VIRUS*

Biological Predator

with an Appendix on Bacteria

(An Investigative Review of Covid-19)

by

Gerald F Pillay

30 September 2021
(cut-0ff)

. *

National Library Board, Singapore Cataloguing in Publication Data
Name(s): Pillay, Gerald F., 1934-
Title: Virus* biological predator with an appendix on bacteria : an investigative review of Covid-19 / by Gerald F. Pillay.
Description: Singapore : Gerald F Pillay, 2021.
Identifier(s): ISBN 978-981-18-3046-4 (PDF)
Subject(s): LCSH: COVID-19 (Disease) | COVID-19 (Disease)--Prevention | COVID-19 Pandemic, 2020-
Classification: DDC 614.592414--dc23

***

Publisher
Gerald F Pillay
139A Lor 1A Toa Payoh
#01-48
Singapore 311139
gfpillay@singnet.com.sg

***

Printing and Publication
An e-book, 285 pages, self-published on **15 Dec 2021** at https://geraldpillay.wordpress.com

***

***

Editorial Note
All currency ($) is stated in United States Dollars (USDs).

***

ABOUT THIS BOOK

The study takes an helicopter view of Covid-19, with close focuses on the virus itself, the history of viral pandemics, and the various responses of us humans. The latter cover the detailed actions of the country of origin, and by the world community. Besides inter-governmental and private-public partnerships, the latter include the outstanding collaboration of the scientific, medical, humanitarian and philanthropic communities .It examines the GOF/Leak Allegations in depth. It ends with Concluding Observations and recommendations for Direction of Change.

Subjects:
(a) **Part One**, Summarises the current state of knowledge of viruses
(b) **Part Two**, Focuses on the past Lesser Pandemics, followed by the past Major Pandemics,
(c) **Part Three,** Deals with the **Covid-19:** its origin, the country of origin and its initial actions; WHO's first responses, its mobilisation of the global communities, and its Three Pillars Strategy – Diagnostics, Therapeutics and Vaccines
(d) **Part Four,** Recounts our Human Defenses and Medical Defenses
(e) **Part Five**, Sizes up where we are under Score Lines, and the road ahead
(f) **Part Six,** Captures the international communities that rallied together to battle the pandemic
Part Seven, includes the Concluding Observations and Directions of Change.

***

FOREWORD

The review takes a deep look at the virus itself. It then looks at the pandemic from various perspectives: historical, geographical, technical, our preparedness and responses, the social impact, and global management.

The virus is a very technical entity, I have therefore had i to resort to biology and molecular science to talk about it. My technical understandings are summarised in Part One. I hope they provide a decent foundation for a non-specialist person to understand the different aspects of Covid-19.

This being my fourth assay into the form, I realise I am a practitioner of a new-generation writing art: the Internet-researched book. It is an ideal mode for dossiers, reports, analysis of current affairs and subject updates, including feisty technical subjects. It is a vibrant and thrilling art. It brings serious writing within the reach of the ordinary person. One is able to write in real-time, while consulting detailed archived material.

If I have erred, it is to have over-laden this review with too much information The result is it is both a compendium as well as a narrative.

I have hyperlinked the important sources. The book is also hyperlinked internally. It is, again, a new way to read a book and get to the bones of the subject in an hour or two.

Gerald F Pillay
15 Dec 2021

Dedication

To Christian, my grandson,
who was 15 on 6 Oct 21.

Introduction

I began this review immediately on completing "Quantum Mechanics, A Non-Technical Brief "[1]. I knew nothing about viruses. Covid-19 had just been declared a pandemic.

I could not have been more intuitive. Between sub-atomic matter and the world's biomass, which embraces all living things, I found a whole third physical universe in the nano scale, the "virosphere". What was amazing was that the virus substantially co-habited and replicated in the biomass - and cannot do otherwise.

The science and technology bequeath to us by Quantum Mechanics, which has enabled us to take control of sub-atomic matter, has now enabled us to study and interact with the virosphere, down to the single virion. There were three technological tools that made this possible.

The first problem was that the virosphere was invisible. It existed at the deep end of the nano scale The smallest viruses, at 20-50 nm[2] (or 0.02-0.05 μm[3]), are about 10 times smaller than the typical bacteria (at 0.5 μm), and 100 times smaller than the typical human cell (at 7.5 μm). It took the electron-microscope, invented in 1931, to open the door to this microcosm. Fifty years before that, we did not even suspect that they existed. Today, the cryo-EM microscope can photograph a fraction of a virus in 3D at 4 Angst[4] (0.4nm), ie about 4 atoms[5].

The second problem was that viruses were biological. We had first to know our biology on their scale. The electron-microscope did indeed enable us to unravel our own cell

---

1 ISBN: 978-981-14-9875-6

2 1 nm= nanometer or 1,000,000,000th or 1X10^{-9} metre

3 1 μm = micron or 1000,000th or 1x10^{-6}metre

4 1 Angst = 0.1 nm or 10,000,000,000th or 1x10^{-10} metre

5 1 atom = about 1 Angst.

biology down to sub-molecular level where the war with the virus was being waged. However, the crucial bio-scientific discoveries of the genome, DNA and its sequencing were yet to come. These were not coherently established until 1977 when the first full genome of a virus (the phX174) was successfully sequenced. These landmark achievements have permitted us to understand the makeup of the viruses and provide some prospect of dealing with them. Full knowledge of the human battleground had still to wait until 2003, when the Human Genome Project was completed. Today[6], with second and third generation gene sequencing and the molecular clock we can scope a virus back to its origins.

And the third problem with viruses was their numbers and their diversity. They came in myriads of classifications and were specialised for the different bio-environments. Without the powerful computers that have emerged (since the late 1980s), classifying and processing the data would not have been possible. (Computers have also featured in other support functions, including the massively parallel sequencing of genes.) Today our major systems are run by supercomputers, and we have half a dozen or so quantum computers in nascent development or gestation. We shall need the latter to fight future viral invasions.

Viruses represent an evolutionary history going back to the beginnings of our planet. Even with the enormous discoveries in the last 70 years, we know little more than the tip of the iceberg about them.

As I progressed, the pandemic evolved; and this became both a virus compendium and a running record. In the end I separated the material for easy access as follows:

---

[6] On 1 Jun 2021, scientists announced they had sequenced the entirety of the Human Genome, including parts (8%) that were missed in the first human genome two decades ago. It increased the number of DNA bases from 2.92 billion to 3.05 billion, a 4.5% increase. But the count of protein-coding genes increased by just 0.4%, to 19,969.
https://www.statnews.com/stat-plus/

In **Pat One**, I summarise the current state of our knowledge of viruses.

In **Part Two**, I focus on the earlier pandemics, the three Lesser Pandemics, followed by the Major Pandemics of Influenza, HIV and the Coronavirus (SARS-Covid-1 and MERS). These provide the experiential history to our present crisis. The major ones are still with us as a living backdrop.

In **Part Three,** I confront **Covid-19**. First, I deal with its origin, the preparedness of the country of origin, its initial actions, and the outbreak. Next I deal with WHO's framework of responsibility, its anticipatory initiatives, its first responses, the mobilisation of the global scientific, donor and humanitarian communities, and finally the massive support of the major governments.

This Part then covers WHO's Access to Covid-19 Tools (ACT), the core of which is the **Three Pillars Strategy** – Diagnostics, Therapeutics and Vaccines, the last the crucial weapon.

Probably the most extraordinary scheme of global co-operation ever put together for humanitarian action is COVAX. Its three components, the Covax Facility, the Covax Marketplace and the Advanced Market Commitment (AMC) provision were brilliant.

Launched by WHO and its partners, CEPI and GAVI, in Apr 2020, and amply supported by government commitments and donor funding, this multi-dimensional scheme targeted to have a vaccine against the Covid-2 virus within one year (as against the norm of 10 years previously), with many more under development and a target of 2 billion doses by the end of 2021 - equitably distributed to the LMICs whether they were able to pay or not.

In **Part Four,** I recount our Human Defences and Medical Defences, The latter reflect those that came through the Three Pillars programme, including **COVAX.**

In **Part Five**, under Score Lines, I size up where we are, and the road ahead, while **in Part Six,** I capture short profiles of the international community that rallied together to battle the pandemic. Without them, WHO could not win this war. I cannot single out one, it must be three: if nothing else read the Bill and Melinda Gates Foundation, CEPI and GAVI.

Finally in **Part Seven,** I set down some Concluding Observations, with an in-depth analysis of China's role as Country of Origin. In Directions of Change, I emphasise the primary need for further research. I also comment on the essentials of the Future Defence Framework and The Next Steps towards it.

With the release of key documents in August and September 2021, I was able to carry out an exhaustive analysis of the Wuhan GOF-Leak Allegations, with my conclusions. Per force, I slotted this report in the penultimate section of the Concluding Observations.

Addendum
in Part Two, I touch on **malaria,** which is non-viral, and remains today the most rampant example of our historical failures. One child dies every minute in Africa.

I make no excuse for including a full-blooded report on **bacteria,** in the **Appendix.** About 30% of our genome are bacteria (as against 8% of viruses). They are remarkably indispensable to the existence of this planet. I also touch on tuberculosis and cholera, two major diseases caused by them, still on-going in modern times.

Gerald Pillay.
15 Dec 21

***

TABLE OF CONTENTS

LIST O F TABLES

PART ONE

Review of Current Knowledge

What Are Viruses?

Viruses are incomplete biological entities. They are encoded to replicate, but are not endowed with the reproductive machinery and resources to do so. They must therefore acquire these by hunting and taking over the cells of living beings to fulfil their reproductive need. Born with the urge but without the necessary genitalia, they hunt to replicate. This is their core identity. Viruses are constitutional predators.

Over time, viruses have become differentiated. Their host range has narrowed They target different species of living things, and different cells in these. By and large they stay dormant or latent in a living entity until they find the right target. Then they go active, become fully "infectious agents" and "pathogenic[7]." It is in this active form that we know them, sadly as in HIV or SAR-Covid-2.

Although biological, viruses have not been classed as living things. Here is the tabulation that explains why:

[7] "Viruses are **obligate intracellular pathogens**. They cannot replicate without the machinery and metabolism of a host cell." (Edited) https://en.wikipedia.org/wiki/Virus#Structure

Table 1
Virus: Living Thing?

	Feature	Living Organisms	Virus
1.	Homeostasis	Maintain internal body environment	**No.**
2.	Internal structure	Cellular. Made up of building blocks	**No**
3	Reproduce	Reproduce independently. “	**No.**.
4	Metabolise	Process nutrients and generate own energy.	**No.**
5.	Grow	Grow and age.	**No.** Virus replicate fully formed
6	Respond to stimuli	Respond to stimuli	**Yes**. Able to detect and infect host cells. Counter defences, change location.
7.	Adaptation (Mutation)	Adaptation is a process that takes place over time.	**Yes.** Can mutate (in fact rapidly against anti-viral drugs, and switch replication methods.
8.	Senescence (gradual deterioration of l biological functions.).	is when a living organism **ceases** performing biological functions.	**No.** **Does not die.** Can be destroyed .

Viruses are not classified as living things by the International Committee on Taxonomy of Viruses (ICTV). In fact, viruses are not even considered "micro-organisms" because they are not "free-living", i.e., they cannot reproduce and carry on metabolic processes without a host cell. Sometimes, editorial license permitting, they are grouped with the others and referred to as "microbes".

Being non-living, viruses are neither prokaryotic (like bacteria) nor eukaryotic (like everybody else.) That also means that they are neither aerobic (need oxygen) nor anaerobic (not need oxygen).

Origin of Virus

Viruses have been around a long time. The increasing belief, indeed new evidence, is that they co-existed with the first life forms, which were the micro-organisms, around 3.7 billion years ago, and of which bacteria are today the most abundant kingdom extant.

One thought stream is that viruses may have been the earliest or early levels of "self-assembly" of living things on the main line of evolution, but went up a cul-de-sac. They may even have been non-oblate (independent) and non-parasitic[8]. But it is not known how much they have modified since nor what route or routes they took from their ancestral forms to today. Even their phylogenetic (family tree) relationships with the other micro-organisms including bacteria have yet to be established. Today, they are oblate noncellular biological non-living things.

Some people view them as an intermediate or "failed" stage in the development of the living cell. Like the *neutrino*, they might be classed as the "waste material" of evolution, the bits that did not make it..

---

[8] Not often described as such, but they are parasites of a kind

Whatever it is, they have since established their own core identity and mode of survival, and have found a place in the scheme of things. They have been taking over and inhabiting living cells since the beginning.

Historical Record

No study of viruses is meaningful without a glimpse into our past experience with them. Mankind has had a long history of epidemics and. pandemics. In the pre-scientific ages, they were ascribed to various causes from supernatural curses to swamp miasma.

In recent times we have been able to identify them as caused by viruses (and their brethren the bacteria). Wiki has compiled a comprehensive list[9]. It seems they have a malthusian role. The breakdown of the 19 worst pandemics, with a million or more deaths, is as follows

[9] See https://en.wikipedia.org/wiki/List_of_epidemics

Table 2
Worst Pandemics in History

	Event	**No**	**Dates**	**Area**	**Cause**
1	Black Death Bubonic Plague II	75-200m	1346-54	Eur, Asia. N Africa	bacterium (Yersinia pestis)
2	Spanish flu	17-100m	1918-20	WW	virus (HINI)
3	Justinian Bubonic Plague I	15-100m	541-49	Byzantine Empire	Bacterium (Yersinia pestis)
4.	HIV/Aids	35m*	1981-	WW	Virus (HIV)
5	Yunan Bubonic Plague III	25m	1885-1960	China India	Bacterium, etc
6	Cocolitizti I	5-15 m	1545-48	Mexico	Virus (Smallpox)
7	Antonine Plague	5-10m	165-80	Roman Empire	Virus (Smallpox)
8	Mexico epidemic	5-10m	1519-20	Mexico	Virus (Smallpox
9	COVID-19	2.9m*	2019-	WW	Virus (SARS-COVID2)
10	Russian epidemic	2-3m	1918-22	Russia	Bacterium tx louse (Typhus)
11	Asian (Guizhou) Flu	1-4m	1957-58	WW	Virus (H2N2)
12	Hong Kong flu	1-4m	1968-9	WW	Virus (H3N2)
13	Cocolitzti II	2-2.5m	1576-8-	Mexico	Bacterium (Salmonella)?
14	Japanese	2m	735-37	Japan	Virus (Smallpox)
15	Persian Plague	2m	1772-73	Persia	Bacterium (Yersinia pestis)

16	Naples Plague IIb	1.25m	1656-68	Italy	Bacterium (Yersinia pestis)
17	Indian Cholera Epidemic III	1m	1846-60	WW	Bacterium (Vibrio cholorae)
18	Italian Plague IIa	1m	1629-31	Italy	Bacterium (Yersinia pestis)
19	Asian Flu pandemic I	1m	1889-90	WW	Virus (H#N8)? Coronavirus OC43?

