoked by stressors. From Simpson & Bosch (2014).

Sleep and immunity

Sleep disorders may promote illness and may influence mortality as a result of varied disorders, often stemming from immune disturbances (Irwin, 2015). The implications of these findings are fairly significant given that 25% of individuals experience a degree of insomnia, with almost 10% meeting the criteria for chronic insomnia (LeBlanc et al., 2009).

Sleep and circadian rhythms contribute to the regulation of immune processes, and sleep disturbances are accompanied by impaired immune functioning (Irwin, 2015). As indicated earlier, sleep has profound recuperative powers, and the lack of ‘restorative sleep’ when accompanied by elevated inflammation may contribute to heart disease (van Leeuwen et al., 2009). Even a single night of sleep loss may be sufficient to disturb immune functioning, reflected by the diminished effects of influenza and hepatitis vaccination (Spiegel et al., 2002), and diminished sleep was associated with increased incidence of the common cold (Cohen et al., 2009). The effects of sleep loss may directly influence immune processes that affect illness vulnerability or, alternatively, the conditions that lead to sleep disturbances can elicit stress-related hormonal disturbances that could influence immune functioning (Irwin, 2015). Either way, like exercise and diet, sleep is an essential element of life-style that affects immune competence.
Stressors and viral illness

Stressful events affect immune functioning, and such experiences understandably affect susceptibility and frequency of viral illnesses (Chida & Mao, 2009), diminish the elimination of a virus, lengthen the course of illness, and favor more frequent infection-related complications (Bailey et al., 2007; Elftman et al., 2010). Among the first ‘formal’ demonstrations of such actions (moms were saying this for ages, but without hard evidence) was that stressful experiences were accompanied by increased occurrence of colds among individuals treated with a low dose of the virus (Cohen et al., 1993), especially if the stressor had been experienced chronically (Cohen et al., 1998). Similar outcomes were subsequently observed in relation to other types of virus, such as the response to cytomegalovirus (CMV), and antibody production upon exposure to Epstein-Barr virus, and stressors that exist at the individual and the neighborhood level may exacerbate the progression of HIV to AIDS (Aiello et al., 2010). In addition, stressors may affect the reactivation of a latent virus, such as HSV-1 (the virus that causes cold sores), that had been in hiding within the trigeminal ganglion. As a result, cold sores associated with infection may recur, often at the most inopportune times. It is largely taken for granted that stressors are causally linked to viral illnesses, but it is not unusual for stressor experiences to be accompanied by other life changes, including altered diet, sleep, and exercise, and the illnesses associated with stressful experiences may reflect the interactive actions of these various factors.

AUTOIMMUNE DISORDERS

Despite the immune system being reasonably effective in protecting us from an assortment of microbes, there are occasions in which it seems confused, and instead of focusing on external challenges, it turns against us, resulting in autoimmune disorders in which our own organs or tissues are attacked. There are about 75–80 disorders that are known or suspected to fall into this class, with their combined overall prevalence being about 8% in developed countries. For most of these illnesses, the frequency is far greater in females (70–90%) than in males. The view is often taken that females carry particular vulnerability factors that place them at increased risk for such disorders, but it is possible instead that males carry a protective factor so that they’re less likely to be affected. The processes responsible for these disorders vary from one another, even though many are comorbid conditions, and the course of the illnesses can be exacerbated by common factors. It is possible, for instance, that autoimmune disorders involve a gene variant that influences T helper cells so that normal cells are attacked more readily, or cells that normally suppress immune functioning aren’t operating efficiently. In conjunction with these operations, still other genetic variants might determine which specific aspect of the body will be attacked. In this regard, the ‘autoimmune regulator’ gene (AIRE) is responsible for training immune cells to ignore self-made antigens, and attack only those that are foreign. However, it was suggested that a child who inherits two mutated versions of the AIRE gene (and it seems that this may even occur with a mutation on one allele) won’t have the ability to examine immune cells as to their competency, and as a result some of them may turn on the body’s own organs (Oftedal et al., 2015). In essence, if immune activity persists when it should be turned off, it can ultimately lead to the immune system attacking the self. As we’ll see in covering several autoimmune disorders, there is currently no cure for most of these conditions; some can be managed to an appreciable extent, whereas others seem to have so far eluded our abilities.
**Sjogren’s syndrome**

This disorder occurs at a moderately high frequency, but estimates of its prevalence have varied widely from 400,000 to 3.1 million cases. *Sjogren’s syndrome* occurs when the body’s white blood cells destroy salivary and lacrimal (tear producing) glands (Borchers et al., 2003). As a result, individuals experience dry eyes and mouth, and they may also experience problems related to blood vessels, various organs (kidneys, liver, lungs, and pancreas) as well as the peripheral nervous system and the brain. The disease usually appears in mid-life (45–55), is more common in women (90%), and often appears among individuals with a rheumatic disease (e.g., rheumatoid arthritis).

