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CRITICAL FOCUS

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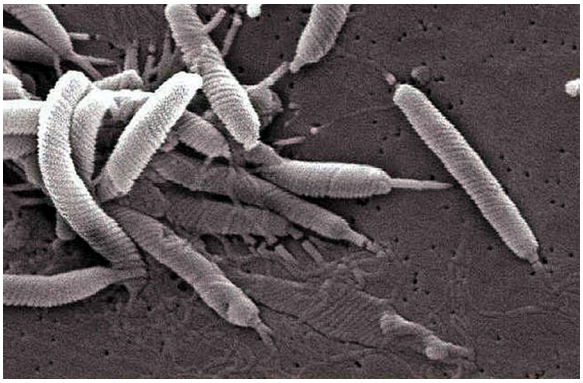
Tomorrow's Infections Today

The optimism of an earlier era — a belief that infectious diseases were on the cusp of defeat — did not last. It has been tempered by the sobering realities of the new millennium.

You might think of the sun-drenched Atlantic Boulevard in Banjul, Gambia, as a carefree haven of leisure. Not me. This vibrant West African locale evokes a far more meaningful association: the headquarters of the Medical Research Council (MRC) where, some four decades ago, I encountered the unforgettable human toll of diseases that we had relegated to the margins of Western awareness. There crouched a village elder, his cheeks etched with the cruel scars of smallpox; a youth robbed of sight by onchocerciasis, river blindness; a bright young mother, her vision extinguished by trachoma — these were not mere case studies but living testimony to the relentless scourge of tropical infections. I was introduced to patients grappling with bilharzia, and the grotesque distortions of elephantiasis.



Gastric ulcers were traditionally related to diet and stress, but *Helicobacter pylori* was implicated when Australian microbiologist Barry Marshall swallowed a broth culture of the bacteria, developed an ulcer, and then cured it with appropriate antibiotics. Surprisingly, this treatment is still not widely recommended by physicians.

At the helm of the MRC's endeavors stood Ian McGregor, a figure whose warmth, erudition, and avuncular demeanor epitomized the archetype of the seasoned scientist. We don't produce them like him any more. A Scot of towering intellect, McGregor devoted 27 years to Gambia, earning reverence across West Africa. Under his stewardship, the MRC's modest nutrition unit in Banjul was transformed into a formidable research complex, complete with a 40-bed research hospital dedicated to unraveling the mysteries of tropical diseases. His particular expertise lay in the study of malaria — its transmission, treatment, and immunological ramifications — though his encyclopedic knowledge spanned the entire spectrum of tropical medicine.

In McGregor's era, the specter of tuberculosis was

receding, thanks to the advent of childhood BCG vaccination. Smallpox, eradicated globally by 1977 with the final case recorded in Somalia, had recently vanished from Gambia's landscape. Yet other plagues persisted. A yellow fever outbreak in nearby villages caused 8,000 cases and claimed 1,600 lives, a crisis McGregor quelled through a rigorous campaign for widespread vaccination.

His pioneering research illuminated critical insights: African children surviving malaria's initial onslaught developed durable immunity, transferable via serum — a discovery that laid the groundwork for modern malaria vaccines. He demonstrated that pregnant women infected with *Plasmodium*, the malaria parasite, could confer protection to their newborns, and that the uterus and placenta adapt to resist malaria in subsequent pregnancies. Defying the prevailing dogma, McGregor proved that malaria infection compromised immunity to other parasitic and infectious diseases, such as schistosomiasis. His work on filariasis, caused by nematode worms like *Wuchereria* and *Brugia*, established diethylcarbamazine as a preventive cornerstone, a strategy later adopted globally.

McGregor's legacy transcends scientific discovery. His empathetic rapport with Gambian communities — forged through humor, patience, and cultural awareness — earned him unparalleled trust. This facilitated his successful vaccination campaigns, and routine blood sample collecting. His creation of a vast demographic database provided an enduring resource for global health research. His investigations exemplified the transformative potential of Western medicine when wielded with empathy, cultural insight and scholarly rigor.

The optimism of that era — a belief that infectious diseases were on the cusp of defeat — was not to last. It has been tempered by the sobering realities of the new millennium. The mid-20th century heralded triumphs: antibiotics had revolutionized the treatment of bacterial infections and vaccines had curtailed many of the viral diseases. Improved sanitation and nutrition further alleviated the burden of illness. In my younger days, conversations about medicine reflected this confidence. A friend's death from cancer prompted a discussion in which one of the group naively concluded that cancer was the only disease we had still to conquer. "And multiple sclerosis," I added. We all nodded, sagely.

In West Africa, the eradication of smallpox, the containment of polio, and the decline of yellow fever had fueled the sense of optimism – and, with the demise of malaria already in sight, the vanquishing of other infections must surely be imminent.

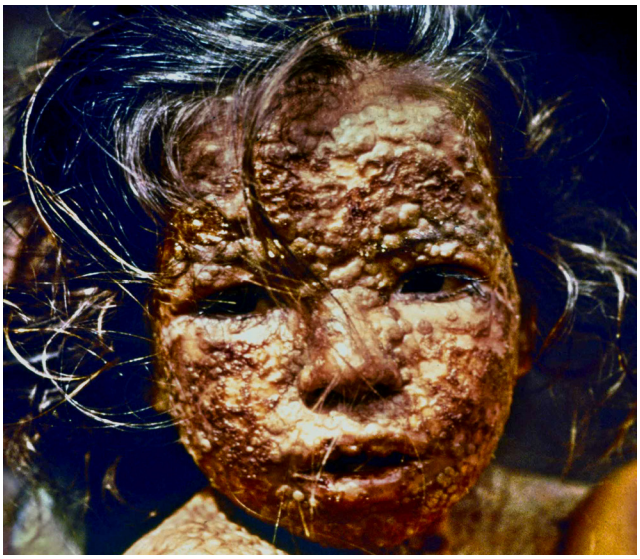
My first experience of endemic tropical diseases came during my first visit to West Africa, where Ian McGregor had established a research hospital treating diseases ranging from bilharzia and malaria, and from yellow fever to elephantiasis. Many of his patients bore the scars of smallpox, which had only recently been vanquished through vaccination.

NEW MILLENIUM, NEW PRIORITIES

The optimism died with the millennium. Polio resurfaced due to vaccine-derived strains, with a rare case reported in Rockland County, New York, in 2022 — the first in the U.S. since 1993. Measles, declared eliminated in the U.S. in 2000, was in resurgence after the anti-vaccine campaigns, with over 600 cases in 2024. A child's had died of measles.

Meanwhile, novel pathogens had been emerging with alarming frequency over the last fifty years. Ebola appeared in 1976. Legionnaires' disease, caused by *Legionella pneumophila*, was first identified in 1977. Gonorrhea was spreading, as was *Chlamydia*, and HIV emerged in 1981 (I published on these: Sexually Transmissible Diseases [in] *Sex and Your Health*, edited by Dr James Bevan, London: Mitchell Beazley, and *El Sexo y la Salud*, Barcelona: Manuales Practicos Planeta, 1985). Both are spreading still. Lyme disease proved to be caused by the spirochete *Borrelia burgdorferi* in 1982, hepatitis C was characterized in 1989, and hantaviruses in 1993. Variant Creutzfeldt-Jakob disease, linked to bovine spongiform encephalopathy (mad cow disease) soon surfaced (see my book: BSE, *The Facts*, London: Corgi Books, 1996).