If not for these devastations, the world population would be a lot larger. The pandemics seem to be associated with the growth , contact and conflict of empires and civilisations, times of heavy population concentrations and movements and the breakdown of hygiene.

Of the 19 pandemics, eight were caused by bacteria - five by a single family line. The remaining 12 were caused by viruses, in fact by only four families Actually, we know very few viruses. And our historical information is incomplete. The cut off also excludes many of lesser but still calamitous effect.

A quick count of the more reliable Wiki data of the epidemics since 1960 gives us 97 events in all. Those with infections of 1,000 or more numbered 27. Of the latter, 21 were viral and six bacteria (mainly cholera).

The decrease in bacterial epidemics has been significant. This has been so particularly with bubonic plague and cholera, through improved public health and sanitation, vaccines and anti-biotics. As for viruses, WHO in 1980 declared that smallpox had been eradicated. Otherwise the battle is very much on. The 27 include the superstars HIV, Ebola, Zika, Influenza, HINIs, SARS-Covidi and Dengue.

Discovery

It is astonishing that, while viruses are eons old, and we have been experiencing their devastation for ages, man had not the slightest knowledge of their existence until 1898.

In that year, Martinus Beijerinck, repeated a 1876 experiment by Adolf Mayer to filter a solution-extract of a tobacco plant infected with “"mosaic disease" ("mozaïkziekte"). through a newly invented ceramic filter. The filtrate remained infectious. He was convinced that the solution contained a new form of infectious agent. He named it “virus”. He thought it was fluid.

By the early 20th century many viruses, as well as the bacteriophage, had been discovered and studied. Viruses were demonstrated to be particles rather than a fluid by Wendell Meredith Stanley. In 1926, Thomas Rivers first defined viruses as “obligate parasites”. And the invention of the electron-microscope in 1931 allowed their complex structures to be visualised.

The second half of the 20th century was the golden age of virus discovery and most of the recognised species of animal, plant, and bacterial viruses were discovered during these years. In the 1950s, improvements in virus isolation and detection methods resulted in the discovery of several important human viruses, including the *rhinoviruses* which causes the common cold, and *hepatitis B* in 1963. *Reverse transcriptase*, the key enzyme that retroviruses use to translate their RNA into DNA, was first described in 1970. This was important to the development of anti-viral medicine – a turning-point in the history of viral infections.

In 1983. Luc Montagnier at the Pasteur Institute , France, isolated the retrovirus now called *HIV*. And in 1989, Michael Houghton discovered *hepatitis C.* These discoveries have continued into the 21st century as new viral diseases have emerged, such as the SARS range, including SARS-COVID 2.

The increasing power of electron-microscopes and the modern computer have given us the tools to fight the virus. Cryo-electron microscopy (Cryo-EM), the most recent

advance, can capture structures with atomic-level resolution, and lies behind the success of the Human Genome Project.

We now have the science to tag the virus and learn not only its genetic history but also its habits and preferences within us. With this increasing depth of knowledge, we have developed effective public health and social prevention measures as our first line of defence. We are able strengthen our immune systems with vaccinations and inoculations as our second of defence. And if they get through, we are building an arsenal of anti-viral drugs.

However, it is also emerging that viruses have formidable abilities, particularly scale of operations, rapidity of replication, and flexibility of mutation – not to mention a non-terminal life span. At this point it is not clear that we have as yet got the upper hand of them in the present pandemic.

(Back to TOC)

Virosphere

Viruses float everywhere, in the air and in the water. They are found on every surface, and in the soil. They subsist in the desert and in the thermal vents of the ocean deep. They are carried around by anything moving, from bees to airline passengers – and with some concern (hopefully not) by astronauts. Viruses are transmitted in a sneeze. Their habitat is the biosphere.

Viruses have invaded the total biomass of the earth. They have invaded all the kingdoms of living things, viz animal, plant, fungi, protists and monera (i.e. prokaryotes) They inhabit the ocean and its creatures, the plant world, the animal world, the entire human population, and every space between them. Specifically, they inhabit the cells of all living things.

We might make mention here that viruses also invade bacteria. They are hunted and taken over by viruses to form bacteriophages or bacterial viruses, also known as phages. Phages are to be found everywhere, in plants and animals, and in humans. The sea is saturated with them. Phages are harmless.

By evolution, viruses are specialised vis-a-vis their respective kingdoms of living things. Plant and marine viruses do not infect or take up residence in humans or animals, nor the latter the plant and marine worlds. The same is true (of their nature) but to a lesser degree as between the human and animal worlds. However, there has been a serious breakdown of the animal to human divide.

Within their respective domains , viruses additionally specialise in their choice of hosts, e.g. monkeys verses cows, pigs verses horses, but with less exclusivity.

Finally, within a body, viruses specialise in their choice of cells, e.g. for instance as between the delights of the liver as against the lung. In a normal healthy body, the number of active viral pathogens at any one time could be relatively small.

Unfortunately, the barriers are coming down. Firstly, as the world gets more populated, urbanised and congested, the opportunities expand for viruses to be involuntarily ingested or attached outside their domain. Secondly, the same increase in human population is cutting back the natural habitats of the flora and fauna of the other kingdoms. Thirdly, travel vastly enlarges the opportunities for humans to carry across their own and third-party viruses. Some species are carriers, in that they are asymptomatic or immune but are vectors, such as bats and flying foxes, and even birds. The overall situation is one of a rising viral threat. Any virus that jumps the barrier is usually a pathogen.

When a virus jumps a barrier, the infections can be catastrophic, for the immune systems tend to be caught off-guard. The current Covid-19 pandemic is one example.

Epidemics within the respective kingdoms can also cause severe economic crises. The “mad cow” disease some years back was an example of an infection transferred within the animal kingdom which seriously threatened the human population. There have been umpteen crop disasters.

Viromass

The biomass covers most of the earth. The viromass saturates the biomass, and most of the rest of the earth. They are by far the most plentiful entity on our planet. We humans are literally swimming in viruses.

Counting all viruses, phages included, it was estimated (in 2018) that the total number in our world is 10 nonillion $1x10^{31}$ - “enough to assign one to every star in the universe 100 million times over”[10] . “If all the viruses on earth were laid end to end, they would stretch for 100 million light years.”[11]

There is no meaningful way to divide this number among the human, animal, plant and ocean biomes. Just to savour the reality of things, one millilitre of coastal water taken from the ocean's surface can contain up to 10 million viruses. The number decreases offshore and deeper into the water, and as we reach the open sea, there are likely to be around 100,000 viruses per millilitre at a depth of 4,000 metres. [12]

I have not found any studies that estimate how the rates of growth of viruses impact the above totals, whether on land or sea. I have no sense of how to divide the totals among those

---

10 https://www.nationalgeographic.com/science/article/factors-allow-viruses-infect-humans-coronavirus

11 Carl Zimmer, Planet of Apes.

12 https://en.wikipedia.org/wiki/Marine_viruses

active (pathogenic), those dormant, those latent and those in the air All I can say is that these totals must have grown since they were calculated, even allowing for destruction.

Classification

It is axiomatic that no one can defeated an enemy without knowing him.

In the long-term, a project that cannot be avoided is launching comprehensive studies to log and classify the total viromass population. It is beyond our practical means at present. Therefore, we must prioritise.

Immediately, we must get a clear picture of the active human pathogens. Firstly, we must nail down mankind's greatest viral enemy today - SAR-Covid-2 and the family variants.

Next, we must prioritise those other categories that are pathogenic to us and prey on the economically valuable components of our animal, plant and marine kingdoms.

Thirdly, we need to know the principle non-pathogenic categories that maraud our other living kingdoms, and what they do.

Lastly, we need to understand viruses in their evolutionary, historical, and global entirety.

Even if we can exclude those that die on replication, the gross numbers are incalculable. They will also be largely historical. They mutate rapidly, and most are therefore non-active. At the front end, however, for the same reason, their numbers are growing at past catch-up speeds. That is where the work lies.

The body responsible for identification, classification and tracking of viruses is the International Committee on the Taxonomy of. Viruses. (ICTV), formed in 1966 and re-constituted in 1975.

They have adopted and adapted the Baltimore System of Classification proposed in 1975 as the basis of their classification.

Their classifications covers viruses of all kingdoms, human, animal, plants, etc. Still, the 2020 ICTV viral taxonomy comprised a meagre 4 families,[13] 9 kingdoms, 18 phyla, 36 classes, 56 orders, 271 families, 2,111 genera, and 6,590 species..

The number of viruses classed as **pathogens** was 219 in 2012. Lately it has been revised to 243, of all categories. In both instances, oddly enough, the figures were not by ICTV. We have a long way to go.

(Back to TOC)

The Human Virome

It has been estimated that there are 380 trillion viruses (380 $x10^{12}$) in one human body, 10 time more than the total number of cells, which is about 37.2 trillion (37.2×10^{12})[14] But, of course, our cells are bigger.

It calls for some contemplation how exactly this whole horde of viruses have entered our bodies and where they are located.

Entry

One obvious route is they float in as we breathe. Viruses are also picked up from every surface and most fluids. Humans can become infected by a virus in contaminated food or water.

---

[13] The small number of families means the number known go back to a few common ancestors.

[14] https://www.nationalgeographic.com/science/article/how-many-cells-are-in-your-body

Human to human transfer is the most common route. Normal people living in the same house share up to 25% of their viruses. They enter our orifices, settle on our skin surfaces and invade our wounds. People infect one another most rampantly during an epidemic.

Lastly, the virus population of the human body is increased by direct “extra-cellular” invasion, (followed by) “intra-cellular” replication. These happenings are known as an “ infection”.

Inside

Once inside, viruses travel via our blood stream to their chosen targets or place of abode. They enter the blood directly through capillaries, by replicating in the blood’s protective endothelial cells or through inoculation by a vector bite. Once in the blood, viruses may access almost every tissue in the host. They do the same via the lymphatic system, by replicating in the latter’s protective endothellal cells. One important ability they appear to have is to be able breach the mucous membrane, on which we humans depend to protect our organs and cells.

The new arrivals, including new replicants, will all be immediately hounded by the immune system. It can be assumed that some will become pathogenic [15] and go into *lyctic* mode[i]. The others will dodge the defences, and go *lysogenic*, namely latent and become resident. The safest place is in a cell, for once they get within the walls of a cell, they are snugly protected from antibodies of the immune system which cannot penetrate the membrane of the cell. Some viruses travel within the nervous system and through neural synaptic transmission.

[15] I use “pathogenic” to mean a virus in “active” infecting mode and includes a replicant which decides or proceeds to infect the next cell.;the others would be technically “latent”, however brief.

In fact viruses have some 200 different types of human cells to choose from. No doubt over the eons (and perhaps based on exposure in different kingdoms) they would have fine-tuned their preferences, recognition skills and knowledge of human anatomy.

Viruses are therefore found everywhere in the human body. They are found in the respiratory, digestive, alimentary and reproductive systems, the liver, in the brain, on the skin, in the cerebrospinal fluid, in the central nervous system - and in the embryo. Needless to say they form much of the traffic in the blood stream[16] and the lymph.

During an infection, a person's virus-count will soar astronomically, with rampant replications. When the infection is overcome, the virus population should revert to "healthy normal". The collection of all viruses in the human body at any one time which do not cause disease is referred to as the "healthy human virome". It consists of three distinct components: (i) viruses that systematically enter primarily with food but do not replicate in humans; (ii) viruses infecting prokaryotes and unicellular eukaryotes (e.g. bacteria) that comprise the healthy human microbiome; and (iii) viruses that actually replicate and persist in human cells.

Pathogens

It is the number of pathogens in our catalogues, not the number of viruses, that matter.

The number of identified human viral pathogens is surprisingly small, for the fiendish damage they do. The following quote from a 2005 study gives a broad picture:

---

16 Whole-genome sequencing data of blood from 8,240 individuals without any clear infectious disease revealed 94 different viruses in 42% of the study participants. https://en.wikipedia.org/wiki/Human_virome

> "There are 219[17] virus species that are known to be able to infect humans. The first of these to be discovered was yellow fever virus in 1901, and three to four new species are still being found every year. Extrapolation of the discovery curve suggests that there is still a substantial pool of undiscovered human virus species, although an apparent slow-down in the rate of discovery of species from different families may indicate bounds to the potential range of diversity."
> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3427559/

The emergence of human pathogens has remained at this relatively sedate order. The database for Mar 2021 of the (US) National Center for Biotechnology Information (NCBI)[18] gives the total figure of viruses docketed as 10, 609, and human viruses as 497 families (of which 243 are co-hosted by other vertebrates, invertebrates and protozoa). The general view is that about 1% of microorganisms[19] are pathogenic.

Our recent experiences reveal that pathogens attack in floods and by more than one species at a time, in fact invariably by related or mixed species, with fast multiplications and mutations. Plurality of participating viruses and mutations promotes net success. SARS-Covid-2 has already produced eight variants in 18 months, and we are still counting

Infection modes

Pathogens employ the following two modes in infection:

. (a**) Lytic** mode. In this, the virus replicates copies in the host continuously, until it "bursts" the cell by *lysis.* killing the host and expelling the replicants,

---

[17] The baseline for this study was 2005. The 219 species, from a list provided by the ICTV, came from 23 virus families. The. highest is the *Bunyaviridae* family with 40

[18] Comprehensively, the lead information aggregator of virus data. https://www.ncbi.nlm.nih.gov/guide/taxonomy/

[19] Viriuses and bacteria would form the vast majority of these.