The causes of this autoimmune disorder are uncertain, but seem to involve genetic and hormonal factors, such as elevated estrogen (Voulgarelis & Tzioufas, 2010), together with a constellation of environmental influences that could affect glandular infection. Psychosocial factors, such as pain catastrophizing, was related to the presence of the disorder, and occurred relatively frequently among individuals who experienced high levels of psychological stress in response to major negative life events, but lacked effective coping strategies, such as social support (Karaiskos et al., 2009). These findings raise the possibility that behavioral interventions to reduce catastrophizing and negative illness appraisals, as well as training cognitive and behavioral coping methods, might be useful in controlling some symptoms (Segal et al., 2014).

**Psoriasis**

Psoriasis, which affects about 2% of individuals, is a chronic, immune-mediated skin disease characterized by itchy red, scaly patches, papules, and plaques that can be localized or may extend to broad sections of the body. Unlike many other autoimmune disorders, this condition appears among males and females equally, initially when they are between 15 and 25 years of age, more commonly among Euro Caucasians than African or Native Americans, as well as among individuals with other autoimmune-based illnesses, such as ulcerative colitis or Crohn’s disease (forms of inflammatory bowel disease). In psoriasis, the immune system mistakenly identifies normal skin cells as a pathogen, and overproduction of new skin cells may develop, sometimes being replaced at a rate 5–10 times faster than normal, owing to a cascade of cytokine alterations (Nestle et al., 2009). Genetic factors contribute to the emergence of psoriasis, but this alone is not sufficient to account for its occurrence, and several environmental factors also have powerful effects on this condition (Krueger & Ellis, 2005). For instance, symptoms may be aggravated by chronic infections, stress, smoking, diet, alcohol consumption, and changes in season (Nestle et al., 2009).

**Inflammatory bowel disease**

Inflammatory bowel disease (IBD) refers to inflammatory autoimmune conditions involving the colon and small intestine, with ulcerative colitis and Crohn’s disease being the most common. Although the latter is often thought of as being restricted to the colon and small intestine, it can also affect the mouth, esophagus, stomach, and anus. These illnesses are distinct from one another, but they share many symptoms related to intestinal problems, such as abdominal pain, vomiting, diarrhea, rectal bleeding, and severe internal cramps/muscle spasms in the region of the pelvis. As well, nonbowel-related characteristics might emerge (e.g., anemia) and several other
autoimmune disorders may co-occur with IBD, such as arthritis and primary sclerosing cholangitis (in which inflammation impedes the flow of bile to the gut, potentially causing cirrhosis of the liver, liver failure, and liver cancer). Recommendations have been made concerning the best foods to eat in order to limit IBD symptoms, including a diet that is limited in fermentable, poorly absorbed carbohydrates and sugar alcohols (Cuomo et al., 2014), but there is some question as to whether there is a specific diet that is most suitable (Hayes et al., 2014).

**Microbial involvement**

The appearance of IBD and ulcerative colitis are promoted by a large number of genes that together account for almost 10% of the variance of each disorder (Jostins et al., 2012). But, there’s obviously more to their occurrence and exacerbation, including influences of gut bacteria, particularly in the form of a reduced number of different types of bacteria (Mukhopadhya et al., 2012). Gut microbiota implicated in the emergence of IBD might also contribute to the comorbidity that occurs with other conditions, even having been linked to psychiatric disorders (Collins, 2014). Epidemiologic studies have consistently indicated that diet can influence the development of intestinal inflammation, and increasingly more studies have been assessing the effects of defined diets in reducing IBD through their microbial actions (Leone et al., 2014). As important as diet alone might be in affecting the microbiota, and hence IBD, we shouldn’t lose sight of the fact that the microbiota is affected by other life-style factors (antibiotic usage, infection, and stress) that ought to be considered in developing treatment strategies for this disorder (Collins, 2014).