The present century introduced us to Severe Acute Respiratory Syndrome (SARS) in 2002, Middle East Respiratory Syndrome (MERS) in 2012, and the Zika virus in 2015. Marburg virus and ebola emerged to compromise public health, *Candida auris*, a drug-resistant yeast, and the chikungunya virus further expanded the roster of threats, culminating in the global havoc



Smallpox could cover a victim with confluent pustules, which often developed a secondary bacterial infection. Meticulous programs of vaccination eventually vanquished the disease. The last case was Ali Maow Maalin, a 23-year-old cook, in Somalia in October 1977. Many of McGregor's patients still bore smallpox scars.

wreaked by SARS-CoV-2, a mutation of the SARS virus that caused the COVID-19 pandemic, first identified in 2019.

THE THREAT OF EMERGENT DISEASES

In recent years, we have become increasingly aware of the problem posed by emergent infections. Many were mentioned in my 2017 article "Tomorrow's Germs threaten Today's Lifestyle" (see: *The Microscope*, 65:2, pp. 85–94, 2017). My main focus then was foodborne diseases, like *Campylobacter* infections. Norwalk virus was a prominent consideration too. But, since the great COVID-19 pandemic, everyone is asking, "What is on the horizon now?" After a century in which we felt that we were conquering diseases, there is a widespread recognition that viruses and bacteria are on the resurgence, with serious consequences for the future of humankind. The pandemic was just a pointer to the future. New infections are continually emerging.

I had lectured on the subject in June 2001, as a presentation to Inter/Micro for An Evening with Brian, entitled "The Disease Revolution," at the McCrone Research Institute in Chicago. I next spoke on the subject at Cambridge University, England, in September that year, and my findings were subsequently published as an article in this journal in 2003 (see: "An Evening with Brian – The Disease Revolution," *The Microscope*, 51:4, pp. 209–220, 2003). The changing face of disease was the subject of a chapter I contributed to a major textbook on the subject in 2004, published in London and the U.S. (see: "Human Behavior and the Changing Pattern of Disease" [in] *The Changing Face of Disease, Implications for Society*, London: Taylor and Francis, 2004).

It is interesting to look back to what I wrote then, and compare it with what has happened since. In some cases, we have managed to hold the front against emergent infections. *Bartonella*, *Clostridium perfringens*, West Nile virus and Kawasaki disease all maintain consistent public health relevance though, in these cases too, we have instituted reasonable methods of control.

But in the quarter century that has elapsed, other pathogens have arisen. Some newly discovered viruses are posing problems we cannot solve, and some that we have known for many decades are currently emerging in new and more virulent forms. The ostensibly harmless organism *Bacillus cereus* has now been found to grow rapidly in cooked rice, causing vomiting and diarrhea from the toxins with which it contaminates the food when left to stand. Novel species of bacteria have been emerging, too.

BACTERIA NEW TO SCIENCE

One of the greatest challenges we face is posed by antibiotic-resistant bacteria. We hear so many reasons given for the increasing incidence of antibiotic resistance, ranging from their overuse in agriculture to their being prescribed to treat virus infections. In my view, the greatest problems come from physicians prescribing antibiotics without prior sensitivity testing. Specific bacteria need particular antibiotics, yet the drugs are customarily administered to treat a range of infections, like sore throat, earache, or cystitis. In my view, no such treatment should be instituted without sensitivity testing (see: "Crisis Point, the Rise and Fall of Penicillin," *The Microscope*, 62:3, pp. 123–135, 2014). In my view, current medical practice breeds resistant bacteria.

Bacterial pathogens were well known to the Victorian microscopists, and they have been extensively studied for two centuries, yet new bacteria are still being discovered. *Helicobacter pylori*, first observed in 1979 by Robin Warren in Perth, Western Australia, was not successfully cultured until 1982. It seemed to be involved in the formation of peptic ulcers, though it took the audacious research of Barry Marshall to prove the point. He showed the organism in culture was sensitive to metronidazole and tetracycline, so he swallowed a potent culture of the bacteria and waited until a serious ulcer had developed. At that point he

self-administered the cocktail of metronidazole and tetracycline – and was cured. The ulcer went away. Other scientists refused to believe the results, and both Warren and Marshall were dismissed as unethical. They had the last laugh, though: both were awarded a joint Nobel Prize in 2005.

New bacteria are suddenly surfacing: *Neoehrlichia mikurensis*, a tick-borne pathogen causing severe inflammatory syndromes, *Lawsonella clevelandensis*, linked to abscesses; *Enterobacter bugandensis*, a hospital-acquired organism; and *Vibrio paracholerae*, associated with marine-related infections. In 2022 alone, *Corynebacterium parakroppenstedtii*, *C. pseudokroppenstedtii*, *Streptococcus toyakuensis*, and *Gulosibacter hominis* were described for the first time, each posing unique clinical challenges. When my column was published in 2017, none of us would have expected new species of bacterial pathogen would be discovered at such a rate.

The relentless emergence of pathogens underscores a humbling truth: the microbial world is neither static nor subdued. As we mark the legacies of pioneers like Ian McGregor, we must confront the dynamic interplay of evolution, environment, and human behavior that perpetually reshapes the landscape of infectious disease. The frontiers of infection are not merely geographical but temporal and they demand constant vigilance. Complacency is our greatest adversary, and ceaseless curiosity our most potent weapon.

OLD FOES, NEW GUISE

Everyone knows of *Campylobacter* these days, and I included it in my presentation in 2001, yet 50 years ago hardly anybody had heard of it. This is a gram-negative spiral bacterium and a leading cause of gastroenteritis around the world. It's everywhere. Yet *Campylobacter* was first observed back in 1886 by Theodor Escherich who studied preparations of the bacteria in specimens from the colon of infants with diarrhea. He observed the organisms, stained them, and recognized them as a species; however he found them impossible to culture on agar media.

100 years ago, similar bacteria were isolated from farm animals including cattle and sheep, and were linked to diseases causing bovine abortion. By 1963, the name *Campylobacter* had been conferred on the genus, but not until 1977 could these bacteria be cultured in the laboratory. There are reasons for this. These organisms demand very unusual conditions before they will grow in culture. They will not thrive if levels of oxygen are above 10% and they require high levels of carbon dioxide, typically 5%. They grow best around 40°C, aligning with the body temperature of the birds which frequently carry the bacteria, but much warmer than a conventional incubator.

CAMPYLOBACTER IN CONTEXT

Recent surveys have shown that over half of the chickens in the U.S. carry *Campylobacter* and a study in 2013 found that 90% of chickens from farmers' markets tested positive for the organism. That, of course, is not representative of commercial supply chains, though these bacteria remain very common.

Turkeys and wild birds also carry *Campylobacter*, though it has also been found in cattle, pigs, sheep, and occasionally in domestic pets. The bacteria are commonly associated with raw or undercooked poultry, unpasteurized milk, and contaminated water which can transfer the infection to leafy pre-packed salad vegetables. Cross-contamination in kitchens through the use of cutting boards remains a significant route of transmission.

Campylobacter causes 100 million cases around the world each year. In the U.S. there are about 1.5 million cases annually, about 100 of them proving fatal. Vaccines against *Campylobacter* are in development, but have never been widely used. Most cases of *Campylobacter* infection resolve within a week. The key is rest and rehydration. In cases of severe infection, which will occur in immunocompromised patients, ciprofloxacin was widely used but antibiotic resistance is now emerging and erythromycin is preferred.

The answer, of course, is hygiene. From the earliest age, children should be shown how to wash their hands thoroughly, how to keep kitchen work surfaces clean, and how to use solutions like dilute hypochlorite to ensure sterility. Pick up a chicken in the supermarket? Regard it as contaminated. It is the only way to avoid infection.