.(b) **Lysogenic** mode. A virus, after replication, remains dormant (short term) or latent (long term) in the host cell or after transfer in another cell. A virus or replicate in this mode may be triggered off and become active and lytic at a future date.

Even where the primary mode is lytic, it may become lysogenic due to immune interference, medication, even a marginal choice of host cell, and finally incomplete mutation responses to these.

(Back to TOC)

Types of Virus

One cannot grasp the extraordinary (microscopic) creature that is the virus without taking a step further and looking at the specific ways they invade their host.

The virus pathogens that we know of (so far) belong to two broad groups:

(a) the “non-enveloped” or classic virus, and
. (b) the .”enveloped” virus (including the retrovirus).

The first category of virus comprises simply a packet of nucleic acid enclosed in a protein membrane. The second additionally has an external envelop enclosing the whole – as well as other internal, constitutional and behavioural differences.

The best known of the latter is the retrovirus, which has caused the worst recent pandemics. The classic virus is possibly the more numerous. These groupings apply in all the kingdoms of living things, but here we focus on them in their human *alter ego*.

At this stage, it is convenient to clarify our terminology. A "virion" is a single virus, usually in the context of an infection.. The term "virus" refers to them generically, in their collective persona as an agent of infection.

The Non-Enveloped (or Classic) Virus

Description

The non-enveloped or classic virion comprises two components: (a) a parcel of nucleic acids[20], and (b) a protein coat, the capsid. The first contains its DNA, encoded with its genome as carried in its chromosomes and genes. The second functions as a shell to protect this genome and as well as provide contact points to attach the virion to receptors on the surface of the host cell. The virion also possesses the capability to dock with and inject its genetic material into its target cell[21]. The classic virion does not have an exterior envelop.

A virion is very small indeed. It ranges from a minimum of about 0.02 -0.05 μm , as against bacteria, typically a minimum of 0.5 μm and the human body cell (red blood cell) at 7.5 μm). To see a virus, it is necessary to use a scanning electron microscope.

[20] Nucleic acids are the molecules that contain and help express a cell's genetic code

[21] Viruses lack the following features to make up a complete living cell: *ribosomes* to translate mRNA codes and build proteins (eventually the replicates), the *mitochondrion* to manufacture ATP (energy), and the suite of enzymes and processes that produce the building blocks.

Mode of Replication

When a virion finds a congenial target, it attacks. We look here at the extra-cellular or external case.[22]. A replicate basically does the same thing.

(a) Entry

Host cells sport a variety of "receptors' on their surface for various purposes. On making contact with a host cell, the virion locks on and joins itself to a receptor on the cell surface, seeking attachment.

Attachment involves two kinds of host proteins on its surface: (1) attachment factors and (2) viral receptors. The attachment factor recruits and hold the viral particle, facilitating entry. On the other hand, the receptors, upon binding to the virion, promote the penetration of viral particles into the cell. It is astonishing that the receptors are virus-specific. Putting it another way, the virion must find a suitable receptor, or it is a no-go.

The classic virion next seeks *penetration*. In penetration the aim is to reach the cytoplasm. In a process called *receptor-mediated endocytosis*, the viral particle-receptor complex forms a coated pit on the plasma membrane of the cell's surface As a result, the particle becomes located inside, in an *endosome* (vesicle). The virion finally ruptures (lysis) this to get in. The classic virus replicates in the cytoplasm.

The last step is uncoating the capsid. Before that, in a processes called *intracellular trafficking*, the virion navigates its way to its objectives which are the *ribosomes* in the cytoplasm. At that point it uncoats.

---

[22] The two major references for this section are:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7158286/
https://bscb.org/learning-resources/softcell-e-learning/ribosome/

.(b) Gene Expression and Replication

After uncoating its capsid, the virion proceeds to inject its genetic material into the host. To effect this, the it makes or "transcribes" a messenger copy (mRNA) of its genome, i.e. its DNA[23], suitably prepared for execution. It then shoots this mRNA into the cytoplasm, targeted for a *ribosome*.

Ribosomes are macro-molecular machines found in large numbers[24] in all living cells. Their function is to perform protein synthesis. On a normal day, ribosomes execute works orders sent by their own host DNA via their own mRNA. The classical virion in effect by-passes the host nucleus and DNA to give the ribosomes an additional[25] "job" direct. It is essentially a takeover.

Two [26]ribosomes sub-units team up on a job, in a complex routine of which we shall say no more, except that the smaller one carefully checks back with the virion's mRNA for accuracy. Their main working tool is the cell's" translator" tRNA strand, of which there are also many free-floating in the cytoplasm. The latter performs two functions; (i) first, it decodes the mRNA for the viral's specifications, a process known as "gene expression" and passes the same on to the smaller ribosome for implementation, and (ii) second it gathers the necessary raw materials, namely amino acids and proteins, available in the cytoplasm. Where a host does

---

[23] DNA and RNA come in a mix of double and single strands and polarity (ds, ss, etc. 0 I have ignored involving these for simplicity.

[24] There could be up to 10 million ribosomes in a human cell at any one time. Their existence is temporary. They combine to do a job and then disengage, and re-combine for another job, or not.

[25] There are about 10 billion protein molecules in a mammalian cell and ribosomes produce most of them.

[26] Production begins at a small ribosome "ranslation sub-unit when the mRNA strand enters through one selective cleft, and a strand of initiator (@ "translator") tRNA through another. This action triggers the small sub-unit to lock-on to a large production sub-unit to form a complete and active ribosome-combo or team.

not have a particular (say) enzyme, the mRNA will direct the ribosomes to synthesise it.

The ribosomes depend on the host metabolic system. Metabolism includes all chemical reactions involved in maintaining the living state of the cells. Metabolic activity can be *catabolic* – the breaking down of compounds, foods, etc or *anabolic* – the building up (synthesis) of compounds such as proteins, carbohydrates, and nucleic acids. Much of this is done by enzymes, some belonging to the virion and some to the host.

All of the preceding requires energy. The host's principal supply comes from its organelles, the *mitochondria*[27], known as its "energy factory". These daddies perform cellular respiration, oxidise food and form *adenosine triphosphate* (ATP), the universal form of energy used by living things.

The ribosomes will manufacture the viral's genome first to specifications, followed by the capsid. These are moved into the cytoplasm. Their assembly can be divided into two processes: capsid assembly and genome packaging. Depending on the virus, these two processes can occur sequentially or simultaneously in a coupled manner. Eventually, the ribosomes complete replication. Voila! a *progeny* virus or replicate.

In a standard situation, the virus DNA codes will require the host to replicate as many and as fast as possible. Therefore, my understanding is that the ribosome-combo then goes on to repeat replicating copies in a continuous run, until space and resources are exhausted and the cell bursts.

I could not confirm whether several combos can be put into production simultaneously by a single virion, and how. More

---

[27] In humans, the mature egg cell, or oocyte, contains the highest number of mitochondria, ranging from 100,000 600,000 mitochondria per cell,

likely, a swarm or "cloud" of identical virions might attack a host simultaneously, and commandeer a whole industrial estate of ribosomes into production.

(c) Exit.

In the classic case, the progeny virions are expelled or released when the host cell dies or bursts (lyse). And the replicates, fully formed, will be expelled into the surrounding cells to do the same.

In a research exercise[28] conducted with the *simian immunodeficiency virus* (SIV) - on a simian cell, what else! - , the "burst size" ranged from 40,000 to 50,000 replicants. In another research paper[29], it was shown in that case that the "cell expansion" before cell burst ranged between 2-5% of its volume.

(Back to TOC)

The Enveloped Virus (including Retrovirus)

Enveloped viruses are conveniently divided into non-retroviruses and retroviruses. The Coronavirus is an example of the first, and Human Immunodeficiency Virus (HIV) the second. Both share the same features described here, except that the **retrovirus** has a significant variation in its genomic equipage and its replication strategy. We shall point out the variations where they occur. Otherwise the descriptions and explanations in this section apply in common to all enveloped viruses.

---

[28] https://bionumbers.hms.harvard.edu/bionumber.aspx?&id=102377 https://pubmed.ncbi.nlm.nih.gov/18025463/

[29] http://book.bionumbers.org/how-many-virions-result-from-a-single-viral-infection/

Description

Like the classic virion, the enveloped virion has a nucleic acid core encoded with its genome, enclosed in a capsid. In addition, the whole is wrapped around by an outer lipid bilayer known as a viral *envelop.* The latter is. In fact a portion of cell membrane taken from its (former[30]) host. (see also below under Exit)

This membrane is studded with proteins coded by both its own genome and the (former) host genome. What we have here is the ripping-off of the enemy's cloak and using it for cover to gain the next entry, a subtlety beyond words! As a result, the virion enjoys better protection from the (next) host immune system, enzymes and certain chemicals. The proteins in the envelop can include *glycoproteins*, which act as receptor molecules, which allow host cells to "recognize" and bind the virions. Most enveloped virions depend on their envelops to infect cells[31].

Enveloped virions can have DNA or RNA as their genetic material. **Retroviruses** have RNA as their genetic material, and in addition the enzyme *reverse transcriptase.*

The genome of an enveloped virus may be encoded in "positive-sense" or "negative sense". Positive-stranded RNA viruses have genetic material that can function both as genome and as messenger; it can be directly translated into protein by the host ribosomes.

---

[30] It never struck me until now that all existing viruses are replicates!

[31] **Gag i**s a polyprotein and is an acronym for Group Antigens (ag). **Pol** is the reverse transcriptase. **Env** in the envelope protein. The group antigens form the viral core structure, RNA genome binding proteins, and are the major proteins comprising the nucleoprotein core particle.

Mode of Replication

.(a) Entry

Like the classic virion, on making contact with a host cell, the enveloped virion locks on and joins itself to a receptor on the cell surface

The enveloped virion must attach to a specific receptor, governed by the attachment proteins in the capsid or the glycoproteins embedded in the viral envelop. This specificity determines the target host (and the cells within the host) - similar to one key fitting only a specific lock to enter. In the case of HIV, the receptor is found on the surface of immune cells and is called CD4.

The next step is penetration. For enveloped virions, one of two mechanisms is used for penetration: direct fusion or receptor-mediated endocytosis.

In direct fusion, the two membranes (ie, the viral envelop and cell membrane) fuse. In this case, the viral capsid in toto is directly delivered to the cytoplasm, leaving the viral envelop behind on the plasma membrane. The **retrovirus**es penetrate by direct fusion.

Receptor-mediated endocytosis is similar to that used by the classic virion.

The intracellar tracking of enveloped virions to their destinations is again similar to that of the classic virion. While the others replicate in the cytoplasm, the **retrovirus** replicates its genome in the nucleus of the host.

For virions that replicate in the nucleus multiple strategies are utilized to enter the nucleus. For those with a smaller genome, the viral capsid itself enters the nucleus. For those with a larger genome, the docking causes a partial disruption of the

capsid or changes the shape of the capsid to allow the transit of the genetic material into the nucleus.

.(b) Gene Expression and Replication

For non-retroviruses, the processes of gene expression and replication are substantially the same as for the classic virus.

With **retroviruses**, however, after entering the host's cell, the virion's RNA genome is reverse transcribed into double-stranded DNA by the enzyme *reverse transcriptase* (RT) present in the virion. Another viral enzyme *Integrase* then searches the host DNA for an appropriate "home", whereupon the integrase clips the host DNA and sews the double-stranded DNA into the host DNA as the *provirus*. Finally, new viral mRNAs are transcribed from the proviral DNA by the host cell's enzymes. These latter may "spliced" to incorporate special exit requirements of the retrovirus.

In the next stage, both the original (full-length) mRNA and the spliced second mRNA made by the host are transported into the cytoplasm. There they are read by the tRNAs and executed by the ribosomes to manufacture the components of the virion replicate, namely the new viral genome and the capsid. The capsid proteins, (Gag, and RT) are translated from the original mRNA. The other components, including the glycoproteins, are translated from the spliced mRNA.

Finally, the new retroviral proteins are transported to a selected spot at the cell plasma membrane, and a new full-length genomic mRNA is incorporated into a budding particle. The nascent or progeny retrovirus-to-be assembles there.

As for the non-retrovirus, the new viral materials are also transported to a preselected spot on the membrane of the cell surface, for assembly.

.(c) Exit

Most enveloped virions are typically released from the host cell by **budding**. Budding enables the viruses to exit the host cell and is mostly used by enveloped viruses which must acquire a host-derived membrane enriched in viral proteins to form their external envelop. It is this process that results in the acquisition of the viral envelop.

E*nvelopment* is a process in which the capsid becomes surrounded by a lipid bilayer derived from the cell membrane, prior to the release. Two mechanisms exist. First, the envelopment can proceed after the completion of capsid assembly In this sequential mechanism, the fully assembled capsids are recruited to the membrane by interaction of the viral capsids with viral envelop glycoprotein. Alternatively, the envelopment can occur simultaneously with the capsid assembly. The **retrovirus** adopts the coupled mechanism.

Zoonotic Cross-overs

Zoonotic refers to an infection or disease transmitted between species, usually by a pathogen[32] that has jumped or crossed over to a human from an animal (usually a vertebrate) – or vice versa.

There is increasing awareness that animal and avian (and perhaps other) viruses make the transition into man over a wide front, with or without the help of a vector. More significantly, when they catch our immunity systems off-guard, they create pandemonium.

The following quotation reflects the growing perception a decade ago:

[32] The term would apply where this was a virus, bacterium or parasite.

> "More than two-thirds of human viruses can also infect non-human hosts, mainly mammals, and sometimes birds. Many specialist human viruses also have mammalian or avian origins. Indeed, a substantial proportion of mammalian viruses may be capable of crossing the species barrier into humans, although only around half of these are capable of being transmitted by humans and around half again of transmitting well enough to cause major outbreaks. A few possible predictors of species jumps can be identified, including the use of phylogenetically conserved cell receptors. It seems almost inevitable that new human viruses will continue to emerge, mainly from other mammals and birds, for the foreseeable future. For this reason, an effective global surveillance system for novel viruses is needed."
> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3427559/

My review of epidemics and pandemics in the last century suggest that the viruses that caused them have been zoonotic. In fact in two out of the three cases, the investigative work has moved into the animal domain. In future, our battle-front surveillance must include animal territory.