It’s still not known which bacteria are principally responsible for the seemingly excessive immune response associated with IBD, although several culprits have been identified. Microbes of a clostridial family, often referred to as ‘clostridial clusters’, act against bacteria such as C. difficile that cause inflammation, diarrhea, bleeding, and massive loss of fluids that can lead to death. It seems that these clostridial clusters also play a fundamental role in limiting immune activation that could be harmful. In ‘germ-free’ mice bred to provide experimental animals that were relatively uncontaminated by a dirty world, strong reactions occurred to antibiotics in that their immune suppressor cells (Tregs) declined precipitously, and they became exceptionally susceptible to an inflammatory bowel condition much like that of IBD in humans. However, if mice were treated with a cocktail of bacteria from the clostridial cluster, the Tregs were reinstated and the bowel disorder diminished (Nagano et al., 2012). Taking the lead from such studies, efforts have been made to deal with such diseases by altering the constituent bacteria within the gut through diet or fecal microbiota transplantation (West et al., 2015).

Analysis of factors related to the microbiome has also provided a better understanding of Crohn’s disease, and has made us take a second look at how the microbiome operates. The view emerged that this disorder might evolve owing to bad gut bacteria provoking inflammation. However, in surgically removed portions of intestine from patients with Crohn’s there was a considerable reduction of a particular bacterium, *Faecalibacterium prausnitzii*. This led to the view that Crohn’s didn’t emerge owing to the presence of bad bacteria, but instead developed owing to specific ‘good’ bacteria being absent (Sokol & Seksik, 2010). Indeed, when these good bacteria were transplanted into mice, positive effects emerged. The question now is what causes these good bacteria to decline to levels that favor the development of illness, and what can be done about this.
Treatment of IBD

The realization that the enteric nervous system may contribute to IBD gave rise to the development of treatments aimed at serotonergic and neurotrophic processes which are plentiful in the gut nervous system (Hansen, 2003; Wood, 2013). Likewise, benzodiazepine-sensitive receptors are present, and stress responses can alter the functioning of the gut, and thus anxiety-related treatments have been used in an effort to control IBD (Salari & Abdollahi, 2011). There have also been a fair number of studies conducted to determine whether fecal microbial transplant, antibiotics, probiotics, and prebiotics can be used to treat IBD. However, most have involved a small number of patients and the results obtained were inconsistent. As a result, there has yet to be significant acceptance of microbe-based treatments for these conditions, although it may be premature to abandon them entirely (West et al., 2015).

Treatment of ulcerative colitis and Crohn’s disease are usually determined on an individual basis. The American Gastroenterological Association has provided guidelines for which treatments are most appropriate, given specific symptoms being expressed, such as presence of constipation versus diarrhea (recommendations entail linaclotide and rifaximin, respectively). When the conditions are relatively severe, immunosuppressive agents may be called for (e.g., TNF-α inhibitors, prednisone). If treatments fail, then surgical procedures may be required, involving removal of large portions or all of the large intestine. It is significant that despite these firm demarcations regarding treatment, there has been a notable increase in a push for individualized treatment of IBD (Mosli et al., 2014).

Celiac disease

Celiac disease, an autoimmune disorder involving the small intestine, affects 1.0–1.5% of Euro Caucasian people, but is infrequent among people of African, Japanese, or Chinese decent. This illness affects individuals of all ages, more commonly women than men, and has a clear genetic component (Gujral et al., 2012). Several genetic factors may contribute to the occurrence of celiac disease, although some individuals without this genetic constitution may also develop the disorder. At one time it was rarely diagnosed, but this increased as the disorder came to be understood and diagnostic procedures became available.

This disease is characterized by pain and discomfort in the digestive tract, chronic constipation and diarrhea, cramping, bloatedness and abdominal distension (owing to the production of bowel gas), weight loss or a failure to gain weight (in children), as well as fatigue and anemia. In the presence of severe celiac disease, pale, loose, and greasy stools may be present, and deficiencies of vitamins are not infrequent, likely owing to the diminished ability of the small intestine to absorb nutrients properly from foods (van der Windt et al., 2010). Typically, celiac disease is determined based on symptoms presented coupled with blood tests, endoscopy (an imaging procedure in which a tube is threaded to a hollow organ or body cavity), and through the determination of vitamin and iron deficiencies. Some patients present with atypical symptoms, but improved assessment methods have allowed for a diagnosis of this disorder to be made, although this may take some time (Pulido et al., 2013).

Symptoms of celiac disease stem from a reaction to gliadin, a gluten protein present in wheat and grains, such as barley and rye, which results in enzymatic changes that cause the immune system to react to small-bowel tissue, provoking an inflammatory reaction. This, in turn, causes the
villi (tiny hair- or finger-like projections) lining the small intestine to become shortened, which undermines the ability of the intestine to absorb nutrients and transfer them to blood vessels to which they are connected (Guandalini & Setty, 2008). It’s possible that early life consumption of wheat, barley, or rye, before barriers within the gut are fully developed, may encourage celiac disease (Akobeng et al., 2006).