THE SAGA OF SALMONELLA

Say *Salmonella* and you're likely to think of *S. typhi*, the causative organism of typhoid fever, or *S. typhimurium* which causes gastroenteritis. They are not the same organism, though it's tempting to think that the name of one is an abbreviation of the other. Although both are gram-negative bacilli some 3-6 μm long, *S. typhimurium* is a flagellated bacterium which causes gastroenteritis lasting about a week, and which rarely needs treatment other than hydration with electrolyte solutions. *Salmonella typhi* causes typhoid. At first sight, the organism looks like *S. typhimurium* un-

Bacteria including *Campylobacter*, *Listeria,* and *Salmonella* often infect chickens across the U.S. Carcasses are routinely rinsed in dilute hypochlorite solutions providing 20-50 ppm chlorine, to control bacterial contamination. Although Europeans won't accept the practice, their packages of prepared salad leaves are regularly treated the same way..

der the microscope, but it lacks flagella and is strictly non-motile. Although antibiotics like azithromycin, ceftriaxone, and the fluoroquinolones can be used, medical practice tends to avoid them because antibiotic resistance is rapidly increasing.

There are vaccines for *Salmonella typhimurium*, and they can be used to reduce contamination in poultry farms. However, they do not protect the human subject. There are two vaccines available for *S. typhi*, both of which are recommended for travelers to areas where typhoid is endemic. Although *S. typhimurium* is zoonotic, and is primarily spread through poultry and eggs, *S. typhi* is human specific, and is most often transmitted through contaminated water or via carriers.

Non-typhoid species of *Salmonella* cause over 1,000,000 cases of infection per year in the United States with about 400 deaths. Although rare, typhoid does occur in the U.S., with over 300 cases per year, most of them related to travel. Hospitalization is necessary in 80% of the cases, though there are very few deaths per year. With treatment, the fatality rate is less than 1%.

Although typhoid is rare in the West, other *Salmonella* infections pose a perpetual problem, particularly among the producers of poultry. *Salmonella enteriditis* was first identified in pigs in 1885. In the 1960s, *S. enteriditis* emerged as a major source of infection associated with egg production. These bacteria are widespread in the intestines of animals like poultry, cattle, and pigs, and can contaminate products like meat, dairy, and water. Cross-contamination during food processing or through incautious food handling is common. These bacteria can survive in low moisture foods, like spices or peanut butter.

Current outbreaks are often linked to undercooked poultry, eggs, or contaminated fruits and salad vegetables. Poultry and eggs should always be thoroughly heated at least to 80° C to avoid infection. The industry relies on strict sanitation, regular testing, and temperature controls.

Episodes of gastroenteritis caused by typical *Salmonella* usually resolve without treatment (apart from rehydration) within a week. Occasional severe cases can trigger bacteremia or meningitis. Ciprofloxacin and azithromycin have to be the antibiotics of choice in these more serious illnesses. It is because of *Salmonella* infections that chicken carcasses are routinely rinsed in dilute hypochlorite solutions in the United States, and this is a reason regularly given in Europe for their refusal to import American chicken. It is a dubious argument. Bags of salad greens are increasingly popular throughout Europe, and they're all washed in dilute solutions of hypochlorite, exactly as are the poultry carcasses in the States. I have never seen this point made in public. It should be.

LISTERIA RISKS

A third organism which frequently causes food poisoning is *Listeria monocytogenes*, found in soil, water, sewage, decaying vegetation, and in animals. This bacterium can contaminate a variety of foods, particularly ready-to-eat products like deli meats, hot dogs, soft cheeses, smoked fish, and pre-packaged salads. What makes this pathogen particularly pernicious is its propensity to proliferate in refrigerators at temperatures only a few degrees above freezing. It can also tolerate high salt concentrations.

The organism was first observed in 1924 in Cambridge, England, as the causative organism of infections observed in domestic rabbits and guineapigs. Blood counts showed an increase in monocytes, and so it was named *Bacterium monocytogenes*. In 1940, it was decided to rename it *Listeria monocytogenes* to commemorate Joseph Lister, who introduced antiseptics in surgery. It was not recognized as a significant foodborne pathogen until the 1980s, following outbreaks in Canada, the U.S., and Europe.

About 1,600 cases of listeriosis occur annually in the United States, with about 250 deaths. Pregnant women may experience fever, fatigue, or flu-like symptoms, with risks of miscarriage. In rare cases, the bacteria causes sepsis or meningitis. What makes it particularly problematic to diagnose is that the incubation period before the infection becomes apparent

The Baroque artist Domenico Gargiulo painted this disturbing study of the Piazza Mercatello in Naples, Italy, to commemorate the outbreak of plague in 1656. To this day, there are surviving obelisks as memorials to this dread disease, and children still sing of the plague in the nursery rhyme: "Ring a ring of roses.'"

may last 70 days. High-risk individuals should never consume unpasteurized dairy products like artisanal cheeses, deli meats, or ready-to-eat meals unless they are heated to at least 80° C. Warmed food is a danger.

Little effort has gone into developing a vaccine. It is not a common disease, so the pharmaceutical companies are aware that the market must be limited. In severe cases, intravenous ampicillin, often combined with gentamicin, is the standard treatment for invasive listeriosis. With prompt intervention, most patients recover fully, but delays can lead to severe outcomes especially in those high-risk groups. And antibiotic resistance is a growing concern. Management is typical for all cases of diarrhea – hydration and fever management, with the option of intensive care for meningitis or sepsis. These infections are expensive: it costs tens of billions of dollars annually in the United States due to health care, food recalls, and industrial safety precautions.

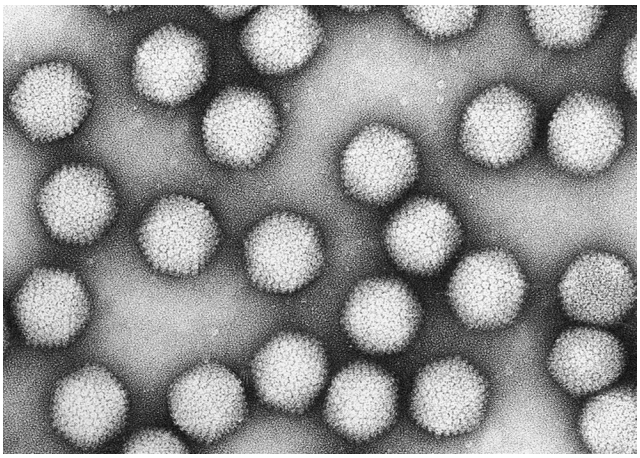
PLAGUE IS HERE TO STAY

A word about the plague. It's a deadly bacterial disease, once feared as the Black Death in Europe, where it no longer exists. Children still sing "Ring a ring of roses, a pocket full of posies," reminding us of the Medieval practice of using fragrant plants to ward off infections, then "Atishoo, atishoo, we all fall down" as the disease reaches its fatal climax. Plague is still found – very rarely – in the States. The causative bacterium was known as *Pasteurella pestis* for many years. The genus was first identified in 1880 by Louis Pasteur, as the causative organism of fowl cholera.

The causative organism of plague was first isolated in 1894 during a pandemic in Hong Kong. By the 1950s, studies had shown that *Pasteurella pestis* had unique metabolic properties that aligned it more closely with the genus *Yersinia*, so *Pasteurella pestis* was formally renamed *Yersinia pestis* 50 years ago, and that's how we know it today.

The first outbreak of plague in the United States was in San Francisco's Chinatown in 1900. This outbreak resulted in 121 cases of infection with 113 deaths, primarily among Chinese immigrants. There was a second outbreak in San Francisco in 1917 and another in Los Angeles in 1924. Since then, the incidence of the disease has steadily decreased and currently fewer than 10 human cases are reported annually, with infection concentrated in the West. There have only been about a dozen deaths from plague in the US during the last 50 years. The case fatality rate for plague is above 50%, though with treatment, the fatality rate falls to only 3%. Early diagnosis is what matters, as delays in commencing treatment greatly increase the mortality rate.

