Frank Ryan is a consultant physician and pioneering evolutionary biologist at the University of Sheffield. He is also the internationally bestselling author of *Tuberculosis: The Greatest Story Never Told*, a *New York Times* book of the year, *Darwin's Blind Spot* and *Virus X*. He pioneered the evolutionary concepts of viral symbiosis and genomic creativity and has contributed to the modern understanding of the evolution of the human genome. He is a Fellow of the Royal College of Physicians, the Royal Society of Medicine and the Linnean Society of London.

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Virusphere

From Colds to COVID-19:
The Hidden World of the Virus

Frank Ryan

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We all play hideous games with each other.
We step inside each other's chalk circles.

Anthony Hopkins

Contents

Introduction

In December 2019 a novel illness came to the notice of doctors in the city of Wuhan, capital of Hubei province, in the People's Republic of China. At first it appeared to be a local outbreak of influenza. But while it was transmitted, like flu, by aerosol spread brought about by coughing and sneezing, this illness differed from the flu in that it often went deeper into the respiratory passages, even as far as the air-sacs where oxygen exchange takes place in the lungs. In the more severe cases this direct infection of the lungs caused a viral pneumonia. As the outbreak worsened, medical authorities realised that they were not dealing with the familiar annual flu virus, but one they had never seen before. It was in the virological jargon, an 'emerging virus' – a hitherto unknown virus causing an illness new to medical science. This mystery virus was subsequently identified as a coronavirus, and attributed the name COVID-19, from Corona Virus Disease and the year of its emergence.

The family of coronaviruses is so-called because, under the extreme magnification of the electron microscope, they appear to be globular with a crown of thorny spikes around their circumference, somewhat like the familiar spiky naval mines. COVID-19

also differs from seasonal influenza in another key aspect: novelty. We have long been exposed to seasonal flu epidemics. This means that if we encounter another flu virus, we are already partially immunised against it. COVID-19 was new to human experience, so we had no advance immunity to it. It was welcome, if a little surprising, that many of those newly infected with COVID-19 suffered a relatively mild illness, with only one in five going on to develop a more severe or life-threatening encounter. This consolation was offset by the fact that COVID-19 was extremely contagious, and so even this minority with severe or life-threatening disease turned out to be more significant in number than was first thought. In Chapter 10, Flu and COVID-19: The Pandemic Threat, we shall examine coronaviruses in more detail while looking at how we can best protect ourselves from them. But, of course, COVID-19 is only one of a number of viruses that threaten human society in the twenty-first century.

Threat of one kind or another is hardly new to life on Earth. For more than half a century we have lived in the shadow of nuclear Armageddon. Today, even as this fear seems to be subsiding, newer worries are surfacing. With climate change, the mass destruction of the rainforests, globalisation of the world into what is effectively a single interconnected 'village' and the pollution and over-fishing of the oceans, the biosphere is under unrelenting threat. This provokes an obvious question: is there a connection between the emergence of new plagues and the effects of human behaviour on the global ecology? Indeed, returning to the subject of the coronavirus pandemic, we might ask the question: why do such plagues emerge to threaten us? At a time when we are still coming to grips with the lethal pandemic of AIDS, it would seem prudent to ask where emergent viruses, such as HIV-1 and COVID-19, really come from? Why do such viruses emerge

in these modern times? And when they do emerge, why do they behave with such fearful aggression? Could it be that through human overpopulation, with its increasing expansion into former wilderness areas, coupled with the toxic effect of climate change and plastic pollution of the biosphere, our human society is heading into an existential crisis?

I have been interested in viruses since I first conducted my own viral research back as a medical student at Sheffield University Medical School. In the 1990s I began my own search for answers to the above questions in a book, *Virus X*. I spent two years visiting leading research laboratories and talking at length with the so-called 'Virus Hunters' of the Special Pathogens Branch of the Centers for Disease Control and Prevention (CDC) in America, Porton Down in the UK, The Pasteur Institute in Paris, the Belgian equivalent in Brussels and the World Health Organization in Geneva. I also interviewed patients who had survived some very perilous encounters. That research changed my perspective of viruses and led me to develop my present interest in evolutionary virology. I became a member of the International Symbiosis Society, which focuses on the evolutionary implications of living interactions. In *Virusphere*, I have returned to take a new look at viruses in general and the worrisome situation of COVID-19 in particular. What we need amidst the confusion and alarm of the present situation is informed facts.

As the entire world is now aware, COVID-19 has developed into a pandemic plague of the like not seen since the so-called Spanish Flu of 1918. Will it provide the lesson that we perhaps need to force us to examine our own behaviour and its impact on the delicate balances of climate, atmosphere and biosphere of our world? We might make a start by seeking to understand entities such as viruses that are capable of seriously hurting us. We

surely need to know *how* they might threaten us, and what we can possibly do to mitigate this threat. Viruses, such as COVID-19, circumambulate our world with the speed of a passenger jet, paying no heed to national boundaries, or circumscribing notions of nationality, ethnicity, race or religion. They pay no heed to social class, or indeed any human hubris of fame, celebrity, wealth or power. To add to the problem, these threatening entities are, for the most part, invisible, even under the most powerful magnification of the light microscope, making them all the more enigmatic – and perhaps also the more frightening. These same invisible entities invade not just our tissues and organs, but, to borrow the metaphor from Anthony Hopkins, they step inside the chalk circles of our most intimate and innermost being: the living cells that are repository of our coding DNA.

Despite all of this, viruses are not evil. They are incapable of thought, or of any considerations of right or wrong, and thus are essentially amoral. Indeed, strange as it might seem, there is even a beneficial side to their presence. Only recently have we come to realise that viruses are integral to the evolution of life on Earth as well as the interdependency of life on the planet, playing key roles in the health of the biosphere. Virologists have invented a new term for the strange and complex interaction between viruses and cellular life (a play on which forms the title of this book). They call it the 'virosphere', which comprises the junctional zones where viruses interact with their myriad hosts, spanning all environments where life is to be found. Viruses are the most abundant biological entities in all the major environments on Earth, exceeding the numbers of cellular life forms, including the bacteria, by one or two orders of magnitude. These viruses are essential to an extraordinary homeostatic equilibrium that not only prevents the oceans from becoming a toxic waste of bacterial pollution,

but also provides the nutritional base of the oceanic and terrestrial food chains.

Contrary to popular belief, we do not rule this world. We share it with the wonderful diversity of life that populates every ecological niche. The emergence of COVID-19 is a brutal reminder of the fact that while life is often harsh, it is also quintessentially interactive. Viruses, and the 'virosphere' that marks the zone of conflict and interaction between us and the viruses, are an essential component of this sometimes harsh, but precious interdependency of life.