Currently, the only way of managing celiac disease is through a life-long gluten-free diet (Fasano & Catassi, 2012). Depending on the degree of damage that has been created, the adoption of such a diet may allow for intestinal healing, attenuation or elimination of symptoms, and diminish the elevated risk for intestinal cancer and osteoporosis that is otherwise present. As the diet must be strictly maintained, the assistance of a dietician is highly recommended, and because the diet can be somewhat unappetizing, patients are encouraged to try new ways of preparing foods (Troncone et al., 2008). Unfortunately, among some patients, more so women than men, some symptoms may persist even with appropriate diets for several years.

### GLUTEN-FREE IS THIS YEAR’S FAD

Have you noticed the very large number of people who are currently on gluten-free diets, although only a small fraction of the population suffers from celiac disease? Some individuals without celiac disease claim heightened gluten sensitivity and report feeling better when not consuming food with gluten in it, but this condition is questionable based on clinical tests (Biesiekierski et al., 2013). Regardless of how this comes about, if it works for them, even if it’s a placebo effect, then that’s fine provided that essential foods don’t go by the wayside.

Gluten intolerance may be accompanied by skin diseases (Humbert et al., 2006), and there are individuals with psoriasis who believe that a gluten-free diet has helped control their symptoms, although it’s possible that this came about owing to weight loss and the consequent decline of cytokines released from belly fat that encourages autoimmune responses (Ricketts et al., 2010).

Being on a gluten-free diet has become a fad (is craze a better term?) encouraged by books that suggest that any product with wheat in it is dangerous, even those containing whole grains. Sports figures and some Hollywood types have also had an impact on the gluten-free movement, even though they might not be the right people to believe with respect to medically-related issues. Some people on this diet feel that it improves their mood, others believe that it will help them lose weight, which might be accurate given that the food is often unappetizing. However, if it’s not a medical necessity, as in those who actually are experiencing celiac disease, it’s probably not useful and can even cause some harm as these diets often lack needed fiber, minerals, and vitamins, and are not fortified by nutrients, such as folate and iron (although these fortified nutrients can be obtained through sufficient intake of other foods). Gluten-free diets are having a substantial popular impact given that big business has responded in a fairly big way, just as they would to any other fad that could mean billions of dollars in sales. Check the supermarkets and you’ll see gluten-free sections (is a gluten-free pizza really a pizza?), and name brand companies are advertising ‘gluten-free products’, even if they had never, ever had gluten in them.
Rheumatoid arthritis

Rheumatoid arthritis, which occurs in about 1% of individuals, primarily women (80%), is an autoimmune disorder that affects synovial joints (i.e., movable joints surrounded by a capsule containing lubricating fluid), the membrane that lines joints, tendon sheaths, and cartilage in the fingers, wrists, knees, elbows, and cervical spine. The disorder is characterized by inflammation of a single or multiple joints, joint pain, muscle aches and pains, general malaise or feelings of fatigue, and may be accompanied by weight loss and poor sleep. Although it is usually considered in terms of joint problems, it may also be accompanied by autonomic nervous system dysfunctions as well as heart problems (Adlan et al., 2014). This disorder usually appears when individuals are 40–60 years old, although systemic inflammation and autoimmunity may begin years before detectable joint inflammation is present (Demoruelle et al., 2014). Depending on the degree of inflammation present, symptoms may wax and wane, and there may be periods that can last months or years during which the symptoms seem to be in remission, only to reoccur (referred to as a flare).

Biological mechanisms

Rheumatoid arthritis is accompanied by the presence of specific antibodies, known as rheumatoid factors (RF), as well as other proteins (citrullinated peptides). Although these biological factors are present prior to the appearance of clinical signs of the illness, they might also be involved in illness provocation and can be used as biomarkers for disease occurrence (McInnes & Schett, 2007). The development of this disorder is also accompanied by a high load of bacterial antigens within the periodontium (tissue that surrounds the teeth), lung, and gut (Brusca et al., 2014), thus implicating a role for microbial factors. In addition, rheumatoid arthritis has been linked to telomere shortening, but once again it’s not known whether this was a consequence of the disorder, the distress created by the illness, or in some fashion contributed to the illness (Dehbi et al., 2013).