The most common form of this dreaded disease is bubonic plague, comprising 80% of all American cases and characterized by swollen painful lymph nodes. It



Computer graphic images of adenoviruses abound across the web, but this is what the negatively stained virions actually look like under the transmission electron microscope. They form as perfect icosahedrons. Each of the 20 triangular facets of the capsid bears 12 hexons, and there are 12 capsomers at the vertices of each icosahedron.

results from flea bites or contact with infected animals. Pneumonic plague is much rarer and is transmissible via respiratory droplets. It causes rapid-onset pneumonia and is almost 100% fatal without prompt treatment. Septicemic plague is particularly insidious for it can occur alone or secondary to bubonic plague. Without treatment, it results in toxic shock, organ failure, and tissue necrosis, and is virtually 100% fatal.

Fortunately, we have antibiotics that will deal with these bacteria: gentamicin and doxycycline are the first line therapies, typically administered for two weeks. People who've been exposed to plague may receive prophylactic antibiotics. Early vaccines were used in India in the late 1800s. They offer limited protection and are not available today. Currently there are several promising vaccine candidates in development, but none has yet received official approval. Plague can devastate rodent populations and cause ecological ripple effects as wild rodents carry the bacteria, so it is unlikely ever to be entirely eradicated. *Yersinia pestis* is a Tier One agent for bioterrorism, due to its potential for distribution as an aerosol. We may think of plague as medieval, but in fact it has never gone away.

VERSATILE VIRUSES

So much for bacterial pathogens, but what of the viruses? I've always liked studying viruses. I learnt to culture them in 1959, when I had a year (in the most junior capacity you could imagine) with the Medical Research Council in Wales. Monkey kidney and HeLa cells were the most popular growth media in those days, and we used bacteriophage viruses only to type staphylococci. Nobody then thought of them as agents of therapy.

Our understanding of viruses has developed vastly since then, though I have pointed out that for some – notably the phages – we seem to have lost sight of the ground-breaking work done a century ago by brave pioneers (see: "Germ versus Germ," *The Microscope*, 69:4, pp. 163–174, 2022). We knew of the great virus epidemics of influenza, smallpox, and poliomyelitis, but only in recent decades has a range of new viruses, literally from A to Z, been recognized.

ENTER ADENOVIRUS

Adenoviruses have been causing recent outbreaks across university campuses and in military bases. In 1953, under the electron microscope they were shown to form perfect icosahedrons. It is a minuscule marvel and looks like a lunar lander.

These viruses cause respiratory infections, conjunctivitis, and gastroenteritis, with severe pneumonia sometimes occurring in immunocompromised patients. For most people, supportive care will suffice, but cidofovir is used in severe cases and there are vaccines which are used to protect military recruits. Currently there are no plans for broader immunization in the US. As of now, these viruses cause up to 20,000 hospitalizations every year, though with fewer than 100 deaths – and those are mostly in vulnerable groups. Recent data suggest a slight upsurge in pediatric cases since 2022, probably related to the reopening of schools after the COVID-19 pandemic.

INSIDIOUS ZIKA

Zika virus was first identified in April 1947, in the Zika forest of Uganda, during a yellow fever survey carried out by researchers from the Rockefeller Foundation. They isolated this previously unknown virus from the blood of rhesus monkeys and named it after the forest where it was found. Within a year, it had been shown that the virus was spread by *Aedes* mosquitoes in the same forest, and these turned out to be the primary vector.

The first human infections with zika virus were reported in Uganda and Tanzania in 1952 and were identified through serological studies. The patients suffered few symptoms, and most were asymptomatic. Over the following 30 years serological evidence indicated that zika could be widely detected in countries including Nigeria, India, Malaysia, Indonesia, Thai-

land, and the Philippines, though no major outbreaks were reported. Symptoms include mild fever, a rash, and malaise, frequently indistinguishable from mild cases of other tropical diseases.

Then, in June 2007, there was a major outbreak on Yap Island in Micronesia. Over three-quarters of the population were infected. Symptoms included fever, conjunctivitis, and joint pain, though there were no severe cases. In 2013 there was an outbreak in French Polynesia affecting 28,000 people, and this was the first to cause neurological complications, including an increase in Guillain-Barré Syndrome (GBS), an autoimmune disorder causing muscle weakness and possible paralysis. Ten years ago, zika reached Brazil. It is believed to have been introduced during the 2014 FIFA World Cup. The virus spread rapidly across Latin America and the Caribbean.

In October 2015, microbiologists in Brazil realized there were insidious effects of the zika virus. They saw a sudden surge in babies born with abnormally small heads and damaged brains. By 2016, this was designated Congenital Zika Syndrome (CZS) and manifested itself as microcephaly, brain abnormalities, and delayed fetal development. This was a turning point, elevating zika to a global health emergency.

We also saw an increase in GBS cases in many countries including Brazil, Colombia, and French Polynesia. Investigators from the World Health Organization (WHO) show that zika could be spread by means other than mosquito bites. Asymptomatic carriers could transmit the disease, and sexual transmission was also implicated. Mother-to-fetus transmission was proved, and in other cases the infection was transferred through blood transfusions.

Over 3,000 babies were affected in Brazil, and a little over 300 in the U.S.. A total of perhaps 5,000 confirmed cases of zika-associated microcephaly have been recorded, a truly tragic total. The true number is likely to prove higher due to underdiagnosis, varying definitions of microcephaly, and limited surveillance in low-income countries. As herd immunity developed, and large proportions of populations were exposed to the virus, zika cases began declining from 2017. No vaccine had been developed by then, and this decline greatly reduced the urgency for vaccine development, stalling progress.

There have been no major outbreaks since 2016. But small clusters persist in India, Africa, Asia, and the Americas. Zika is an insidious virus. No matter how widespread herd immunity might be, it remains a serious threat to the future.

DENGUE, FIRST COUSIN OF ZIKA

Like zika, dengue fever is one we need to note. It was discussed in my 2001 presentation, when it was just emerging as a major problem. One factor that makes dengue fever unusual, in a discussion of emergent infections, is that it has been known for centuries. A second factor is that people don't know how to pronounce it. It's not "deng-you," but "deng-ee," the name deriving from Swahili, for it had been known to the Africans for centuries.

The first Western reports of dengue fever date back to 1779 in Jakarta, followed by an outbreak in Philadelphia the following year. The symptoms included fever, skin rash, and severe joint pain. At the time it was often called Breakbone Fever, due to the intense muscle and joint pain. Dengue virus was first isolated during World War II by researchers in Japan and the United States from blood samples obtained from soldiers in the Pacific. Four serotypes are now known. An infection with one serotype will provide lifelong immunity only to that type of the virus, but not to the others. After WWII, urbanization and global travel increased the spread of dengue around the world, particularly in Southeast Asia, where epidemics became ever more frequent. Then, in the 1980s, it spread to the Americas.

During the era of DDT, *Aedes* mosquitoes had been almost eliminated, but in subsequent decades, after the pesticide was banned, the mosquitoes re-emerged and triggered major outbreaks in Latin America and the Caribbean until, by the 1990s, dengue had become endemic in over 100 countries. It has continued to increase in prevalence. There are some 300 million dengue infections every year, with half a million cases of severe dengue and 40,000 deaths, mostly in little children.

