A report from our Bristol Correspondent

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When the coronavirus started impacting on the UK, I ordered 2 books: *The Plague* (*La Peste*) by Albert Camus, which was one of my French A level texts years ago, and I remembered it as being weirdly uplifting, showing (as I remember) a doctor struggling on regardless against seemingly impossible odds – sounds familiar? I haven't started the book yet …

… as I started reading the second book, *Spillover - Animal Infections and the Next Human Pandemic* by David Quammen, all about zoonoses [*Ed: Zoonoses are infectious diseases caused by a pathogen - an infectious agent, including bacteria, viruses, parasites and prions, that has jumped from non-human usually vertebrate animals to humans.*] As he presciently says in 2012, "Some knowledgeable and gloomy prognosticators even speak of the Next Big One as an inevitability … Will the Next Big One be caused by a virus? Will the Next Big One come out of a rainforest or a market in southern China? Will the Next Big One kill 30 or 40 million people?" Gulp!

It is a really fascinating book, moving between different levels: explaining the science, a bit of history of virology and the mathematics behind it; interviews with experts; fieldwork in various countries and continents, interviewing survivors of pandemics in villages in the Democratic Republic of Congo; helping with fieldwork, e.g. collecting bat faeces samples. I'm not a physical scientist but I found it accessible. He also has a nice line in descriptive writing: "At a crossroads known as Mambele Junction, with a central roundabout defined by three truck tyres piled up like coins, we dined by kerosene lantern at a small cantina, eating smoked fish in peanut sauce and drinking warm Muntzig beer."

I couldn't possibly do it justice with a synopsis, but here are 7 "gems". Apologies if it's old news to you and if I've got something wrong.

- Viruses are very small, 10 times smaller than bacteria; they can only be seen by electron microscopes. They have been described as "a piece of bad news wrapped up in a protein". The bad news is the genetic material, which is very limited but allows it to mutate more easily than if it were a more complicated genome. It is generally RNA (RiboNucleic Acid - a polymeric molecule, a single strand folded onto itself) rather than DNA

(DeoxyriboNucleic Acid - a molecule composed of two polynucleotide chains that coil around each other to form a double helix carrying genetic instructions), which has the same effect. The protein wrap is called a capsid, protects the viral innards and defines its exterior shape. Some are spherical, others ovoid, globular or like bullets. “A plate of Ebola virions mixed with Hendra virions would resemble capellini in a light sauce of capers”.

- Viruses act by entering a cell and commandeering its genetic machinery to make copies of itself. A bacterium is a cellular organism. Antibiotics work by preventing bacteria from building cell walls (Penicillin, Amoxicillin) or by interfering with the process by which bacteria manufacture new proteins for cell growth and reproduction (Tetracycline). They are ineffective on viruses which lack cell walls. However, if we are infected we can produce antibodies, molecules that stick onto the spikes of the coronavirus capsid and prevent the virion from grabbing a cell.
- Viruses often lurk within a reservoir host, a living organism that harbours the pathogen while suffering little or no illness, in a sort of ecological equilibrium. Bats are often highlighted as being a reservoir host of many viruses. Sometimes the virus spreads to an amplifier host, a creature which can be relatively easily infected by the virus and yet transmit it abundantly, e.g. by sneezing or coughing. It becomes an intermediate link between the reservoir host and some other victim, who requires higher doses or closer contact to become infected – such as a human in the coronavirus case. Some examples of amplifier hosts of viruses are pigs, horses, civets, chimpanzees, other types of monkey, mice, birds and the poor old pangolin which seems to be blamed for the present outbreak.
- Why are bats often identified as reservoir hosts? Well, the order Chiroptera encompasses 1116 species, which amounts to 25% of all the recognised species of mammal. Yes, one in four species of mammal is a bat. They have an ancient lineage, evolving to their present form about 50 million years ago, allowing scope for a long association between bats and viruses. They are very social and roost in huge numbers very close together, allowing for easy transmission. They fly, dozens of miles every night, and some species of bat migrate according to the seasons. An infected flying fox can, for example, eat a fruit, drop it onto the ground where it is eaten by a horse, which contracts Hendra virus which is transmitted via its breath to its trainer.
- How can science make predictions and say, “the peak of corona virus in the UK is likely to occur over Easter”? (Apparently for Bristol it is supposed to be in May - we always were behind the times). The answer is mathematical modelling. “The evolutionary success of a bug is directly related to its rate

of transmission (R_0 is the basic reproduction rate) through the host population and inversely but intricately related to its lethality, the rate of recovery from it, and the normal death rate from other causes." [Anderson and May (1992*) Infectious Diseases of Humans*] In this blog (April 19th), Angela Merkel gives a pretty good exposition of the process. It's worth noting that different viruses have different transmission systems - airborne (coughing, sneezing), blood-borne, sexual, oral-faecal, vector borne (e.g. mosquitoes with malaria).

- There is a Critical Community Size (CCS) for different infectious diseases, a critical minimum size below which it can't keep circulating indefinitely. For measles this is about five hundred thousand people; for whooping cough it is about two hundred thousand. This is because, as Quammen puts it, it has "consumed its opportunities among susceptible hosts".
- The $64,000 question - Why zoonoses? Why now? There has been a modern era of emerging zoonotic diseases- Machupo, Marburg, Lassa, Ebola, HIV-1 and 2, Sin Nombre, Hendra, avian flu, Nipah, West Nile, SARS, swine flu. They represent the unintended consequences of what we are doing. By no means exhaustive examples are:
    - Factory farming. As evolutionary biologist Rob Wallace put it in his book *Big Farms Make Big Flu*, "Industrial livestock appear ideal populations for supporting virulent pathogens. Growing genetic monocultures of domestic animals removes whatever immune firebreaks may be available to slow down transmission. Larger population sizes and densities facilitate greater rates of transmission. Such crowded conditions depress immune response. High throughput, a part of any industrial production, provides a continually renewed supply of susceptibles [those animals who can catch the germ], the fuel for the evolution of virulence [deadliness of germ]."
    - Destruction of natural ecosystems at an alarming rate. So much to say here, all of which is very much in the media. Infectious disease can be thought of along ecological lines as a struggle for existence between man and micro organisms, much like competition between species in nature. Environmental disruption by man releases epidemics. "When the trees fall and the native animals are slaughtered, the native germs fly like dust from a demolished warehouse. A parasite microbe, thus jostled, evicted, deprived of its natural host, has two options, to find a new host, a new kind of host, or go extinct. We, human animals, are abundantly available and a

wonderful target for any organism that can adapt itself to invading us."

- Opportunities for cross species contamination, as in the so-called wet markets, e.g. Wuhan. Observers of Chinese culture have called the trend for eating unusual wild animals in southern China 'the Era of Wild Flavour'. In the UK, BSE (mad cow disease) is thought to have been caused by feeding to cows meat and bone meal containing cattle and sheep remains.

In his concluding chapter, Quammen unsurprisingly does not offer specific 'solutions', although he clearly believes that our impact on the natural world is largely negative at present and, in terms of zoonotic infections, potentially catastrophic. But as he says, "the purpose of this book is not to make you more worried. The purpose of this book is to make you more smart." In other words, that humans can change things if they want to. What people do even as individuals has a large effect on R_0. The government is at present telling us and is likely to go on giving similar advice throughout this year at least.

As Barack Obama said a couple of days ago (posted in this blog, April 19th), hopefully this can be a time for reflection. The world is on pause. What kind of world do we want to emerge from the global lockdown, and how can we work together to achieve a better world?