Multiple sclerosis

Multiple sclerosis (MS) most often occurs among women, typically appearing during early adulthood. In this disorder, immune responses are directed toward myelin, the sheath that surrounds brain and spinal cord axons, resulting in the slowing of electrical signals within neurons. Thus, MS symptoms comprise sensory and motor disturbances, such as loss of sensitivity or tingling, pricking, or numbness, as well as fatigue, muscle weakness, difficulty moving, disturbed balance and coordination, and it’s not unusual for cognitive impairments and depression to manifest as the disease progresses. In one form of the illness, the relapsing-remitting type, discrete episodes may be followed by intervals extending to months or years before another incident occurs. At these times individuals might misconstrue the illness as being on hold, or even diminishing, but unfortunately, the neurological disturbances may persist and even worsen. A variant of MS that affects 10–15% of those with the disorder, primary progressive MS, appears at about age 40 and is not accompanied by periods of apparent remission, often leading to disability earlier than in the relapsing–remitting form of MS. Secondary progressive MS, also known as ‘galloping MS’, appears like relapsing–remitting MS, but a progressive neurologic decline occurs between episodes (Compston & Coles, 2008).
Biological mechanisms

As in the case of other autoimmune disorders, the processes that instigate MS have yet to be fully determined. One hypothesis is that in the presence of particular genetic determinants, infections may operate as a trigger for the disease (Venkatesan & Johnson, 2014). Although several such pathogens have been suggested, Epstein-Barr virus (EBV) has received particular attention given that MS is approximately 15 times higher among individuals infected with EBV during childhood and about 30 times greater among those infected in adolescence relative to those who were not infected (Ascherio, 2013). These findings, together with detection of EBV-infected B-cells in patients’ brain, have been consistent with the suggestion that immunopathology in MS stems from chronic EBV infection (Salvetti et al., 2009). Confirmation of a causal relationship between these factors, however, requires prospective studies that assess the fate of those who had (or had not) experienced EBV as well as other concordant factors (e.g., genetic profile).

Systemic lupus erythematous (SLE)

Systemic lupus erythematous (SLE), which is far more common in women than in men, typically appears at about 15–35 years of age and affects about 0.5% of the population, varying across ethnic populations. Lupus may affect almost any portion of the body, including joints, blood vessels, skin, liver, kidneys, heart, lungs, and the nervous system. Moreover, with disease progression, numerous comorbid illnesses may develop, ranging from infections, osteoporosis, through to cardiovascular disease and cancer, and in about half the cases it appears along with arthritis (Cervera et al., 2009). A diagnosis of lupus, at least early on, can be difficult to make because the symptoms expressed are nonspecific (e.g., joint and muscle pain, fatigue, and recurrent, unpredictable bouts of fever), and due to the fact that some symptoms might appear and then disappear, leading to it initially being mistaken for other illnesses.

As the illness progresses, flares are usually preceded by signals, such as elevated fatigue, pain, rash, fever, abdominal discomfort, headache, and dizziness. At this point, marked neurological and psychiatric manifestations of the disorder are detectable, notably white matter (referring to glia and myelinated axons) hyper-intensities in certain brain areas as well as hemorrhages, lesions, cell loss, and cell atrophy. In some instances, microstructural abnormalities can be detected in the brain that likely contribute to disturbed memory, executive functioning, and the speed of information processing. Despite the gravity of the illness, mortality attributable to lupus has been declining over the years (Bernatsky et al., 2006), particularly in developed countries. This is largely due to better health care access, education, physician availability, and treatment compliance, suggesting that the management of lupus may have to do with life-style factors rather than medications alone (Lisnevskaya et al., 2014).

Biological mechanisms

As in the case of other autoimmune disorders, several candidates have been identified that may contribute to the development and progression of lupus. There has been the suggestion that lupus arises owing to disturbances in the clearance of debris stemming from cells that have died or been destroyed, and the subsequent development of antinuclear antibodies (antibodies that attack inner portions of our own cells) (Lisnevskaya et al., 2014). As lupus is often associated with compromised
blood–brain barrier functioning, auto-antibodies (self-directed antibodies) might gain access to brain sites where they can cause damage (S. Williams et al., 2010), thereby promoting the development of depressive-like symptoms and cognitive disturbances (Kowal et al., 2006). Alternatively, these auto-antibodies might cross-react with aspects of glutamate (NMDA) receptors, leading to cell death (Faust et al., 2010). Since lupus occurs primarily in women, there has also been the view that estrogen might be a causal agent for this illness and/or that testosterone has a protective effect in this regard. Finally, environmental factors may contribute to the emergence of lupus. For instance, low levels of exposure to sunlight can provoke vitamin D deficiency, which is accompanied by elevated disease activity (Kamen & Aranow, 2008). Other triggers include cigarette smoking, infection, administration of estrogen, certain drugs and pesticides, as well as phthalates, which are incorporated into plastics to increase flexibility and durability.