(Back to TOC)

Major Viral Pathogens

There have been three major[33] pandemic within a century, caused **by a different virus each time**.

.- 1. The first was the **Influenza A virus,** which caused the Spanish flu major pandemic in 1918-20, killing an estimated 18 to 100 million people world-wide. A string of sub-types have caused three other pandemics and three epidemics in the last 60 years, and is endemic seasonally in the northern and the southern hemispheres.

.- 2.The second one was the **Human Immunodeficiency (HIV),** which pandemic which started in 1981 and is still on-

[33] I use "major" to mean over 1 million deaths.

going, with 76 millions infected and the death-toll 37.4 millions so far. And,

.- 3. The third is the **Coronavirus SARS-Covid-19** pandemic, which started in 2019, is still ravaging the world, and has already been responsible for 3,398,302 deaths and 163,869,893 people infected world-wide, as at 19 May 2021. SARS-variants have been responsible for four other epidemics in the last 60 years.

In Part 2, I review the pandemics in some detail. Here I provide a profile of the viruses responsible for the above pandemics.

Influenza

The Influenza virus is a major daddy of a pathogen. It ranks as a top endemic public health concern and constant potential pandemic threat.

Taxonomy

The Influenza viruses belong to the viral realm: *Riboviria*[34] Below that we find subdivisions into kingdom, phylum, class and order, and finally below that the family: *Orthomyoxviridae*, with seven genera, four of which are hosted by humans (*h*Ifluenza A)

The genera *Alphainfluenza* has only one species, *h*Influenza A, which is responsible for all our pandemics and epidemics of this name.

---

[34] Riboviria includes all viruses that use a homologous RNA-dependent polymerase for replication. It includes RNA viruses that encode an RNA-dependent RNA polymerase; and, it includes reverse-transcribing viruses (with either RNA or DNA genomes) that encode an RNA-dependent DNA polymerase.

*h*Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus*: hemagglutinin* (H) and *neuraminidase* (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes (H1 through H18 and N1 through N11, respectively). While there are potentially 198 different Influenza A subtype combinations, only 131 subtypes have been detected in nature.

Current subtypes of *h*Influenza A viruses that routinely circulate in people include: A(H1N1) and A(H3N2).

Influenza Invasions

Over the last century of years, the *h*Influenza A viruses have launched seven major and minor outbreaks, in addition to their seasonal visits, see Table 3

Table 3
***h*Influenza A Pandemics and Epidemics**

No	Epidemic/Pandemic	Year(s)	Deaths	Region
1	Spanish Flu Influenza A H1N1	1918-20	18 million	WW
2	Asian Flu Influenza A, H2N2	1957-58	1 -4 million	WW*
3	Hong Kong Flu Influenza A H3N2	1968-68	1-4 million	WW
4	London Flu Influenza A, H3 N2	1972-73	1,027	US
5	Russian Flu Influenza A, H1N1	1977-79	700,000	WW
6	Swine Flu Influenza A, H1N1	2009	284,000	WW
7	Indian Epidemic Influenza A, H1N1	2015	2,035	India
8	Seasonal Flu Influenza A and B	2017	60,000	USA

* = world-wide **= Not in Wiki list, added separately

These have been contained, even the annual flu season (in which Influenza B participates) to an extent. Many variants of the Influenza are zoonotic. The H5N1, one of a number of viruses of avian pedigree, is threatening to bring on the next pandemic.

Constituent Design

The **Human Influenza A** (*h*Influenza) viruses are enveloped viruses, the characteristics of which genre are described in a relevant section preceding this.

*h*Influenza A viruses are encoded in negative-sense single strand RNA, and have the features and extra tools that go with it.

It is, like the Coronavirus, armed with spikes on the outside, but different. The first set comprises *hemagglutinin (H)* that mediate the binding of the virus to target cells and entry of the viral genome. The second set comprises *neuraminidase (N)*, an enzyme involved in the release of the progeny or the replicated virus by cleaving the sugars that bind the young viral particles at their points of emergence.

The hemagglutinin (H) and neuraminidase (N) are key targets for antibodies and antiviral drugs, and they are used to classify the different *h*Influenza A viruses. It is now believed that the Spanish Flu was caused by the *h*Influenza A variant (H1N1).

The nucleocapsids of negative-strand viruses contain minor proteins that possess enzymic activity. These nucleocapsids remain intact within the host cell during the entire infection cycle and serve as machines that make viral RNA.

Following replication of the new viral component proteins and sub-genomic RNA synthesis, the new viral structural proteins encapsulate the total new virion, via budding.

The exit procedures follow those of the enveloped virus.

Transmission

Human to human transfer is the most common route. *h*Influenza A viruses most commonly transmit by coughing and sneezing. Viruses are also picked up from every surface and most fluids.

Normal people living in the same house share up to 25% of their viruses. People infect one another most rampantly during an epidemic.

Influenza flourishes in temperate conditions. It has now become endemic in the northern and southern hemispheres in winter.

Pathogeny

Influenza and the common cold[35] share many symptoms, often indistinguishable: fever, cough, headache, muscle and joint pain, sore throat and a runny nose. It is as contagious as the common cold. Most people recover within a week without requiring medical attention. But influenza can cause severe illness or death especially in people at high risk.

Zoonotic Relationship

The virus co-inhabits independently in the human, animal and avian domains, It seems conclusive that the Spanish flu was triggered by the zoonotic avian flu (H1N1).

Influenza A viruses are thought to possess zoonotic potential as they are able to infect different avian and mammalian animal hosts, from which they can be transmitted to humans. People can be infected without an outbreak by viruses circulating in animals, such as the avian influenza virus subtypes A(H5N1)[36] and A(H7N9), and swine influenza virus subtypes A(H1N1) and (H3N2). Other species including horses and dogs also have their own varieties of influenza viruses.

Even though these viruses may be named as the same subtype as viruses found in humans, all of these animal viruses are distinct from human influenza viruses, and do not easily transmit between humans.

In Part 2, we review our successes and our failures against the actual pandemics.
(Back to TOC)

[35] The common cold is usually caused by the rhinovirus, a milder non-enveloped single strand positive sense RNA virus.
[36] Currently a major threat.

(b) Human Immunodeficiency Virus (HIV)

The **Human Immunodeficiency Virus (HIV**) ranks as the deadliest virus we humans have ever and hope never to experience again.

Taxonomy

This virus also belongs to the viral realm: *Riboviria*. But, further below, we find different subdivisions into kingdom, phylum, class and order, family and finally the sub-family *Orthoretrovirinae,* with seven genera.

The genera fall into three basic groups: the *oncoretroviruses* (oncogenic retroviruses), the l*entiviruses* (slow retroviruses) and the *spumaviruses* (foamy viruses). The first group are able to cause cancer in some species, the lentiviruses are able to cause severe immunodeficiency and death in humans and other animals, and the last are benign and not linked to any disease in humans or animals.

The Lentivirus is a subgenus has 10 species, Of these eight are hosted by animals and two humans. The best known is the **Human Immunity Deficiency Virus (HIV**) There are two species: HIV-1 and HIV-2. The first is the cause of the world-wide pandemic disease **Acquired Human Immunodeficiency Syndrome (AIDS),** and is the one we refer to herein as HIV. The second species is of lower infectivity, and is largely confined to West Africa.

HIV Invasion

There has been only one HIV pandemic, and it is has been the most colossal one humans have experienced, Covid-19 not excepted.. The outbreak started in 1981 and the pandemic is still on-going., see Table 4 below:

Table 4
HIV Pandemic

Epidemic/ Pandemic	**Year(s)**	**a. Infections b. Deaths c. Still living infected**	**Original Region**
HIV pandemic (180 countries) Virus: HIV	2081 – On-going	a.76.5 millions b.37.6 millions c.37.4 millions	Africa US (WW)

It is a straight infection, with no intermediaries.

Constituent Design

HIV is an enveloped virus, the characteristics of which are described in a relevant section preceding this.

The HIV is a **retrovirus**. It is composed of two copies of positive-sense single-stranded RNA that encode the virus's genes, which is enclosed by a conical cover composed of 2,000 copies of the viral protein (p24).

The nucleocapsid houses and tightly binds the single-stranded RNA proteins and the enzymes needed for the development of the virion, such as reverse transcriptase, protease, ribonuclease, and integrase. A matrix composed of the viral protein (p17) surrounds the capsid ensuring the integrity of the virion particle.

Entry is as per normal for enveloped viruses, except that the HIV targets the host's cell receptor CD4. On entry, being a retrovirus, the HIV nucleocapsid heads for and unpacks in the host cell's nucleus and creates a "provirus". Next it substitutes the latter in place of the host's DNA, makes the

necessary mRNA of itself, takes over the host's operating systems and commands the host to replicate itself.

HIV has very high genetic variability. This diversity is a result of its fast replication cycle, with the generation of about 10^{10} virions every day, coupled with a high mutation rate of approximately 3×10^{-5} per nucleotide base per cycle, and due to the recombinogenic properties of reverse transcriptase.

This leads to the generation of many variants of HIV in a single infected patient in the course of one day. This variability is compounded when a single cell is simultaneously infected by two or more different strains of HIV.

When simultaneous infection occurs, the genome of the progeny virions may be composed of RNA strands from two different strains. This hybrid virion then infects a new cell where it undergoes replication.

Upon replication, the HIV virus follows the exit strategy typical of the enveloped virus

Lentiviruses[37] can also become endogenous (ERV), integrating their genome into the host's germ-line genome, so that the virus is henceforth inherited by the host's descendants.

Pathology

Once the HIV virus enters a person's body, it attacks the **immune system**. HIV targets the white blood cells called the **CD4** cells. It enters the CD4 cells, and makes copies of itself. Then, it kills the cell, and the new HIV replicates move on to find other CD4 cells to do the same.

[37] Lentivirus is use synonymously with HIV, The former genus has only one species, the latter.

The immune system tries to control the HIV by making more CD4 cells, but is usually not fast enough. When the viral load reaches a certain point, and the immune system weakens, the person can no longer combat opportunistic infections. The person progressively acquires the AIDS syndrome. Th unique feature of HIV virus is that the incubation period could be long.

There are four stages of HIV -

Stage 1: Infection
HIV quickly replicates after infection. Some people develop short lived flu-like symptoms, for example, headaches, fever, sore throat and a rash within days to weeks after infection. During this time the immune system reacts to the virus by developing antibodies – this is referred to as 'sero-conversion'.

Stage 2: Asymptomatic
This stage of HIV infection does not cause outward signs or symptoms. A person may look and feel well but HIV is continuing to weaken their immune system. This stage may last several years (an average of 8 to 10 years.)

Stage 3: Symptomatic
As the immune system becomes damaged and weakened, symptoms develop. Initially they can be mild but they do worsen. Symptoms include fatigue, weight loss, mouth ulcers, thrush and severe diarrhoea. The symptoms are caused by the emergence of opportunistic infections. Some examples of opportunistic infections are PCP, toxoplasmosis, TB and kaposi sarcoma.

Stage 4: AIDS/Progression of HIV to AIDS
There is no single test for AIDS.

Transmission

HIV is transmitted by exchange of bodily fluids and this tends to be mainly sexual. It is also transmitted by blood, often by sharing of medical instruments not properly sanitised, one example being injection needles among drug addicts. It is also transmissible by an infected mother to child.

Fortunately one cannot catch it through a sneeze by an infected person.

Treatment

Today, there is a range of medications to keep the viral balance and the onset of AIDS in check. No cure

Zoonotic Relationship

Detailed research has now confirmed that the human HIV virus originated from the Simian Immunodeficiency Virus (SIV), in non-human primates in Central and West Africa. The current pandemic had its origins in the emergence of one specific strain – HIV-1 subgroup M – in the Congo in the 1920s.. The line of cross transmission was humans eating the meat of wild chimpanzees, who themselves fed on two other smaller species of monkeys. These were found to host the mutated virus *SIVcpz*, which was almost identical to HIV 1 and could be passed on to humans, . HIV is therefore zoonotic. There were sporadic reports of infections from the 1950s onwards in Central and West Africa. The epidemic broke in US from 1981.

From recent research, Lentiviruses are found in apes, cows, goats, horses, cats, and sheep. Recently, lentiviruses have been found in lemurs, rabbits and ferret, as well. Lentiviruses and their hosts have worldwide distribution.

I found no information whether HIV viruses are hosted by bats.

(Back to TOC)

Coronavirus

Coronaviruses are a large group of related viruses. We focus here on the human coronaviruses.

Taxonomy

The **Coronavirus** also belongs to the viral realm: *Riboviria*. But, further below, we find different subdivisions into kingdom, phylum, class and order, family, the sub-family and finally the genus *Betacoronavirus.*

The genus Betacoravirus includes the five following subgenera:
.1 *Embecovirus* (e.g. HCoV-OC43, HCoV-HKU1),
.2 *Hibecovirus* (e.g. Bat Hp-betacoronavirus Zhejiang2013),
.3 *Merbecovirus* (e.g. **MERS-Covid**, Pipistrellus bat coronavirus HKU5, and Tylonycteris bat coronavirus HKU4),
.4 *Nobecovirus* (e.g. Rousettus bat coronavirus HKU9), and
.5. *Sarbecovirus* (e.g. **SARS-Covid-1, SARS-Covid-2** and bat SARS-batCovid, HKU3).

There are seven human Coronaviruses identified in the Lentivirus taxonomy. The seven include HCov-229E, HCov-NL63, CCov-OC43 and HCov-HKU-1; the others being SARS-Covid, MERS-Covid-1 and SARS-Covid-2. The last two caused acutely infectious pandemics earlier, while the third became the cause of our the present pandemic.

The taxonomy[38] also shows that there were another 15 animal virus species, eight bat viruses and seven avian viruses, all within the same coronavirus sub-family.

Using molecular clock analysis, investigators estimate that the most common ancestor (MRCA) of all Coronaviruses appeared in about 8100 BC, and the genera appeared in approximately 2400 BC, 3300 BC, 2800 BC, and 3000 BC, respectively. They were therefore around from at least the time of early civilised man and in animals before that.

The earliest reports of a Coronavirus infection in animals occurred in the late 1920s, and an animal virus was fully cultivated for the first time in 1937.