Three-quarters of all dengue cases are asymptomatic, or cause only a mild fever, which makes tracing an epidemic ever more difficult. The symptoms of regular dengue fever include headache, rash, limb pain, and orbital pain lasting up to a week. But in 5% of the cases, often during secondary infections, abdominal pain, hemorrhage, plasma leakage and shock can ensue with a case fatality rate of up to 20% without treatment. The first vaccine was released in 2015, but it is not suitable for general use, though other vaccines are in trial at present. Global warming is adding to the rate at which the mosquitoes spread, and attention should always be paid to isolated areas of standing water in barrels and bowls, pools and puddles. Dengue has become the most widespread mosquito-borne disease and over

50% of the world's population is now at risk. Mostly it is a harmless infection, but occasionally it is as serious as any we know.

CHIKUNGUNYA ON THE RISE

So similar are the symptoms of these virus diseases in the tropics, that differential diagnosis takes time and effort. Chikungunya virus was first identified in Tanzania in 1952, and, like dengue, its name is derived from the local word for the disease in the Makonde language. The virus was first detected in Uganda and Nigeria, and in parts of Asia, including Thailand and India. But these early outbreaks were small, in rural areas, transmitted by *Aedes* mosquitoes, and dismissed as of local interest only. The symptoms included high fever and rash, though it is debilitating joint pain that characterizes chikungunya disease.

The first major epidemic began in 2004 on the Kenyan coast, spreading later to the Indian Ocean islands including Mauritius, and then moving on to India. A minor mutation in the virus had enhanced its transmission by mosquitoes, expanding its geographic range. Since then it has spread widely across Southeast Asia, then entering Europe in 2007, and the Americas in 2013.

The acute phase is marked by sudden high fever, often over 102° F (39° C) with rash, headache, and excruciating bilateral joint pain. The symptoms appear up to a week after the mosquito bite and may last for a week thereafter. However, half of patients develop persistent joint pain, arthralgia, which can last for years, particularly in older adults and those with comorbidities. In some rare instances serious complications including encephalitis and myocarditis can ensue, occasionally extending to organ failure. These cases occur mostly in the elderly or neonatal patients, though overall fatality rates worldwide are fortunately less than 0.1%.

Here too, we have no specific antiviral treatment, and management is supportive by administering acetaminophen and electrolyte fluids. The first chikungunya vaccine was approved by the Food and Drug administration (FDA) in the US in 2023. This shows 99% protection at 28 days, and 96% after 6 months in trials. The vaccine has been approved in Canada and Europe, as well as the US, specifically for travelers to endemic areas.

The Americas have seen several outbreaks in the last couple of years. There were a quarter of a million cases of chikungunya in Brazil in 2023 and 140,000 cases in Paraguay the same year. There are also reports of chikungunya in the US. 81 cases were reported in 2024, all of them related to travel in infected areas. Chikungunya has continued its global penetration and is now epidemic in over 100 countries. There are many millions of cases annually; their exact numbers are unclear due to unreporting and confusion with dengue and zika. These viruses may have been with us for a long time, but it is only now that they pose such a serious global threat to the future health of humanity. Research currently centers on mRNA vaccines. These have shown promise for the future, though none has yet been licensed.

BLAME THE BATS FOR NIPAH

One of the new pathogens featured in my 2001 presentation was nipah virus, which had been first identified in 1998 during an outbreak among pig farmers in a village of that name in Malaysia. This zoonotic paramyxovirus is primarily transmitted by *Pteropus* fruit bats via intermediate hosts like pigs. It also spreads human-to-human, making it a high-priority emerging pathogen. Nipah causes a very severe disease, with fatality rates up to 75%, manifesting as encephalitis, respiratory distress and neurological complications, with survivors often facing lifelong sequelae. One outbreak in India during 2018 had 19 cases with 17 deaths. No licensed vaccines or treatments exist, though mRNA vaccine trials are currently underway. South Asia remains a hotspot due to bat populations and human-animal interactions.

This is a priority pathogen. In recent decades, isolated outbreaks have occurred in Malaysia, Singapore, India, Bangladesh and the Philippines. Rapid response by local medical authorities has limited the spread, but recrudescence remains a current concern. There have never been any outbreaks of nipah virus in the United States. The absence of flying foxes and fruit bats that carry the virus means there is no primary means of transmission. The virus could be spread through pig farming, but practices in the US are so very different from those in Malaysia where the virus first emerged. Surveillance systems continue to check for imported cases, but no such examples have yet been reported. Research into mRNA vaccines has raised the hope that vaccination could quickly curtail an outbreak should it occur in the future. Make no mistake: nipah virus is serious, pernicious, and deadly.

RIDING ON RODENTS – LASSA FEVER

Lassa fever was first recorded in Lassa, Nigeria,

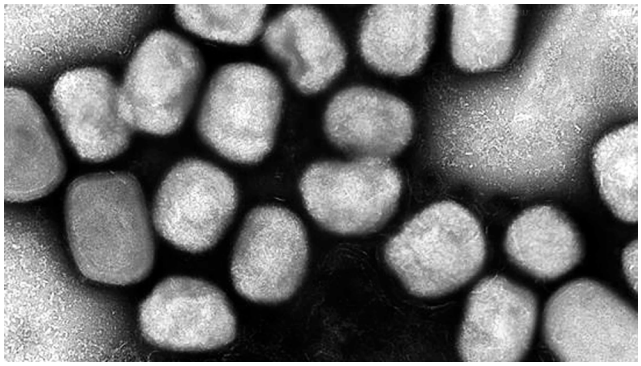
in 1969 when a nurse succumbed to a mysterious fever. The electron microscope revealed the virus as pleomorphic particles. They are transmitted via the multimammate mouse *Mastomys*. The disease causes fever, sore throat, and in 20% of the cases hemorrhagic collapse. The internal organs break down and hemorrhage issues from the ears, eyes, and mouth. There is no vaccine, though ribavirin will offer hope if given sufficiently early. Cases occur in the U.S. though they are very rare (perhaps one per year) and there have been no American deaths in recent decades. However, international travel and climate-driven rodent spread are sparking private concerns after a case in Iowa in 2023. Lassa fever will be back.

HOW NORWALK VIRUS BECAME NOROVIRUS

The first outbreak of norwalk virus was in 1968, a local epidemic of gastroenteritis in Norwalk, OH. The name didn't last. At the International Congress of Virology in 2002, it was decided to rename it as norovirus. It has been said that the city of Norwalk did not want to be associated with a disease-causing agent, and it was also pointed out that 'norovirus' was much simpler to spell. Infections with the virus trigger short-lasting vomiting and diarrhea – it doesn't last more than 48 hours. Outbreaks thrive in confined communities, from cruise ships to schools and colleges. There is no vaccine, nor an antiviral for treatment; rest and hydration are the mainstay of therapy. This virus gets everywhere. It is particularly common on cruise ships. On one vessel where I was lecturing about microbes, we had a major outbreak that resulted in large numbers of passengers and crew being confined to their quarters. I didn't catch it. Nor did a nurse I knew who was responsible for preventing cross-contamination in operating theaters, showing that meticulous attention to hygiene can prevent spread.

Each year the U.S. sees about 20 million cases, with fewer than 1,000 deaths (primarily among the elderly and vulnerable). In the last 2 years, there has been a 15% rise in outbreaks, which seem to be linked to post-pandemic social mixing. This is a virus that needs a wise-eyed microscopist to identify. High-resolution imaging of viral particles in fecal samples remains critical to confirm an outbreak of this virus. No serotyping is necessary; it is the electron microscopist who alone proves the point.

MONKEYPOX CHANGES ITS NAME



Monkeypox is a virus that is very similar to smallpox. They share 90% of their genes, so vaccination against one protects against the other. They are indistinguishable under the scanning electron microscope, and at 250 nm long, the virions are large enough to be just at the limits of resolution of the light microscope.