**Factors that exacerbate autoimmune disorders**

**Stressors and psychosocial contributions**

Despite the characteristic differences that exist across autoimmune disorders, they share several common features. Many have a genetic basis, often running in families, and those with one autoimmune disorder may also be afflicted with others. It is also thought that even if genetic factors contribute to autoimmune disorders, an external agent (a second hit) is necessary to get the process rolling. These may comprise viral infection or other illnesses, toxicants (chemicals in the environment, including the workplace, smoking, drugs, and even particular hair dyes), some foods, and traumatic events.

Life stressors are probably not responsible for the initiation of an autoimmune disorder, but such experiences have been implicated in the appearance of flares or exacerbations of the illness, and in MS patients these flares may be accompanied by an increase of brain lesions (Mohr et al., 2004). Early studies assessing these relationships involved only a small number of patients and comprised retrospective analyses of stressor experiences; however, subsequent prospective studies confirmed that flares were often preceded by stressful events (Brown et al., 2005). The important element in promoting flares wasn’t necessarily the severity of the stressors, but the frequency of their occurrence. The relationship between MS symptoms and stress responses were, predictably, moderated by the coping methods that individuals adopted, being most prominent among individuals who focused on their illness through emotion-based coping, and least apparent among those who coped through avoidance/distraction (Mohr et al., 2002). Having good social support resulted in improved psychological adjustment, although full symptom remission typically was not achieved.

Like many patients with serious illness, those with rheumatoid arthritis frequently attributed their illness to stressful experiences or believed that stressful events worsened their symptoms (Affleck, Pfeiffer et al., 1987). Once again, the results of retrospective reports were confirmed through prospective studies (Evers et al., 2014). Workers with rheumatoid arthritis reported that their perceived pain was especially intense on days that involved many work-related stressors, and were most severe among individuals with jobs that entailed high ‘strain’. Predictably, the negative effects of day-to-day hassles were buffered by having adequate social support (Straub et al., 2005). Given the differential actions of mild and strong stressors as well as acute and chronic stressors on circulating cytokines and corticoid functioning, it is possible that these factors play a prominent role in affecting the course of autoimmune disorders.
Eating and autoimmune disorders

Interventions based on diet have been proposed in relation to many illnesses, and autoimmune disorders are no exception. As dietary factors influence metabolic and inflammatory processes, it would be expected that diet would affect the development and/or progression of autoimmune disorders. Recommendations have been made regarding what to eat and what not to eat in relation to autoimmune disorders, including foods that could affect the microbiome, thereby influencing MS, rheumatoid arthritis, and IBD (Vieira et al., 2014; Yeoh et al., 2013). Other foods have been recommended that act against inflammation, oxidative stress, and angiogenesis (new blood vessel growth) that may be associated with MS. Some of the most notable are polyphenols (bioactive molecules found in vegetables, fruits, spices, herbs, soy, tea, wine and other fruit-based beverages), carotenoids that are obtained from vegetables, omega-3 polyunsaturated fatty acids (PUFA) from fish, and vitamins, such as vitamin D and niacin (Van Meeteren et al., 2005). It was also recommended that the diet should discourage inflammatory responding, and thus should include moderate protein and energy content, but rich in minerals (especially antioxidants) and mono/polyunsaturated fatty acids.

Contradictory evidence

Inconsistent data have been reported regarding the link between foods and autoimmune exacerbation. It is difficult to reconcile many of these findings, but it is important to bear in mind that focusing on the impact of any single dietary category may be counterproductive. Several studies have indeed examined whether broader diets would have positive effects on arthritis symptoms, and while several studies that assessed vegetarian, Mediterranean, and elemental eating plans yielded positive outcomes, they typically comprised samples that were too small to permit reliable conclusions (Smedslund et al., 2010). If nothing else, however, diet-related treatments might offer people with illness an opportunity to gain a sense of control over their condition, and thus may have important psychological benefits (Stamp et al., 2005).