The first human coronaviruses were discovered in 1961. In 1965, the virus was successfully cultivated using a then new technique of organ culture in the human embryonic trachea.

Coronavirus Invasions

As far as can be made out, the Coronavirus first invaded the domain of humans in this 21st century, and have done so three times in succession, see Table 5

38 https://www.avma.org/sites/default/files/2020-02/AVMA-Detailed-Coronoavirus-Taxonomy-2020-02-03.pdf

Table 5
Coronavirus Epidemics/Pandemic

	Epidemic/Pandemic	Year(s)	Infections Deaths	Original Region
1	**SARS-Covid epidemic** (30 countries) Virus: SARS-Covid1	2002-03	8,096 774	Guangdong China (Asia)
2	**MERS-Covid outbreaks** MERS-Covid outbreaks MERS-Covid outbreaks (27 countries) Virus: -MERS-Covid	2012 2015 2018	(2494 ((858	(Jordan, (Saudi (Arabia (ME)
3	**SARS-Covid-19 pandemic** (180 countries) Virus: SARS-Covid-2	2019 On-going	5 millions On-going	Wuhan China (WW)

All three Covid pathogens are human, under the same genera Betacoronavirus. The two SARS-Covids are our primary interest. They belong to the same subgenera, have been matched up to 79% in genotype, share a similar constituent design, have similar infectious histories and even suspected sources of origin.

MERS-Covid belong to a different subgenera. While their constituent design and infectious characteristics are similar, their source of origin is different. These generalised introductory descriptions reflect their shared “coronoviral” features. Information on each used for specific purposes should, however, be checked against authoritative sources.

Constituent Design

Human[39] Coronaviruses are enveloped viruses, the characteristics and functions of which genre are described in

[39] Most coronaviruses share the common features, but in view of their wide diversity, individual non-human subspecies should be verified individually.

the relevant section preceding. Only distinguishing features are mentioned here.

They are encoded in a positive-sense[40] in single-stranded RNA genome.

They are roughly spherical and have characteristic club-shaped spikes that project from their surface, like solar flares, from which their name derives. They attach themselves to their target cells with these spikes. The primary human-side receptor of the virus is *the angiotensin-ceonvertinng enzyme 2 (ACES)* and *hemaglutinin (HE).*

The core of the virus is the nucleocapsid, which in the human Coronavirus contains only one major structure, the nucleocapsid protein. It binds and encapsulates the viral RNA, and there are no other proteins within.. Being positive-strand RNA they do not need to carry enzymes to initiate infection.

After entry ,the virus' nucleocapsid is discharged into the host cytoplasm. There it unpacks, prepares its mRNA and other non-structural proteins, and engages the ribosomes and other host manufactories to replica, by-passing the host nucleus and controls.

Following sub-genomic RNA synthesis, the viral structural proteins encapsulate the total new virion, and export it via budding.

The exit procedures follow those of the enveloped virus.

---

40 Positive-strand RNA viruses have genetic material that can function both as a genome and as messenger; it can be directly translated into protein in the host cell by host ribosomes.

Pathology

SARS-Covid causes the medical condition **Severe Acute Respiratory Syndrome (SARS)**, for which strangely I could find no neat definition, and which I like to think could not be worse than ARDS defined below

> "Acute respiratory distress syndrome (ARDS) is a lung condition often caused by severe infection or trauma, and marked by fluid build-up in the lungs' air sacs. The resulting damage leads to a substantial decrease in oxygen reaching the bloodstream and rapidly developing difficulty with breathing. Patients are usually hospitalized and placed on a life-supporting ventilator. ….ARDS survivors often have long-lasting impairments such as cognitive dysfunction, mental health issues and physical impairments, all of which may affect employment." (Edited)
> https://www.hopkinsmedicine.org/news/media/releases/the_high_cost_of_surviving_acute_respiratory_distress_syndrome"

Coronaviruses mainly target epithelial cells of the respiratory tract. The infections are similar for both SARS, with Covid-2 being more severe.

Stage 1
Asymptomatic state (initial 1–2 days of infection)
The inhaled virus SARS-CoV-2 binds to epithelial cells in the nasal cavity and starts replicating. The symptoms are not unlike a common cold.

Stage 2
Upper airway and conducting airway infection (next few days)
The virus propagates and migrates down the respiratory tract along the conducting airways. Nasal swabs will yield the virus as well as early markers of the innate immune response. The infection is clinically manifest.

For about 80% of the infected patients, the disease will be mild and mostly restricted to the upper and conducting airways. Conservative symptomatic therapy would generally be sufficient.

Stage 3
Progression to ARDS
About 20% of the infected patients will progress to stage 3.

The virus will lead initially to non-specific symptoms such as fever, myalgia, headache, and respiratory symptoms. The virus can also cause temporary loss of taste and smell.

Further deterioration will lead to developing pulmonary infiltration, progressing to ARDS. Older people and those with prior medical conditions are most at risk.

The distribution of ACE 2 receptors in various tissues attracts the virus and explains gastrointestinal symptoms, cardiovascular, and other organs complications. Some patients experience septic shock and multi-organ dysfunction.

Transmission

Coronaviruses are most commonly transmit by coughing and sneezing.

Transferring infection from contaminated surfaces to the mucosa of eyes, nose, and mouth via unwashed hands is a well-used route especially in communal facilities.

They enter our orifices, settle on our skin surfaces and invade our wounds. People infect one another most rampantly during an epidemic

Treatment

As SARS is a viral disease, antibiotics do not have a direct effect on them. However they are used against bacterial secondary infection.

With improved technology, a number of vaccines have been developed to combat Covid-19, to strengthen the immune system. Likewise, anti-viral drugs are being deployed to the same end.

Medical defences are dealt within some detail in Part Four.

Zoonotic relation

SARS-CoV-1 is close to the bat viruses Bat CoV BtKY72 and Bat CoV BM48-31, and is additionally related by 82.8% to 96.0% to three species of the Chinese rufous horseshoe bat virus. SARS-CoV-1 is 99.8% similar to the Civet SARS-CoV. Finally, SARS-CoV-2' s genetic sequence is 79% similar to that of SARS-CoV-1

For its part, SARS-CoV-2 is close to the bat Coronavirus RaTG13 (96.2%). It is additionally related as above to the three species of the Chinese rufous horseshoe bat virus, and one of them by 81% to the same in Japan.

Finally, SARS-CoV-2 is 89% to 91% related to the Pangolin SARS-CoV smuggled to China from South East Asia, which in turn related by 91% to 96.1% to the Chinese rufous horseshoe bat from Cambodia, Thailand as well as China.

The preceding indicate that the SARS-CoV is probably zoonotic, but not proved. The further questions still not determined are whether in the case of Covid-2 the cross-over came from civet or pangolin to human, bat to human, or from lab (enhanced)to human.

(Back to TOC)

Other Forms of Viral Entry

.(a) Endogenous Viral Element (EVE)

An endogenous viral element (EVE) is a viral DNA sequence present within the germline of a non-viral organism. EVEs may be entire viral genomes, known as proviruses, or fragments of viral genomes. They arise when a viral DNA sequence becomes integrated into the genome of a germ cell that goes on to produce a viable organism. The newly established EVE can be inherited from one generation to the next as an allele (gene variant) in the host species, and may even reach fixation (permanency.)

EVEs that occur as proviruses can potentially remain capable of producing infective viruses. Replication of such 'active' endogenous viruses can lead to the proliferation of viral insertions in the germline.

For most non-retroviral viruses, germline integration appears to be a rare, anomalous event, and the resulting EVEs are often only fragments. Such fragments are usually not capable of producing infectious viruses, but may express themselves in other forms, as protein or RNA and even cell surface receptors.

By and large, EVEs lack a transposon[41] function, are typically not infectious and are often defective. They are referred to as "fossil viruses".

---

41 Transposon = class of genetic element that can "jump" to different locations within a genome.

.(b) Endogenous Retroviruses (ERVs), (HERVs)

Retroviruses integrate their genome into the genome of the host cell in the latter's somatic[42] region, but sometimes in its germline. In both instances, they duplicate with and as part of the cell's DNA when the latter undergoes cell division. Where they enter the germline, they integrate with the embryonic cells. Thereon they are transmitted down the line to the human's descendants as part of their genetical inheritance.

In the first case, they are latent but could be re-activated by environmental changes. These are properly viruses and are called *endogenous retroviruses* (ERVs)[43].

In the second cases, they are inactive, whether damaged or otherwise. These are also regarded as viral elements, and are called *human endogenous retroviruses (HERVs).* They are more commonly defined thus: human endogenous retroviruses (HERVs) are a family of viruses within our genome with similarities to present day exogenous retroviruses[44]. HERVs have been inherited by successive generations and it is possible that some have conferred biological benefits. HERVs however lack most transposon functions, are typically not infectious and are often defective.

HERVs represent the footprints of previous retroviral infections and have been termed "fossil viruses".

---

[42] A somatic cell is any cell of the body except sperm and egg cells. Somatic cells are diploid, meaning that they contain two sets of chromosomes

[43] Though budding does not immediately destroy the host cell, this process will slowly use up the cell membrane and eventually lead to the cell's demise. Thus, the host can be expected to divide so son after.

[44] In 2021, it has been demonstrated that the k-mer composition of endogenous RNA virus resemble that of their exogenous counterparts. As a result, it is now possible to identify novel groups of endogenous RNA viruses whose exogenous relatives have become extinct.[6]

.(c) Cell-to Cell Transmission

After direct entry or by replication, viruses can spread in the human body via either a *cell-free mode or cell-to-cell transmission*. The latter is a cell-associated mode involving direct cell-cell contact.

.(i) Cell-free mode

Cell-free spreading is basically aqueous. For this mode to be efficient, a virally infected cell would have to release large numbers of virions and so reach distant areas by diffusion. These particles must be sufficiently stable, not quickly cleared and, importantly, still able to efficiently bind to and infect uninfected target cells. If viruses are not efficiently released into the extracellular milieu, spreading by the cell-free mode would be unsuccessful.

(ii) Cell-Cell Transmission

On the other hand, retention of a young virion on a host cell may not necessarily inhibit transmission.

Viral gene expression may be too low in certain cell types to allow efficient particle generation. Some released viruses may be too unstable to allow for cell-free spreading, but may be able to undergo rapid spreading via cell-cell contact. As an alternative, such weak released viruses may be captured and stabilized by cell surface or extracellular matrix components, and rescued at sites of cell-cell contact by locally enhancing virus assembly and release resources.

Extracellular components at these sites may similarly promote efficient virus binding and infection of cells.

There are several advantages associated with direct cell-to-cell spread. The first is speed: the entire extracellular replication cycle can proceed quickly at sites of cell-cell contact and exploit the host's cytoskeletal forces for the

purpose of spreading. The second is immune evasion: limited extracellular exposure can allow evasion of neutralizing antibodies Third, exploiting cell-cell communication is an effective way to overcome the various physical and immunological barriers within an organism.

On the other hand, a cell-free virus is not restricted to specific cell-cell interactions and may facilitate spread from person to person. As such, it is possible to imagine that some viruses, notably HIV, may have come up with mechanisms to switch between cell-free and cell contact-dependent modes of spreading.

.(d) Long term Infectivity

EVEs that occur as proviruses can potentially remain capable of producing infective viruses in their endogenous state. Replication of such 'active' endogenous viruses can lead to the proliferation of viral insertions in the germline.

For most non-retroviral viruses, germline integration appears to be a rare anomalous event, and the resulting EVEs are often only fragments of the parent virus genome. Such fragments are usually not capable of producing infectious virus, but may express proteins, RNA and even cell surface receptors

I could not verify that HERVs share the above characteristics as EVEs, but have no reason to doubt that that they do.

.(e) Viral Genetic Fragments -Viral Fossils

The net result is that the human genome is embedded with HERV and EVE fragments, amounting to 8% of its genes. They are in fact records of past infections, or *viral fossils.* In much commentary, EVEs are taken to include HERVs.

With cryo-electron photography and DNA sequencing technology, we have been able to look at their DNA directly,

read their genetic evolution from pre-historic times, and construct their phylogenetic relationships. As a spin-off, we are able to template EVE's/HERVs against their genetic profiles and identify their historical association with us and our ancestors.

.(f) Vertical Transfer

The last method of transfer is vertical, from mother to child. Viruses have been found in breastmilk and in the human embryo. This is the route by which our primal ancestors passed their genes down to us.

It is astonishing that in the viral remnants embedded in us there are traces of their own ancestors, prokaryotes and eukaryotes the viruses took over eons ago.

(Back to TOC)

PART TWO

Earlier Pandemics

Historical Perspective

There have been pandemics, epidemics and outbreaks continuously in the last century of years.

This is the third time within that century that a virus has struck humans by a mega-scale pandemic, a different virus each time.

.- 1. The first was the **Influenza A** Spanish flu pandemic in 1918-20, killing an estimated 18 to 100 million people world-wide.

.- 2.The second one was the **HIV** pandemic which started in 1981 and is still on-going, with a death-toll so far of 32.7 million, and with 75.7 millions infected as at end 2019. And,

.- 3. The third is the **Coronavirus SARS-Covid-19** pandemic, which started in 2019, is still ravaging the world, and has already been responsible for 3,398,302 deaths and 163,869,893 people infected world-wide, as at 19 May 2021. This last continues.

In addition, there have been 13 other outbreaks with deaths of 1,000 or more each, since 1960. Table 6[45] provides a picture:

[45] See, https://en.wikipedia.org/wiki/List_of_epidemics

Table 6
Pandemics and Epidemics since 1960[46]

No	Pandemics/Epidemics	Year(s)	Deaths	Region
1	Poliomyelitis	1948-52	9,000	US
2	Small pox	1974	15,000	India
3	Yellow Fever	1940	1,627	Sudan
4	Yellow Fever	1986	5,600	Nigeria
5**	Yellow Fever	2013	45,000	Africa
6	Ebola	2013-16	11,323	Congo, W Africa
7	Ebola Kivu	2018-20	3,280	Congo Uganda
8	Measles	2010-14	4,500	Congo
9	Measles	2019-20	7,018	Congo
10	Dengue	2006	1,000	Philippines
11	Dengue	2018-20	3,93-	Pacific Latin Amer
12	Hand-Foot-Mouth Disease HFMD	2008-17	3,322	China
13	Japanese Encephalitis	2017	1317	India.