Monkeypox is closely related to vaccinia and the smallpox virus. The virions are large and brick-shaped, and can survive for prolonged periods in the environment. This virus was first identified in 1958 in monkeys used for research in Denmark, hence the name monkeypox. Not until 1970 was it known that the virus could also cause disease in humans, when the first case was reported in the Democratic Republic of the Congo. We now know that the virus is endemic in central and West Africa, particularly in the rainforest regions. It likely originated in rodent reservoirs, squirrels, rats, or dormice, though the exact reservoir remains unknown. Primates, including humans, act as incidental hosts. Infection is caused by the monkeypox virus entering the body through broken skin, mucous membranes, or via the respiratory tract. Primary infection often results from direct contact with infected animals or their bodily fluids. Human-to-human transmission can occur through close contact with lesions or respiratory droplets. After a prodromal phase lasting less than a week, in which the patient suffers fever, chills, headache, and muscle aches, macules form which develop into papules and eventually into vesicles and pustules just like smallpox, though monkeypox produces swollen lymph nodes, a key feature to distinguish it from smallpox. The illness usually lasts two or three weeks, though symptoms range from mild to severe. Treatment focuses on hydration and nutritional support, with pain and fever management using acetaminophen. Secondary bacterial infections often occur, and these need treatment with antibiotics. Tecovirimat and cidofovir are antivirals that can be used against all the pox viruses, but they are limited both by availability and potential toxicity. Vaccines have recently been introduced and, if given before exposure to the virus, can eliminate up to 90% of infections and curtail an out-

break.

There have been 35,000 cases in the U.S. since 2022. Although monkeypox is the obvious name, since the virus was first isolated from monkeys, there were claims that the name might be linked to stigmatizing narratives, particularly affecting communities of color. The use of the alternative term mpox was spearheaded by the WHO, who said it was the preferred term in November 2022. They said that for 20 years the guidelines on naming viruses have discouraged terms that reference specific places or groups, though many viruses are named after where they were found and, since everyone knows that the origin of the name mpox has nothing to do with people, it's impossible to see how it could discriminate against anyone. Currently both terms are found, though mpox is clearly the way ahead. Everybody knows what it really means.

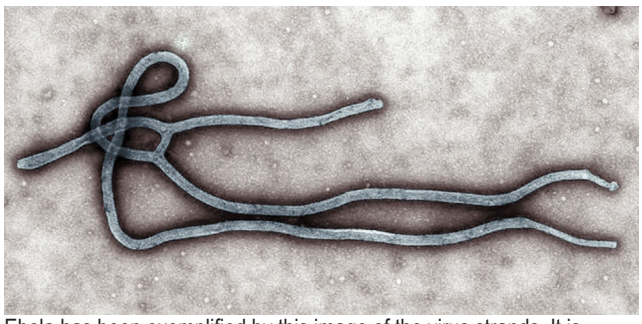
CURSE OF EBOLA

During 1976, there were simultaneous outbreaks of serious infections in the Democratic Republic of the Congo, near the Ebola river, and in South Sudan. The causative agent turned out to be a thread-like virion under electron microscopy. Outside its host, ebola virus is fragile, being inactivated by heat, ultraviolet, and by disinfectants. However, it can persist in bodily fluids, such as semen and breast milk, for many months after a patient recovers.

An infection with ebola typically has an incubation period of about a week, followed by the sudden onset of fever, fatigue, muscle pain, and sore throat. At this stage, it is often mistaken for malaria, but after a week vomiting and diarrhea appear, and severe cases then develop hemorrhagic symptoms with bleeding from the gums, nose, ears, or eyes, or from injection sites. These dire manifestations are seen in about 50% of the patients.

The infection may then move to the critical phase in the second week, involving organ failure, shock, or severe neurological complications in the worst cases. The illness typically lasts for 3 weeks, and recovery begins 1 or 2 weeks after onset in those who survive. However, a post-ebola syndrome involving joint pain, loss of vision, and fatigue, may persist for months. Fatality depends on the specific virus causing the disease. In Zaire, mortality is up to 90%, whereas in Sudan it is about 50%. This is a killer.

Ebola virus is not transmitted through casual contact or respiratory droplets in the air, unlike influenza or mpox; but handling of dead bodies during traditional burial rituals in affected regions can contribute



Ebola has been exemplified by this image of the virus strands. It is assumed by most people to be a new discovery, but this scanning electron micrograph was taken by Frederick A. Murphy at the Centers for Disease Control on October 13, 1976, almost 50 years ago. It shows a virion isolated from a specimen collected in the Democratic Republic of the Congo.

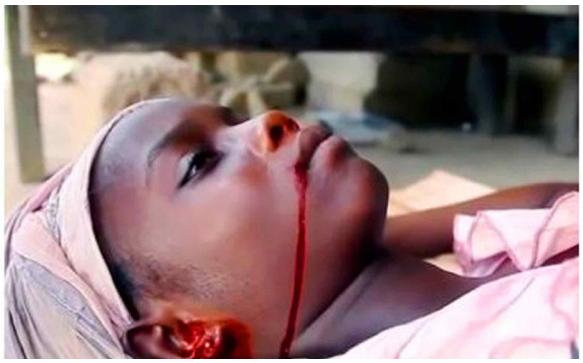
to transmission, as corpses remain highly infectious long after death. The good news is that several vaccines have recently been introduced. Healthcare workers, first responders, and high-risk communities are now being offered prophylactic vaccination. During outbreaks, ring vaccination is used in which a protective zone around the center of the outbreak is established. There is no drug that can cure ebola, but early intervention with monoclonal antibodies significantly improves survival rates, especially for the Zaire ebola virus infections. Survivors develop immunity to this specific ebola species, though reinfection with a different virus is possible. Ebola cases in the U.S. are currently very rare. There were four cases in 2014, one proving fatal, but no sustained community transmission has ever occurred within the U.S.. We need to be watchful; there is currently an outbreak of ebola in Sudan, and this dreaded disease is not going away.

Marburg virus is similar, though there have never been substantial outbreaks. There is one in Biharamulo, Tanzania, in early 2025, though with only a handful of cases. Only one person in America ever came home with the infection. That was in 2008; he recovered.

ALL FLU IS BIRD FLU

Influenza viruses are not grown in tissue culture, but in hens' eggs. It seems a curious choice, until you reflect on the fact that influenza originated in wild birds. All flu is bird flu. The virus was first described in 1878 in Italy, as the cause of fowl plague. But it is the H5N1 subtype that currently causes us most concern and that was first detected in humans in 1997 during an outbreak among poultry in Hong Kong. These viruses reveal various forms under the electron microscope, and can be spherical, filamentous, or even pleomor-

Because all influenza viruses have avian origins, they are routinely cultured in hens' eggs. The Indian authorities issued this photograph to illustrate their ongoing research, during the current outbreak of avian flu in Maharashtra, Andhra Pradesh, and Kerala. Vast poultry flocks are culled, though fortunately only one human fatality has been reported.



Patients suffering from hemorrhagic fevers are soon seen to bleed from every orifice. The organisms attack the tissues, causing systemic structural breakdown and widespread organ destruction. Ribavirin has shown potential as an antiviral, but the essential supportive treatments still consist of fluid support with electrolyte solutions.

phic. Their genomes are segmented, which encourages genetic reassortment that can lead to new strains. Flu viruses survive in cool, moist environments, like water or bird droppings, but they are inactivated by heat, ultraviolet, and routine disinfectants. However, they can persist in contaminated environments for many weeks.

Bird flu has an incubation period of about a week, and then produces fever, cough, sore throat, muscle aches, and conjunctivitis. Patients feel fatigued. About 1,000 herds of dairy cows have been infected with H5N1 bird flu across the U.S. last year, with 70 human cases. The single fatality was a Louisiana chicken owner in December, 2024.