Multiple sclerosis, vitamins, and dietary factors

Despite the certainty that seems to be apparent in some quarters, the links between several dietary factors and autoimmune disorders is not particularly strong. By example, the involvement of vitamin D in relation to MS has received particular attention, and there is some evidence that deficits of this vitamin may contribute to some autoimmune disorders (e.g., SLE, rheumatoid arthritis) and disorders that are organ-specific (i.e., type 1 diabetes, primary biliary cirrhosis) (Agmon-Levin et al., 2013). However, the research suggesting a causal link between the progression of MS and vitamin D has not been convincing (von Geldern & Mowry, 2012). Similarly, PUFAs either did not affect disease progression (Farinotti et al., 2012) or provided only small positive effects (von Geldern & Mowry, 2012). Several other nutritional factors were initially said to influence MS, including antioxidants (uric acid, vitamins A, C, and E, lipoic acid), milk proteins, probiotics, polyphenols, as well as ginkgo biloba extracts and curcumin, but once again the data have not been convincing and statements about their efficacy need to be constrained (von Geldern & Mowry, 2012).
Drug treatments of autoimmune disorders

It is unfortunate that for most autoimmune conditions a cure isn’t presently available, but ‘disease-modifying treatments’ can often minimize symptoms or delay the illness’s downhill course. In other instances, such as the progressive-remitting form of MS, positive effects in delaying illness progression have been limited. In the case of MS and rheumatoid arthritis, physiotherapy and life-style changes are sometimes recommended, but for the most part, symptoms are managed through drug treatments that reduce inflammation and by pain-relieving medications.

Like so many other illnesses, autoimmune disorders are physiologically heterogeneous, and it may be necessary to devise personalized approaches, using genetic and other markers, to provide optimal treatments for patients. For the moment, however, most patients receive a standardized course of treatments. Ordinarily, nonsteroidal anti-inflammatory drugs (e.g., prednisone) are used to deal with mild symptoms, whereas stronger drugs that affect immune functioning are used to deal with relatively severe symptoms. These include corticosteroids, and immunosuppressants such as cyclophosphamide, but because of their potential adverse effects, drug development efforts have targeted specific types of immune cell (e.g., belimumab or atacicept, which inhibit B-cell activity) rather than acting broadly on immune functioning. Treatments may also include immunosuppressive agents, or antibody immunomodulators as well as those that influence cytokine functioning (e.g., Kamal, 2014; Kaneko & Takeuchi, 2014).

Promising results in slowing down disease progression have been reported using disease-modifying antirheumatic drugs (DMARDs), including agents that inhibit proinflammatory cytokines (IL-1β and TNF-α), although in some instances the disease is not responsive (refractory) to treatments and many patients do not experience symptom remission (Polido-Pereira et al., 2011). In MS cases that are not responsive to any treatments, high dose immunotherapy may be tried in an effort to diminish the immune system’s attack, although this procedure in itself can have negative consequences (Paz Soldán & Weinshenker, 2015). It is nonetheless significant that when high dose immunotherapy was followed by transplants of the patient’s own hematopoietic stem cells (the types of cell that give rise to varied other blood cells), 75% experienced relief from relapsing–remitting MS that was still apparent 3 years later (Nash et al., 2015).

Despite the generally negative outlook regarding a cure for autoimmune disorders, occasional breakthroughs have been made that hold promise for the future. In the case of MS, by administering incrementally higher doses of specific antigens that are being attacked by immune cells, it is possible to re-educate these immune cells so that they cease attacking, but without diminishing their ability to eliminate other dangerous antigens (Burton et al., 2014). An alternative approach has been to focus on a substance, SIRT-1, that is essential in regulating the balance between T cells involved in attacking tissues and those involved in regulating the responses of other T cells (Lim et al., 2015). As multiple pathways might contribute to diseases, lupus treatment was attempted based on low dose tolerance therapy with a cocktail of several agents that activated regulatory T cells and suppressed interferon gene expression. In this way several immune-related processes related to lupus could be triggered concurrently in an effort to attenuate illness (L. Zhang et al., 2013).

Novel compounds are also being developed to provide relief from autoimmune disorders. One approach focused on reestablishing the presence of myelin on nerve fibers rather than attempting...
to reduce inflammatory responses (Miron et al., 2013). Another approach, so far assessed only in mice with an MS-like condition, revealed that transplantation of human embryonic stem cells (that may differentiate and repair the myelin sheath) caused a reduction of neuroinflammation and behavioral signs of MS in less than 2 weeks (L. Chen et al., 2014), and encouraging results have been reported regarding other autoimmune conditions, such as rheumatoid arthritis. Trials using gene therapy and stem cell transplantation to treat severe autoimmune conditions have been conducted across countries for more than 15 years, and some of the findings have been encouraging (Li & Sykes, 2012; Shu et al., 2014). This approach is still in its infancy and there’s still much that needs to be done, including analyses of the clinical efficacy of the treatments as well as their safety, the side effects that can be expected, and the long-term benefits that are obtained. Ultimately, there is the hope that this approach would not only diminish or eliminate symptoms of autoimmune disorders, but might lead to the creation of a cure (Liao et al., 2015).