* = world-wide **= Not in Wiki list, added separately

There have been some successes. In 1980, WHO declared that *smallpox* had been eradicated. In 2015 it was able to declare the wild *poliovirus* type 2 (WPV2) had be eradicated, and in 2019 that the type 3 (WPV3) had also been eradicated.

The overall all picture however is one of increasing frequency and virulence. The underlying question is whether we have a

[46] Excluding the three mega-pandemics (Influenza, HIV and SARS)

growing monster. The associate questions are what can we learn from their past behaviour and our past mistakes.

(Back to TOC)

The Limited Pandemics

Yellow Fever, Dengue and Ebola share features in common. They are arboviruses[47]. Although not the most massive in outbreaks, they have been the most lethal in mortality rates. Ebola became our direct run-in to Covid-19. We also touch here on the related subject of Malaria.

(a) Yellow Fever

Flavivirus[48] is a genus of enveloped positive-sense single strand RNA virus, which includes species that cause Yellow Fever, Dengue fever, Zika and others, some of which can cause encephalitis.

The Yellow fever virus is transmitted to humans through the bite of an infected *Aedes aegypti* mosquito The virus is taken up by the female mosquito when it ingests the blood of an infected human or primate. Humans and mammals are the natural hosts. The mosquito is the vector. Yellow fever is not contagious as between humans. In 1927, yellow fever virus was the first human virus to be isolated.

Yellow fever in most cases causes only a mild infection of a few days, with fever, headache, chills, muscle pain, nausea, and vomiting. But, in about 15% of cases, people enter a second, toxic phase, leading to jaundice, liver damage, bleeding and kidney failure. Among the latter, fatality can be

[47] "Arbovirus," short for "arthropod-borne virus", refers to a type of virus transmitted via insects that bite and feed on blood.

[48] Also of the realm of *Riboviria*

20% to 50%, while the overall fatality rate is about 3% to 7.5%.

As with other Flavivirus infections, **no cure is known** for yellow fever, except symptomatic treatment.

The first line of defence has therefore been prevention of infection by the mosquito. This always starts at the domestic and social levels. The primary infrastructure must be good drainage, sanitation and public health services. But next, the most important measure has to be public education and information, right down to how to eliminate breeding, use larvicides, insecticides, and protective clothing, and correctly dispose of waste.

The common experience with mosquito-borne diseases is that they spread urban-ward with the shrinkage of the jungle habitat.

The second line of defence is control, and if possible, elimination of the vector. This goes beyond yellow fever. There are a number of mosquitoes that feature as vectors causing major diseases, and a history of attempts to control and eliminate them, some quite promising. I shall deal with them when reviewing Dengue fever. Provided the domestic and social defence lines are working, this defence Is not so critical here.

There has been **a vaccine since 1938**. WHO recommends routine immunisation of children in all countries where the disease is common. No one today travels to an endemic country without a vaccination, and countries increasingly require it.

Yellow fever is endemic in tropical and subtropical areas of South America and Africa. WHO estimates that 200,000 cases of disease and 30,000 deaths a year occur.

Despite recent increases in some South American and African countries, yellow fever is not presently a pandemic threat.

(Back to TOC)

(b) Dengue Fever

The Dengue virus, also of the genus Flavivirus, is likwise an enveloped positive sense single-stranded RNA virus.

There are four types of the Dengue virus. These are vector-spread by different species of the Aedes mosquito.
Until a few hundred years ago, they subsisted mainly in the "sylvatic cycle" [49], between mosquitoes and non-human primates. Their primary lifecycle has now migrated to between humans and mosquitoes, in what is recognised as the " urban cycle".

Dengue fever causes the same symptoms as yellow fever, plus a rash. With early detection, most people recover within a week. In a small proportion of cases, the disease develops into dengue haemorrhagic fever, with bleeding, loss of platelets, dangerously low blood pressure and shock syndrome. The risk of death among those with severe dengue is 0.8% to 2.5%.

Before 1970, only 9 countries had experienced severe dengue epidemics. WHO report that there has since been a dramatic increase in infections to 129 countries. Some 70% of the burden is carried by countries in South East Asia, South Asia, South America and the West Pacific.

---

[49] The sylvatic cycle, also enzootic cycle, is a portion of the natural transmission cycle of a pathogen refers to the fraction of the pathogen population's lifespan spent cycling between wild animals and vectors. Humans are usually an incidental or dead-end host, infected by a vector. This is opposed to a "domestic" or "urban" cycle, in which the pathogen cycles between vectors and non-wild, urban, or domestic animals.

WHO's database is not updated, but Wikipedia reported that 2019 saw an all-time global record of 4.7 million infections. The number of deaths however was 3.2%. These country figures are worth capturing

Table 7
Dengue Epidemic 2019-20 (May)[50]

Rank	Country	Cases	Deaths	Mortality Rate
1	Brazil	2,225,461	780	
2	Philippines	420.4553	1,565	
7	Malaysia	127,407	178	
9	India	157,3§5	166	
18	Singapore	15,998	20	
Total (2019)	60 countries	4,700,522	3,244	(0,007%)
Total (2020)*	60 countries	1,461,672	686	(0.005%)
Total (20119-20)	60 countries	6,162,144	3,930	(0.006%)

* = Up to May 2020

There was indeed a pandemic over 60 countries, extending into 2020.The mortality rate, however, was 0.006%. Dengue is active world-wide, and has surfaced to threatening levels in the underdeveloped world.

Dengue is not person to person contagious. Again, the first-line of defence is prevention. The essential infrastructure and measures are simply the same as in the case of yellow fever. These measures are internally affordable for developing countries.

The second line of defence is elimination of the vector. There is an history of attempts to control and eliminate mosquito vectors, some quite promising. Their main attraction is that they are also affordable for developing countries.

[50] See https://en.wikipedia.org/wiki/2019–2020_dengue_fever_epidemic

Malaria is a fever disease caused by the parasite *plasmodium relictum* (not a virus or bacterium) and is transmitted by the *Anopheles* mosquito. This was established in 1896. Man's earliest successes with its control and elimination was by spraying DDT, a chemical compound. This was found to be toxic to humans and wildlife, and is now banned in most countries. Today, there are a wide range of approved larvicides. Other inventions include larva and mosquito traps, and using natural vector predators, such as fish. These constitute the weaponry for the war of protection, and apply to both yellow fever and dengue fever.

Each year, an estimated 390 **million** dengue infections occur around the world. Of these, around 500,000 cases develop into severe dengue or dengue haemorrhagic fever, which result in up to 25,000 deaths annually worldwide (Malaria is still the most lethal mosquito-borne disease. In 2019, there were 229 million cases, but 409,000 deaths, 94% in Africa. **In Africa, a child dies every minute of malaria.)**

There have been a wide range of explorations into genetic means to exterminate the mosquito population. Amongst these is the Sterile Insect Technique (SIT). Radiation is used to disrupt DNA to produce sterile males who are then released. When these mate no offspring is produced.

Since 2011, the World Mosquito Program (WMP), a non-profit organisation, has been developing the *Wolbachia* project, which appeals to me. Herewith the essential details:

.(a) The project offers a way to reduce the ability of the *Aedes egypti* mosquito to host (and transmit) the viruses that cause yellow fever, dengue, Zika, and chikungunya .

.(b) They have identified the *Wolbachia,* a common bacteria that occur naturally in 60% of insect species, including some mosquitoes, fruit flies, moths, dragonflies and butterflies. Wolbachia live inside the host's cells and are passed from one generation to the next through the host's eggs.

.(c) Aedes egypti mosquitoes do not normally carry Wolbachia. However, it has been found that when the Aedes aegypti mosquitoes does carry Wolbachia, the bacteria competes with viruses like dengue, Zika, chikungunya and yellow fever in the eggs. This makes it harder for viruses to reproduce. Therefore when Aedes aegypti mosquitoes carry Wolbachia, the transmission of viruses is reduced.

.(d) So, at the WMP, they breed Wolbachia-carrying mosquitoes. Then, in partnership with local communities, they release them into areas affected by mosquito-borne diseases. In time the entire Aedes egypti population will carry the Wolbachia, and the viral population is reduced.

.(e) The first mosquitoes were released in 2011, and the programme is under test in 11 countries, with encouraging results. It's attraction is that it is natural and self-sustaining. It does not suppress the mosquito population or involve genetic modification (GM).

I conclude this diversion by citing the following good news: **"First concrete evidence for the presence of Wolbachia in malaria-transmitting mosquitoes" 14 April 20**21.[51] My surprise is that after over a decade, the results have not been more evident.

A vaccine against dengue viruses has been on the market since 2015. Disastrous experience of its use in the Philippines led to its review, inter alia **by** WHO. The latter has since approved it, in 2018, subject to conditions of use. In May 2019, the US FDA finally approved it for people aged nine through 16 who have had a previous infection and who live in endemic areas.

[51] https://www.lshtm.ac.uk/newsevents/news/2021/first-concrete-evidence-presence-wolbachia-malaria-transmitting-mosquitoes

What this means is that **there is no generally approved vaccine for dengue fever.** I do not see WHO, the medical and pharmaceutical industries, or the politico-regulatory sectors rushing around to supply a suitable vaccine as early as possible. There are also no approved direct antiviral treatments for dengue fever. Perhaps, because the market is the developing world, there is less enthusiasm to invest in high-end solutions.

For diseases where there is no effective cure, vector control remains the only way to protect the human population.

(I am appalled with the situation as regards malaria, and make no apology for injection these comments although malaria is neither a viral disease nor technically a pandemic, and therefore not within the scope of this dossier.. After nearly 125 years, this is all Wikipedia can report on the status of a vaccine:

> "The only approved vaccine (for malaria) as of 2021 is RTS,S/AS01. It requires four injections, and has a relatively low efficacy. Due to this low efficacy, WHO does not recommend the routine use of the vaccine in babies between 6 and 12 weeks of age.
>
> Research continues with other malaria vaccines. The most effective **malaria vaccine** discovered so far is R21/Matrix-M, with 77% efficacy shown **in initial trials.** It is the first vaccine that meets the WHO goal of a malaria vaccine with at least 75% efficacy." (edited)
> https://en.wikipedia.org/wiki/Malaria_vaccine

(Back to TOC)

(c) Ebola

The Ebola virus (EBOV), is the deadliest of the four species within the genus *Ebolavirus*[52]. The latter and *Marburgvirus* are twin genera in the taxonomic family home of *Filoviridae.* Viruses in this family form filamentous infectious viral particles (virions) and encode their genome in the form of single-stranded negative-sense RNA

Like most other RNA viruses, Ebola's molecules are structured in a way that makes them more prone to genomic errors and mutations.

The Ebolaviruses and Marburg viruses cause severe and often fatal haemorrhagic fever in humans and animals, known as "filovirus" diseases. The former caused the Ebola Virus Disease (EVD), which was the cause of the most recent epidemic in Western Africa, in 2013-20.

These diseases have a high risk of death, killing 25% to 90% of those infected, with an average of about 50%. All filoviruses have accordingly been classed as "select agents" by WHO and placed in Risk Group 4 Pathogens, requiring Bio-Safety Level 4 (BSL4) equivalent containment[53].

EDV is contagious. It spreads through direct contact with body fluids, including droplets and excreta – and infected fruit. Fruit bats are believed to be the normal carrier in nature, able to spread the virus without being affected by it.

Human-to-human transmission of EBOV through the air has not been reported, neither from primates to primates. Pigs with EVD get very high concentrations in their lungs, and can spread the disease through droplets when they sneeze or

---

[52] Also of the realm *Riboviria*

[53] List of BSL4 organisms, see https://en.wikipedia.org/wiki/List_of_biosafety_level_4_organisms

cough. By contrast, humans and other primates accumulate the virus throughout their body and specifically in their blood

Spread of EBOV by water or food, other than bushmeat, has not been observed. No spread by mosquitos or other insects has been reported.

Bats are likely a natural reservoir for the Ebola virus, but little is known about how the virus evolves in bats.

The disease was first identified in 1976, in two simultaneous outbreaks: one in Sudan and one from a village near the Ebola River in the Congo (hence its name), and has been essentially confined to Central and West Africa.

The largest outbreak to date was the epidemic in West Africa in 2013-16, with 28,646 cases and 11,323 deaths. It broke in Guinea, and spread to Liberia and Sierra Leone. WHO called for world help reporting that, "The Ebola epidemic ravaging parts of West Africa is the most severe acute public health emergency seen in modern times. Never before in recorded history has a Bio-Safety Level 4 a pathogen infected so many people so quickly, over such a broad geographical area, for so long." By mid-Aug 2014, Doctors Without Borders reported the situation in Monrovia was "catastrophic" and that fears of Ebola among staff members and patients had shut down much of the city's health system, leaving many people without medical treatment for other conditions. The epidemic was only contained in Jan 2016,

After nine earlier spasmodic outbreaks in the Democratic Republic of the Congo[54] the second largest outbreak in Africa began there in May 2018. In Jul 2019, WHO declared the Congo outbreak a world health emergency. On 18 Nov 2020, Congo declared the end of the Ebola Virus Disease (EVD) outbreak, after a tally of 2,313 and death rate of 64%

[54] Previously known as Zaire. I use “Congo” for simplicity, and because I never much cared for Patrice Lumumba in his time.

The US Food and Drug Administration (FDA) approved the **Ebola vaccine** (rVSV-ZEBOV) on December 19, 2019. This is the first FDA-approved vaccine for Ebola.

We can be grateful that Ebola and the Marburg[55] viruses are not at this point pandemic threatening, and are both under BSL4 containment. Their death rate figures reflect the poverty levels of the African countries where they mainly break.

(Back to TOC)

The Major Pandemics

(a) Influenza[56]

For convenience, I have placed the information component of this topic separately in Part 1 – Summary of Current Knowledge. (Read First).

The Influenza viruses belong to the viral realm: *Riboviria*[57] Below that we find subdivisions into kingdom, phylum, class and order, and finally below that the family: *Orthomyoxviridae*, with seven genera.