Public health measures include surveillance of farmers and workers, and swab samples are frequently taken. Infected flocks are always culled, though that could be ineffective since wild bird reinfections are without doubt a prominent means of transmission. Although H5N1 influenza has spread from birds to mammals, and occasionally to humans, no sustained human-to-human transmission has yet been reported. There can be little doubt that, before much longer, humans may transmit this virus among themselves. Although no vaccine is generally available for public use, medical authorities have been stockpiling vaccines in order to be ready for a pandemic of the virus. Moderna and Pfizer are among the pharmaceutical enterprises that are developing mRNA vaccines. Current research is aimed at developing vaccines that could inactivate flu virus components, like the stalk of hemagglutinin, which would work not only against H5N1, but also other influenza viruses yet to emerge.

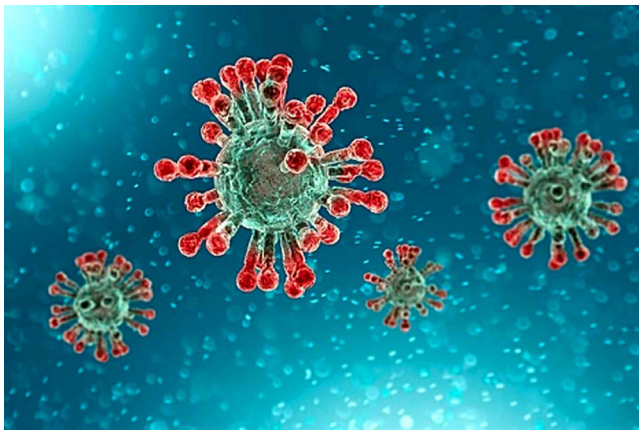
Vaccines for poultry are already used in China, Vietnam, and Egypt, though they have not been introduced in the U.S.. Vaccinated poultry may test positive for flu, which would complicate exports. And, although they reduce mortality, they might still allow for the silent spread of the virus. The current 2025 outbreak of bird flu has resulted in the culling of 20 million birds in a month, and is focusing attention on trials of new poultry vaccines. One of the most pressing problems is that current vaccines can take months to manufacture, whereas mRNA platforms would shorten this considerably. And an all-purpose anti-flu vaccine remains our eventual aim.

CRIMEAN-CONGO HEMORRAGHIC FEVER

Hemorrhagic fevers are the worst of all infections, and this disease is another example of a virus that can trigger the breakdown of the internal organs and cause widespread hemorrhage throughout the body. This virus was first identified in 1944 in Crimea, during an outbreak of disease among farm workers. An outbreak in the Congo in 1956 proved to have the same cause, and by 1969 this was known as Crimean-Congo hemorrhagic fever. This disease is endemic in Africa, the Balkans and the Middle East, and in parts of Asia including Pakistan and Afghanistan. The virus is maintained in a zoonotic cycle and is transmitted through Hyloamma ticks. They do not occur in the U.S., so the disease cannot be directly transmitted in America. The virion contains a segmented genome, much like that of influenza, and this is one reason for concern, since segmented genomes encourage genetic reassortment that could lead to new strains of higher pathogenicity.

After an incubation period of about a week, the pre-hemorrhagic phase brings on fever, chills, headache, and muscle aches; patients are fatigued and suffer severe abdominal pain. Serious mood changes may

occur, and photophobia is often encountered. During the second week, hemorrhage appears. This may result in petechiae in the skin and nose bleeds, which can progress to gastrointestinal bleeding or massive internal hemorrhage. Severe cases show disseminated intravascular coagulation, which is invariably fatal. Most patients recover after about 3 weeks, but fatigue and weakness can persist for months. The case fatality rate is about 30%. Antivirals are of limited use, and although experimental vaccines have been tested in animal models, none is yet available for clinical use. In recent years, there have been many major outbreaks; one in Iraq in 2022 involved over 1,000 infected individuals. One fatal case in Portugal was an 83-year-old man who was misdiagnosed as suffering from Mediterranean Spotted Fever caused by *Rickettsia conorii*. So often these diseases are hard to distinguish clinically, one from another.



Computer graphic images of coronaviruses are now familiar to everyone. The virion measures about 60–140 nm across and has characteristic crown-like spike proteins protruding from the surface, each measuring 9–12 nm. These glycoprotein structures facilitate attachment to host cells and are evenly distributed across the virion.

ENTER THE CORONAVIRUS

Coronaviruses were first observed, and named, by women microscopists whom I discussed in a previous article (see: "Forgotten Women who Lit the Way," *The Microscope*, 68:3/4, pp. 139–150, 2020). I remember being shown images of these curious virions in the electron microscope in 1967. They had been isolated from a boy with a cold – but it wasn't a typical cold. He was suffering from severe malaise, and it soon became clear this was an unrecognized infection. A young physician named David Tyrell, whom I knew well, soon isolated the causative virus. It was something new. As I explained in that earlier column, a brilliant young technician, June Almeida, found how to make the virions visible under the electron microscope. At the time, this was a strange new virus; nobody had any idea that a coronavirus would become familiar to everyone as the agent of a global pandemic.

SARS RAISES ITS HEAD

It was in November 2002 in Guangdong, China, that a clutch of cases of severe pneumonia were first reported. It turned out that the causative agent was a coronavirus very similar to the one Tyrrell had originally discovered. Biologists named it Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-1). This was a single-stranded RNA virus with spike proteins that covered the surface. The virus could survive in aerosols for hours, and on surfaces for days; like most other viruses, it was inactivated by heat, ultraviolet and common disinfectants.

The disease had an incubation period of about a week, during which time fever, chills, headaches and aching limbs appeared. In the second week, a dry cough would emerge, along with shortness of breath possibly progressing to pneumonia in severe cases. The worst suffered acute respiratory distress. In most instances the illness had gone in a month, though severe cases required prolonged hospitalization. In this initial outbreak there were 8,098 cases, 774 of them fatal.

The initial cases almost certainly came from contact with civets, but, once the outbreak was established, human-to-human spread came to dominate. Aerosol droplets proved to be the primary mode of transmission, though contact with contaminated surfaces was also significant. One interesting observation is that some individuals acted as super-spreaders. For some reason these individuals infected scores of people around them.

There was no vaccine. There was no cure. Antivirals like interferon were tried, but showed little benefit. Supportive therapy was all that could be offered, with mechanical ventilation or oxygen therapy for those finding it difficult to breathe. Secondary infections were problematic, and antibiotics were used to reduce those. This initial epidemic of SARS primarily affected China, Taiwan, Singapore and Vietnam, though it also occurred in Canada, and there were fewer than 30 cases – all travel related – in the United States. No community transmission occurred in the US, and the only American to die was in Hong Kong. Meticulous hygiene prevented the disease from spreading further, and taxis I used in Singapore had notices advising im-

mediate transport to hospital if symptoms appeared during a ride. In China there was a complete ban on the trade in civets. Airport screening was begun in 2002 and by July 2003 isolation, quarantine, and travel restrictions were introduced, and the outbreak was over by May 2005.

CORONAVIRUS AND THE CAMEL

Saudi Arabia was next. In September 2012 an unusual case of severe pneumonia was documented in a 60-year-old man. The virus was isolated and turned out to be another coronavirus. It was named MERS-CoV and was thought to be zoonotic, with bats as the likely reservoir. Investigation showed that dromedary camels were the intermediate host and the illness could also be spread through camel milk. Human-to-human transmission was limited, but became significant in outbreaks.