A PLACE FOR MEDICAL MARIJUANA

There is evidence that marijuana’s primary active ingredient, THC, may cause epigenetic changes that act against inflammation and could thus be beneficial for a variety of autoimmune disorders (X. Yang et al., 2014). However, the anti-inflammatory effects attributable to the use of marijuana during teen years may subsequently flip, so that during later adulthood the predominance of pro-inflammatory processes might contribute to autoimmune disorders (Moretti et al., 2014).

Whether these new findings will hold up and whether there are actually negative repercussions for well-being will have to await further studies in humans. For the moment, however, there have been reports, often being played and replayed by newspapers and television, regarding ‘medical marijuana’ use for an assortment of illnesses, as a pain reducing agent, as a method to keep PTSD in check (Neumeister et al., 2013), to diminish intraocular pressure associated with glaucoma, as well as to diminish side effects associated with medical treatments (e.g., nausea related to cancer therapy). It was unexpectedly observed as well that individuals who experienced severe trauma were less likely to die if they had tested positive for THC (Nguyen et al., 2014), possibly owing to increased blood flow provoked by THC and hence elevated nutrients delivered to the brain, or because THC inhibits glutamate, thereby limiting neuronal damage that might otherwise have occurred.

Given increasing moves regarding the legalization of marijuana, we can pretty well count on a new arsenal of treatments becoming available for immune-related disorders as well as those related to stress and trauma. No doubt, this will require improved standardization of the product, and risk–benefit analyses will be needed considering the adverse effects that can occur regarding CNS functioning (Yadav & Narayanaswami, 2014), including stunted development of white matter associated with its early and chronic use (Filbey et al., 2014; but see Weiland et al., 2015). This will become that much more important with increased use of high-potency (‘skunk-like’) cannabis (Di Forti et al., 2014).
SUMMARY

The immune system is obviously tough, resilient, and well designed. But the enemy it faces is equally sly and resourceful, and as the immune system learns ways to deal with challenges, microbes learn new ways of getting around immune defenses. More than that, numerous factors can compromise the ability of the immune system to deal with threats. Eating the wrong foods or encountering chronic stressors may diminish immune functioning, thereby altering risk for the emergence of pathological conditions, more so among individuals who have inherited particular genes. The presence of toxicants can also affect immune functioning, and may create tissue disturbances or gene mutations that can cause illness. It also seems that these environmental events or our experience may cause adverse outcomes as a result of changes within the microbiome or by altering hormonal and neurochemical processes. Thus, identifying these specific mechanisms, and determining why these factors differ across individuals, could result in the development of targeted treatments to deal with a variety of challenges. This said, it would be far better to adopt behavioral strategies to prevent disease occurrence, although it is certain that there are many conditions for which this isn’t possible. Besides, in relation to illnesses and its causes, we often simply don’t know what we don’t know, and, for this reason, maintaining healthy life-styles is a fairly good tactic.

Finally, in considering emerging threats, especially viruses and bacteria with potentially devastating outcomes, it is essential to act quickly and decisively as half measures don’t work. Some diseases, such as Middle East respiratory syndrome (MERS), airborne H5N1 influenza, and H7N9 avian flu, have crossed the line to affect humans, although they haven’t yet posed widespread threats, as they aren’t being passed from human to human. In contrast, Ebola, which likely came from animals, has had profound negative effects in some parts of Africa. This disease first appeared about 40 years ago, so one has to wonder why more attention wasn’t devoted to it earlier. Clearly, to deal with potentially transmissible diseases, active efforts need to be undertaken before the problems become too large to handle. Likewise, illnesses such as polio, although largely eliminated, persist in some countries, and vaccine-resistant strains have appeared (Drexler et al., 2014); and TB, which affects 8 million people yearly (and 1.3 million die), needs to be attended to more rigorously, especially as treatment-resistant forms of TB are also around. It is also essential for proper infrastructure to be present to contain viral spread, including high levels of cooperation across countries as well as among people within any particular locale. Conspiracy scenarios or false information being passed around, irrespective of whether it’s Ebola or measles, are counterproductive in dealing with viral or bacterial spread.