The genera *Alphainfluenza* has only one species, *Influenza A,* which is responsible for all our pandemics and epidemics. The latter has in turn evolved many sub-types. It is now known that the variant H1N1 was responsible for the Spanish Flu.

---

[55] I have not reviewed the Marburg virus (MARV). Although belonging to the genera Marburgvirus, it is, like Ebolavirus, an enveloped negative sense single stranded RNA virus.

[56] For editorial ease, influenaza = *h*Influenza A in this section.

[57] Riboviria includes all viruses that use a homologous RNA-dependent polymerase for replication. It includes RNA viruses that encode an RNA-dependent RNA polymerase; and, it includes reverse-transcribing viruses (with either RNA or DNA genomes) that encode an RNA-dependent DNA polymerase.

The Influenza A virus has been our constant companion and most consistent viral enemy over the years. It is convenient here to recall its record (see Table 3 here reproduced for convenience)

Table 3 (repeated here)
***h*Influenza A: Pandemics and Epidemics**

No	Epidemic/Pandemic	Year(s)	Deaths	Region
1	Spanish Flu Influenza A H1N1	1918-20	18 million	WW
2	Asian Flu Influenza A, H2N2	1957-58	1 -4 million	WW*
3	Hong Kong Flu Influenza A H3N2	1968-68	1-4 million	WW
4	London Flu Influenza A, H3 N2	1972-73	1,027	US
5	Russian Flu Influenza A, H1N1	1977-79	700,000	WW
6	Swine Flu Influenza A, H1N1	2009	284,000	WW
7	Indian Epidemic Influenza A, H1N1	2015	2,035	India
8	Seasonal Flu Influenza A	2017	650,000 a year	USA, temperate zones

* = world-wide **= Not in Wiki list, added separately

The Pandemic

Besides the Spanish flu[58], Influenza A has caused not less than six pandemics and epidemics world-wide over the last century of years, and it still results in massive seasonal outbreaks in the northern and southern hemispheres annually. It ranks as a top endemic public health concern.

Fortunately, our surveillance and preventive systems, medical defence armouries and our levels of public preparedness are in place against this virus. The battle against Influenza A has

[58] I have not reviewed the Spanish Flu, 1918-20. Because it happened during World War 1, the information is patchy. It was not actually "Spanish". It started in an army camp in Kansas. But is spread world- wide. Estimates of infection and deaths vary wildly, up to 500 million and 100 million respectively. It was unquestionably, though, the world's our worst viral pandemic ever.

provided useful experience and resources for combating our present pandemic.

Influenza (the A is dropped when referring to the human infection) is seasonal. In temperate climates, seasonal epidemics occur mainly during winter, while in tropical regions, influenza may occur throughout the year, causing outbreaks more irregularly.

The CDC estimated that the during the 2018–2019 season about 35.5 million people in US caught Influenza, 16.5 million went to a health care provider, 490,600 cases resulted in hospitalisations, and there were 34,200 deaths. In industrialised countries most deaths occur among people aged 65 or older. 99% of deaths in children under 5 years of age, with influenza related lower respiratory tract infections, are found in developing countries.

WHO estimates that, worldwide, the annual epidemics result in about 3 to 5 million cases of severe illness, and about 290,000 to 650,000 respiratory deaths. (The latter figure works out to 1.23 per minute, beating children in Africa with malaria.)

Vaccine

For more than 50 years, WHO has been collaborating with scientists and policy makers on a global scale to develop a unified approach to manufacturing, testing and regulatory oversight of influenza vaccine development as well as their efficient use and distribution. In 2011, researchers reported an antibody effective against all types of Influenza A, and there is **now an effective vaccine, which is updated annually** to catch up with mutations. (I get my flu jab every year in May).

GISRS

The battle against Influenza has been the longest on-going waged by WHO and the world – perhaps because it is endemic in the big as well as developed countries, and kills massively, regularly and annually.

The UN signalled the need for a Global Influenza Programme as early as 1947, and WHO has had **a Global Influenza Surveillance and Response System (GISRS)** in place since 1952.

It has grown with t experience, improving technology and participation. GISRS members include institutions, formally accepted by WHO, in 114 WHO Member States. Today, it comprises:-

. 144 National Influenza Centres (NICs) – on the frontlines of surveillance and monitoring

• 6 WHO Collaborating Centres for Influenza (CCs) – international centres of excellence that carry out detailed analyses and risk assessment.

• 4 WHO Essential Regulatory Laboratories at the interface of influenza surveillance and vaccine development

• 13 WHO H5 Reference Laboratories (H5RefLabs) at the human–animal interface to support countries and WHO in early detection and confirmation of novel viruses.

There is also a **Flunet** serving the system, by which viral data is uploaded for common reference and research.

GISRS is now a routinised round the clock system of surveillance and global alert , with shared viral intelligence gathering and common reference data-bases. No thanks to the Influenza viruses, it is today our primary guardian at the zoonotic divide.

Since March 2020, GISRS has included first testing of SARS-CoV-2 specimens collected from influenza surveillance sources. The sub-systems established for influenza virus detection, risk assessment and sharing of virus materials and data, have provided ready platforms to monitor the circulation of SARS-CoV-2.

Since January 2021, the genomic sequencing of systematically sourced sentinel specimens under the Influenza system has been expanded to monitor SARS-CoV-2 variants and to bridge the critical evidence gaps.

GISAID

GISAID is the acronym for what began as the **Global Initiative on Sharing Avian Influenza Data**.

GISAID was a global initiative in 2008 which began as a consortium of some 70 research entities to freely share genomic data of avian influenza viruses among themselves on an open-ended basis. (We may assume there were some bureaucratic inhibitions in the governmental GISRS system.) The idea caught on. GISAID was officially launched in May 2008 at the 61st World Health Assembly, as a publicly-accessible database rather than a consortium requiring membership.

Since its establishment, GISAID has been recognized for accelerating the rapid exchange of outbreak data among scientists. This included the H1N1 outbreak in 2009 and the H7N9 outbreak in 2013.

It was immediately engaged to confront the SARs-CoV-19 pandemic In 2020. WHO's chief scientist called it "a game changer". On 10 Jan, 2020, 10 days after China reported the outbreak, the first whole genome sequences of the SARS-COV-2 virus were made available on GISAID, by China.

GISAID has also facilitated genomic epidemiology and real-time surveillance to monitor the emergence of new COVID-19 viral strains as fast as the virus has been able to mutate them.

The Initiative ensures that open access to data in GISAID is provided free-of-charge to all individuals that agreed to identify themselves and agreed to uphold the provisions governing the GISAID sharing mechanism

GISRS and GISAID complement one another. . The one is the routine information gatherer and country sentinel, and the other the hotline of the global scientific community.

China and Influenza

China was one of the countries affected by the major Influenza pandemics of 1918, 1957, 1968 and 2009. They estimated 4-9.5 million died from the first, the Spanish Flu. The 1957 and 1968 pandemics were first identified in China. China now also participates in the seasonal epidemics, in fact having three outbreaks, the third at mid-year in the mid-latitudes. China's experience with the above forms relevant background to its involvements with the two coming SARS pandemics.

China established its first influenza epidemiology office and laboratory in 1954. A second pandemic wave spread across China in the latter half of 1957, prompting the government to establish the Chinese National Influenza Center (CNIC) to lead in control efforts.

After becoming a WHO member country in 1972, China invested in CNIC's research infrastructure and formed international collaborations for surveillance. In 1981, China joined the Global Influenza Surveillance and Response System (GISRS).

The Chinese Center for Disease Control and Prevention (China CDC) was formed in 1983. In 1988, China initiated

influenza laboratory capacity. In 2000, with WHO support, China expanded its influenza surveillance network with more sites.

As near as I can make out, in January 2002, the Chinese Academy of Preventive Medicine, which housed the CNIC, became the National Institute for Viral Disease Control and Prevention **(NIVDC**) a statutory board under the Chinese Center for Disease Control and Prevention (CCDC).

Later that year, Guangdong Province reported the first cases of a typical influenza, later identified as the SARS. The CCDC was still nascent, and failed to identify it, to their mortification.

As a result, China invested in a nationwide network of CDCs at the national, provincial, prefecture and county levels. In April 2004, China launched a real-time web-based reporting system.

By 2005, CNIC had further expanded its national influenza surveillance network to all 31 provinces. The 2009 pandemic triggered further government investment in China's influenza surveillance network, which, by the end of 2009 included 411 laboratories and 556 sentinel hospitals.

NIVDC has a long standing reputation in the field of medical virology. NIVDC has several WHO Collaboration Centres and Laboratories, including:

.a WHO Influenza Collaboration Reference Center
.b WHO Western-Pacific Region (WPR) Polio Reference Laboratory
.c WHO WPR Measles and Rubella Reference Laboratory,
.d WHO WPR Japanese Encephalitis Reference Laboratory, and
e. WHO WPR Rotavirus Reference Laboratory, Chinese Center for

In October 2010 CNIC was designated as the **fifth and latest WHO Collaborating Centre for Reference and Research on Influenza** under the GISRS. CNIC's surveillance network

collects 200,000–400,000 specimens and conducts antigenic analysis on approximately 20,000 viral strains annually.

Barring information to the contrary, it seems the NIVC- CNIC is the party responsible for the first line processing of reports of unknown influenza (or other) viruses.

Avian Flu

In 2005, China identified the highly pathogenic avian influenza *A(H5N1)* virus in numerous poultry outbreaks and several human infections. So far outbreaks have been contained.

The Influenza virus with the highest pandemic potential to date, the avian influenza *A(H7N9),* has also been identified in China.

Both these predators need watching, see the following extract:

> **"**The most striking aspect of H5N1 is its high mortality rate, observed from surveillance of sporadic outbreaks between 1997-2019. Of the 861 confirmed cases, 455 people have died making the mortality rate 53% (world-wide figures). Unlike many circulating strains, H5N1 has a lower age curve, with the median age of infection being 19, more similar to that of Spanish influenza, in which 50% of deaths were adults between the age of 20 to 40. In contrast, H7N9 has a lower-case fatality rate of 40%, in which two thirds of deaths are over the age of 50, but even so this is still significantly higher than seasonal and even Spanish influenza"
> https://www.gavi.org/vaccineswork/next-pandemic/h5n1-and-h7n9-influenza

From 2013–2017, China experienced annual epidemics of human infections with A(H7N9), with a cumulative total of 1,537 human cases identified through September 2019.

Because most (90%) humans infected with avian influenza A(H7N9) had been exposed to live poultry within the two

weeks preceding illness onset, China initiated poultry industry reform, including banning live poultry markets in major cities and promoting market sanitation.

With 20% of the world's population and the world's largest poultry production of 5 billion chickens and ducks per year, China is a major zoonotic frontier of the avian H5N1 and avian H7N9, both assessed to have high human pandemic potential. Fortunately, in its long battle with Influenza, China has developed a strong defensive research backbone and surveillance network.

As of November 2017, China CDC consisted of 3,481 units and 877,000 public health professionals serving at all levels of government.

China's importance in this respect is doubled in that it also houses a major bat population which hosts the Coronavirus.

(Back to TOC)

(b) Human Immunodeficiency Virus (HIV)

For convenience purposes, I have placed the information component of this topic separately in Part 1 – Summary of Current Knowledge. (Read First.)

The Pandemic

The HIV virus originated in non-human primates in Central and West Africa. The pandemic had its origins in the emergence of one specific strain – *HIV-1 subgroup M* – in the Congo in the 1920s. There were sporadic reports of infections from the 1950s.

The medical condition AIDS was first diagnosed in 1981. Around the same time, the first human retroviruses were discovered in T cells. In 1983, Luc Montagnier's at the

Pasteur Institute in Paris discovered the HIV virus and established the association. In 1984, Robert Gallo, of the National Cancer Institute in Bethesda, Maryland, did the same from a larger group of patients.

By 1990, because of the long incubation, HIV infection and AIDS emerged full blown, rampant and world-wide. Statistics for that year give 873,625 people living with HIV/AIDS, nearly 2.02 million new infections and 348,600 deaths.

The counter-measures focussed on antiviral drugs, first to prevent the virus from killing the CD4 cells, and second from replicating[59]. The year 1987 saw the first partial offensive, the drug . called *azidothymidine* (AZT), which blocked the enzymes he virus needed to replicate. Over the next several years, the FDA approved several other drugs that worked similarly to AZT. They belonged to a drug class called *nucleoside reverse transcriptase inhibitors* (NRTIs).

In 1995, the FDA approved a different anti-HIV drug class called *protease inhibitors*. Like NRTIs, protease inhibitors (PIs) stopped the virus from copying itself, but at a different stage during the infection.

A year later came yet another class of antiretrovirals, called *non-nucleoside reverse transcriptase inhibitor* (NNRTI). These also shut down HIV by targeting the enzymes it needed to multiply. I believe there ae also some entry inhibitors.

These drugs paved the way to a new era of combination therapy, dubbed **Highly Active Antiretroviral Therapy** (HAART). It became the new standard of care for HIV in 1996. HAART greatly lengthened the life span of people with AIDS. in 1997, the FDA approved a pill called that contained two anti-HIV drugs and was easier to take.

---

59 https://www.webmd.com/hiv-aids/hiv-treatment-history

Two decades after the emergence of HIV and AIDS, a dozen antiretroviral drugs were on the market.
New HIV drug classes kept coming out. In 2007, the FDA approved the first integrase inhibitor, *raltegravir (Isentress).* This type of drug offers a different way to shortcut HIV from making copies of itself. In 2012, the FDA approved a drug for pre-exposure prophylaxis, (PREP)which could lower the risk of catching HIV to almost zero.

Today, more than 30 HIV medications are available. Many people are able to control their HIV with just one pill a day. Early treatment with antiretrovirals can prevent HIV-positive people from getting AIDS. HIV drugs also stop people who have the virus from passing it to their partner during sex.

There is still no cure for AIDS. But with the right treatment, people who are HIV positive can live a normal life span.

I place special emphasis on pregnant women with HIV. There are antiretroviral drugs for them, and for their babies. With proper treatment, the baby will not be infected.

Annual new infections peaked in 1998 at 2.8 million people and annual deaths peaked in 2004 at 1.8 millions. By 2020, new infections had dropped to1.5 millions (by 47%), and deaths to 690,000 (by 61%).