The incubation period was about a week, with fever, cough, shortness of breath, and sore throat. Some infected people went on to develop pneumonia, kidney failure, and septic shock. These severe cases were more common in older adults or those with comorbidities, though 30% had no symptoms at all. Milder cases resolved within a fortnight, but the severe cases required weeks of intensive care. This virus is a killer. There were 2,494 cases between 2012 and 2020 resulting in 858 deaths, a fatality rate of over 33%. Death was due to renal failure, multi organ collapse, and coagulopathy.

Patients with kidney failure were treated with dialysis, and those enduring respiratory distress were given oxygen therapy or mechanical ventilation. Further prevention was limited by quarantining contacts for 14 days. There is no cure, and still there is no vaccine for MERS. Only two cases were reported in the U.S., when health care workers returning from Saudi Arabia in 2014 developed the disease, but both recovered, and there was no secondary transmission. Personal measures to limit the spread of the virus focus on hygiene and avoiding contact with camels or unpasteurized camel's milk.

REMEMBER THE PANDEMIC?

The third coronavirus outbreak was of COVID-19. None of us can forget that. I analyzed the pandemic in a previous article (see: "Stop Covid Beyond the Mask," *The Microscope*, 68:2 pp. 59–70, 2020). The virus was named SARS-CoV-2 and the pandemic sparked an unprecedented global health response. The rapid development of mRNA vaccines was an extraordinary medical achievement which saved countless lives. But the pandemic triggered political controversy in the press, with online objections to vaccines involving members of congress and official representatives who challenged the value of vaccination.

Common claims circulated through social media included the idea that vaccines would alter our DNA, or even contain microchips, an absurd notion linked to Bill Gates. It was claimed that vaccines didn't work, or that they would cause widespread harm ranging from autism to infertility. It was said that natural herd immunity was all we needed, and even that the virus was a hoax. These campaigns had a marked effect on the public response to the pandemic. In 2021, some 30% of American adults were reluctant to be vaccinated, particularly in Conservative regions. This reluctance had measurable mortality: hundreds of thousands of Americans may have died needlessly, some 40,000 of them in Texas alone. The surveys confirmed that vaccine refusal was most marked in red states where strong antivax activism was most apparent. Major figures like Robert F. Kennedy amplified the skepticism, by raising concerns about public health. Marjorie Taylor Greene, a leading U.S. member of congress, rejected the idea of vaccine safety and effectiveness. To her, claims of vaccine benefits were "bullshit." Other Republican lawmakers including Rand Paul and Ted Cruz questioned the validity of vaccination, prioritizing personal choice over public health, and claiming that vaccines didn't work. The result was clear. Some 10% to 15% of Democrats did not trust vaccines, though well over 40% of Republican voters refused to use the vaccine. People died in droves as a result.

President Donald Trump initially called COVID-19 a hoax and he persistently downplayed the effectiveness of vaccines, though he later went on to endorse them and his mixed messages confused supporters. In other countries, leaders like Jair Bolsonaro in Brazil and Narendra Modi in India minimized the severity of COVID-19 and delayed the rollout of vaccines, which simply amplified online skepticism. By contrast, leaders like Angela Merkel in Germany and Jacinda Ardern in New Zealand strongly endorsed the vaccines and a disinclination to vaccinate was unusual.

Since the pandemic started, there have been over 100 million cases in the U.S. with about a million deaths. More than two-thirds of Americans were fully vaccinated. This reduced hospitalization by some 90% when we compare vaccinated versus unvaccinated populations. Worldwide there were 700 million cases with 7 million deaths reported by the WHO, a figure which is likely underreported globally. Vaccination is found in 80% of the population in high-income coun-

tries, and only 30% in countries with low incomes. It is estimated that vaccination saved up to one and a half million lives in the U.S. and that the vaccines reduced severe outcomes by at least 80%. The mRNA vaccines produced by Pfizer and Moderna are claimed to have prevented more than 90% of hospitalizations in 2021 to 2022.

The authorities supporting vaccination regularly claimed that the vaccines against COVID-19 were both safe and effective, though no vaccine is ever fully effective, nor can they all be perfectly safe. There have been serious side effects with the COVID-19 vaccines, as there always are with them all. Cases of myocarditis were reported in young men, typically after the second injection. The official world instinctively tried to cover it up. About 0.03% of young males were found to have suffered myocarditis, usually mild, according to Moderna scientists, but they didn't pass on the information.

The CDC even prepared a document warning of the risk but never sent it out. They were concerned with emphasizing the benefits.

Clearly, there would have likely been a reaction against vaccination if everyone knew of these reports, but openness and honesty are prerequisites if we are to avoid claims of cover-up. At its worst, the reported risks were far smaller than those we all accept. Lasik eye treatment, for instance, is successful in 99.5% of cases, but the 1 in 200 that result in serious effects can be deeply distressing. People have committed suicide because of the symptoms they experience. Honesty must always prevail, though our acceptance of everyday risks casts a shadow on reality. Tell a patient that the risk of a procedure is less than 1% and they'll shrug it off. Say there's a 1:1,000 risk with a vaccine, and they'll campaign against it.

Thrombosis was another problem noted with the viral vector vaccines produced by Johnson & Johnson and AstraZeneca, at an incidence of about 3 per 1,000,000 doses. Anaphylaxis was seen in up to 5 cases per 1,000,000 doses, a condition immediately treatable with epinephrine. This is much the same level as all vaccines. Guillain-Barré Syndrome (GBS) was another rare side-effect with 1 per 1,000,000 doses linked to the Johnson & Johnson vaccine. Overall, serious side-effects are reported to have occurred in less than 0.05% of the doses that had been administered around the globe by 2023. The risk of death from contracting COVID-19 is between 1% and 2% of unvaccinated people, which far outweighs any risk from the vaccine.

Officials overstated the benefits. President Joe Biden insisted that "If you get the vaccine, you're protected." CDC Director Rochelle Walensky stated that "vaccinated people don't get sick." Both must have known this is wrong. The most effective vaccines we have are against measles, and even those protect only 95% of vaccinated persons. The COVID-19 vaccines were meant to greatly reduce incidence of the disease, and this they did. Overall, the COVID-19 vaccines may have saved up to 20 million lives globally, and 1½ million in the U.S. alone. Vaccination had the effect of reopening economies by reducing the incidence of severe cases, saving trillions in healthcare and in lost productivity. We have to note that protection against infection drops to below 40% after 6 months, requiring booster injections. Yet the legacy of the antivaxxers still persists. In the U.S., 40% of all vaccinated adults skipped their boosters in 2023, purely due to distrust.

Facemasks were heralded as an answer to spreading the pandemic virus. However, a moisture-control expert from Vermont, Chad Roy, used freezing air to show how ineffective masks can be. Although the fabric may trap water droplets, most of the breath bypasses the popular masks and their use may owe more to medieval traditions, rather than medical efficacy.

The development of mRNA vaccines in such a rapid time is unprecedented and we can only hope that the responses of the producers are as effective next time. If medical history repeats itself, as it has a tendency to do, then it is worth noting that these coronavirus outbreaks have happened every 7 to 8 years. If this trend continues, we can expect another one by 2030. Even if a new coronavirus doesn't cause an outbreak, some other virus will. A major pandemic could wipe out most of humankind, and it's a question of when, not if.

Official spokesmen during the COVID-19 pandemic underplayed the risks and overplayed the benefits, compromising public trust. The antivaxxer campaigns can only discourage people from obtaining vaccines when a new pandemic threatens, and that would have massive global consequences. Millions of people may die because they do not trust the authorities and are intimidated by the campaigners. Yet you may be certain that those who protest will buy one of those disease-carrying chickens without a second thought. Risks are relative, and that is a lesson we have yet to learn. ■