The total number living with HIV/AIDS would of course keep growing the longer they lived. In 2020, they grew to 37.6 millions, of whom 20.6 millions lived in Africa. Of the global total of 37.6 millions, 27.4 millions or 73% had access to antiretroviral therapy. Of those in Africa, 16.1 millions had access to the therapy. The pandemic was global and affected 169 countries. But the virus was effectively halted.

UNAIDS

WHO[60] launched a Global Program on AIDS in 1987.Superceding and enlarging it, in 1996 the UN and co-operating partners launched a Joint United Nations Programme on HIV/AIDS. Its mission was to lead, strengthen and support an expanded response to HIV and AIDS that included preventing transmission, providing care and support to those already living with the virus, reducing the vulnerability of individuals and communities to HIV and alleviating the impact of the pandemic. It established a **Global Fund** to Fight AIDS, Tuberculosis and Malaria.. No doubt UN leadership contributed immensely to their success.

Emboldened by the latter, in 2014, under UN Sustainable Development Goal 3, UNAID launched its Fast- Track Strategy[61], a set of targets around which all countries, agencies and organisations could co-ordinate their efforts in two stages:

.
(a) Target 90-90-90. By 2020,
.- 90% of all people living with HIV will know their HIV status.
.- 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and .
.- 90% of all people receiving antiretroviral therapy will have viral suppression.

(b) Target 95-95-95. By 2030
.- 95% of the first group
.- 95% of the second group
.- 95% of the third group
.- Thereafter: Get to ZERO.

---

60 I could not find when. WHO declared HIV a pandemic, if they did.

61 www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

In 2016, the United Nations General Assembly's Political Declaration on Ending AIDS committed countries to the 90–90–90 targets,

As at 2019, the levels achieved were 81%, 67% and 59%. UNAIDS' assessment: good progress, but the world was off-track for hitting the 2020 targets.

US Funding

The US government, through PEPFAR (the President's Emergency Plan for AIDS Relief) has been the single largest donor to international HIV efforts in the world. In 1981, almost all of the then smaller (I could not get the figure) US federal budget for HIV was spent on research. By 2017 the federal budget, which had grown to $32.9 billion, was disbursed as follows:. care and treatment, 60%; global funding (UNAIDS) accounts, 20%, cash and housing assistance, 9%, and research, 8%, with prevention, 3%.[62]

Bottom Line

The bottom line at end 2020 was 75.0 millions people were infected since the outbreak. Of these, 37.4 millions died and 37.6 millions were living with HIV needing medication.

In 2020 alone, there were 1.5 millions new infections, nearly 60% in Sub-Saharan Africa. Their links to poverty and difficulty of access to antiretroviral drugs are evident.. Things are far from over. Discrimination is additionally a major social dimension affecting the quality of life of those living with HIV.

The main obstacle to complete elimination of HIV is that it is able to integrate itself into the DNA of host cells and rest in a latent a state, while antiretrovirals only attack actively

[62] https://www.ajmc.com/view/the-past-present-and-future-of-hiv-funding

replicating HIVs. The cells in which HIV lies dormant are called the viral reservoir. There is work being done to activate reservoir cells into replication so that the virus can be attacked by the host immune system.

The so-called “Berlin patient” has been potentially cured of HIV infection and has been off of treatment since 2006 with no detectable virus. This was achieved through bone marrow transplants, which carry their own significant risks

Observations.

In this case, the medical battle seems to have been won outright. **The HIV virus seems so far to have been unable to out-mutate the antiretroviral drugs**. There has been no use of a vaccine, nor is there one, except one on trial.

I am unable to evaluate the situation, and so take this extract from Wikipedia as representing the current view of things: “Vaccination has proved a powerful public health tool in vanquishing other diseases, and an HIV vaccine is generally considered as the most likely, and perhaps the only way by which the HIV pandemic can be halted”.[63]

Under present strategies, HIV leaves a heavy and accumulating legacy of living infected persons, who need constant treatment. A vaccine would, even an annual vaccine, would help.

There seems no doubt that the HIV virus crossed over to humans via the animal kingdoms – perhaps not always vectored, and not always on their own volition or compulsion; and quite possibly pressured to do so by human encroachment of their natural habitats. My scans did not

[63] This article discusses the problems of HIV vaccine development in some detail.. https://en.wikipedia.org/wiki/HIV_vaccine_development

disclose any methodical research in this direction vis-à-vis HIV.

Nowhere either did I find any mention of gain-of-function (GOF) research in connection with HIV. It seems the medical war was over before the emergence of the furor over funding GOF, which surfaced around 2011 – in the next era of the Influenza and Coronavirus[64] bugs. It does not mean it did not happen.

US federal GOF research funding was suspended in 2015, but was resumed in 2017 with fresh guidelines and controls. I failed to find legislative controls governing private GOF research then or now – apart from non-approval of federal grants.

I am far from naïve to believe that individuals in the science community, whether encouraged from within their community or pressured by their governments have not, with the best of intentions, ventured across the line. The framework of international controls and surveillance is weak. I imagine HIV research is far from over. We still need to kill the virus.

The SARS-Covid-19 pandemic also could have an impact on viral load. Early modelling showed that a severe disruption in HIV treatment could result in additional AIDS-related deaths in sub-Saharan Africa. Some countries have reported reductions in medicine collections of up to 20% in some areas and there have been multiple reports of people living with HIV not having enough antiretroviral medicine for a lockdown of more than 60 days, as well as reports of people having abandoned their HIV treatment due to a lack of food.

(Back to TOC)

[64] On the off-chance I decided to check and was not surprised that the coronavirus, influenza and HIV all belong to the same realm: Riboviria.

(c) Coronavirus

For convenience purposes, I have placed the information component of this topic separately in Part 1 – Summary of Current Knowledge. (Read first).

SARS-Covid-1 and **SARS-Covid-2 virus** are the two closely related Coronavirus viruses that cause the **Severe Acute Respiratory Syndrome (SARS).**

The first caused the SARS-Covid epidemic in 2002-03, which originated in Guangdong, China.

The second has caused the on-going SARS-Covid-9 pandemic which originated in Wuhan, Hubei, China in 2019.

There is a third Coronavirus virus ,MERS-Covid, of a different subgenera, which caused the SARS-like Middle East Respiratory Syndrome and was responsible for the outbreaks in 2012-2018.

As the facts now unfold, all three throw important light on our ongoing engagement with the Coronavirus virus. Table 5 is repeated here for convenience.,

Table 5 (repeated here)
Coronavirus: Epidemics/Pandemics

No	Pandemic/ Epidemic	Year(s)	Infections Deaths	Original Region
1	SARS-Cov-1 (30 countries)	2002-03	8,096 774	Guangdong, China
2	MERS-Covid MERS-Covid MERS-Covid (27 countries)	2012 2015 2018	(2494 ((858	(Jordan, (Saudi (Arabia

SARS-Covid 1

This was the **very first Coronavirus** to invade and be discovered by man. It was the first of the viruses of the 21st century to attack us.

It was the investigations into this virus that disclosed that many species of Coronavirus, and indeed of many other viruses of pathogenic interest, co-habited in animals, birds and bats as well as humans, each in their own variant, and that bats formed a natural reservoir or gene pool for coronaviruses.

The Pandemic

The timeline of this epidemic is worth reviewing:

.- On 16 Nov 2002, the first case was reported of a person with atypical pneumonia in Foshan, Guangdong (bordering Hong Kong), China. This was thought to be one of a number in an outbreak of influenza.

.- On 5 and 11 Dec 2003, WHO requested information about the reported influenza outbreak

.- On 12 Dec 2002, WHO received a detailed report on data collected at Chinese influenza surveillance sites, indicating that 23 influenza virus isolates were confirmed type B strains in all but one and that the number of cases was consistent with the seasonal pattern in previous years.

.- On 31 Jan 2003, The first “super-spreader”, a fishmonger checked in to the San Yet Sen Memorial Hospital in Guangdong, where he infected 30 nurses and doctors. The virus soon spread to nearby hospitals.[\

. On10 Feb 2003, China notified WHO about this outbreak, reporting 305 cases including 105 health-care workers and five deaths.

.- On 22 Feb 2003, the Liu family (visiting from Guangdong) checked into Metropole Hotel, Hong Kong, and the next day checked into Kwong Wah Hospital very sick. They became Hong Kong's "super spreader", subsequently infecting 20 hospital staff and an American businessman.

.- On 26 Feb 2003, a Chinese-American who stayed at the Metropole, checked in sick at the French Hospital, Hanoi, and infected 38 staff.

.- On 28 Feb 2003, an American businessman reported with an unknown form pneumonia in Hanoi, and by 10 Mar 2003 had spread it to 22 hospital workers.

.- On 28 Feb 2003, WHO was notified of the preceding (probably by Hong Kong)

.- On 28 Feb 2003, another Metropole guest returned to Toronto, Canada, and spread the infection, including to staff of Scarborough Grace Hospital.

.- On 1 Mar 2003, another Metropole guest was admitted to Tan Tock Seng Hospital, starting the outbreak in Singapore.

.- On 12 Mar 2003, WHO issued a global alert, and on 15 March an heightened global health alert about a mysterious pneumonia with a case definition of SARS. The alert included a travel advisory .The (CDC) also issued a travel advisory.

.- ON 13 Mar 2003, WHO notified GOARN (see section further down)

.- On 17 Mar 2003, an International network of 11 leading laboratories was established to determine the cause and develop potential treatments. There were 14 cases in US.

.- On 24 Mar 2003, CDC identified Coronavirus as likely cause of SARS.

.- On 28 Mar 2003, the POC (Provincial Operating Centre) in Ontario established a set of SARS-specific recommendations and suggestions for all hospitals (in Toronto) in order to guide them on how to best avoid the transmission of SARS among staff.

.- On 3 Apr 2003, WHO-sponsored team of international infectious disease experts arrives in Guangdong province to investigate the outbreak. The team found evidence of "super spreaders" who were capable of infecting as many as 100 persons.

.- On 12 Apr 2003, the Michael Smith Genome Sciences Centre, Canada completed sequencing of the new virus

.- On 16 Apr 2003, WHO issued a release that the Coronavirus identified by a number of laboratories was the official cause of the epidemic. The virus was officially named the SARS virus.

.- On 20 Apr, 2003, the Chinese Health Minister was replaced. Beijng cases increased to 407, against 37previously, and the city was closed down.

On 17 May, WHO extend travel warning to all affected countries

.- On 9 Jul 2003, last travel ban was lifted, all countries having no cases in the previous 20-30 days.

Compared to the current, the outbreak was modest in scale affecting 8,110 people in 30 countries. Exceptionally, 95.5%

of the cases were concentrated in the East, with 65.5% in China and 30.0% in South East Asia. The death rate was on the high side, with 10.0% world-wide and 6.6% in China. Canada had the largest number outside the region with 251 cases and a 17.5% death rate

In May 2005, Jim Yardley of the *New York Times* wrote[65]:

> "Not a single case of the severe acute respiratory syndrome has been reported this year [2005] or in late 2004. It is the first winter without a case since the initial outbreak in late 2002. In addition, the epidemic strain of SARS that caused at least 774 deaths worldwide by June 2003 has not been seen outside of a laboratory since then."

Observations

From the first atypical case on 16 Nov 2002 to the first "super-spreader" on 31 Jan 2003, who infected 30 staff at the San Yet Sen Memorial Hospital in Guangdong, was two and a half months, with a further month before notification to WHO on 28 Feb 2003.

It is my impression that the Chinese communicable diseases fraternity were genuinely caught off guard. They knew nothing about the SARS-Covid (nobody did). Therefore, when the first outbreaks occurred, they concluded it was a novel influenza and routinely reported it to WHO to be so. It was only on the subsequent outbreak of the index case and the rampant infection of the medical staff that they (someone) reported the occurrence of a new deadly disease.

All I need say is that the GISRS influenza early warning system in China failed to identify this new bug and they took too long in trying to do so before reporting. It is hard to say if the Chinese scientific brotherhood over-sold their technical advance to their political compatriots or the whether the latter

---

65 https://en.wikipedia.org/wiki/2002–2004_SARS_outbreak

had held back their development. In the outcome, whether the latter were complicit in the delay, they had much to rue for it, for China was the most affected country in the epidemic that followed. One evidence of their frustration was the extensive reforms of the Health and CCDC system that followed, down to installation of a national web-based information reporting network.

The international scientific community responded, and passed samples around. Canada completed the DNA sequencing 12 Ap 2003. WHO identified the virus as the Coronavirus and officially named it the SARS virus on 16 Apr 2023. All this was quick work.

This epidemic brought to light that this new SARS was a highly infectious virus. Hospital staff and healthcare workers were exceptionally vulnerable, and it showed a capacity to spread along the routes of international air travel. Severe cases needed oxygen. There was no cure, and a vaccine was years still in the making.

Fortunately, the countries affected had learnt a few important things from their influenza experiences. China, Singapore (234 cases) and the other infected countries masked up, closed schools and went into lock-down. Contact tracing became the key tool. The safety manual for healthcare workers produced by the Canadians must have become the norm. Above all, I think the travel bans were the most effective instrument, both as internal controls by China and international travel bans by WHO. Fortunately, despite the delays, the outbreak was caught early enough, before it spread.

On 9 Jul 2003, the last travel ban was lifted by WHO, as all countries had no cases in the previous 20-30 days. It was remarkable that the epidemic was halted **within four months of WHO declaring it to be so, with no therapeutic drugs or vaccines discovered.** (This was even before Ebola, which would sharpen our research skills.)

I have no doubt, the epidemic's quick halt was due to its being largely in China. They have the secret of social regimentation. to snuff out pandemics, and would do so again in the first year of Covid-19..

GOARN

In a remarkably opportune move, WHO's Department of Communicable Diseases Surveillance and Response and its Regional Offices had earlier initiated the formation of an international **"Framework for Global Outbreak and Response" (GOARN).** This was adopted by 67 institutions[66] at a meeting on 26-28 Apr 2000, " to contribute resources, coordination, surveillance, and technical assistance towards combating diseases. The network was to be financed by voluntary funding.

GOARN was therefore available and running, and was put to the test in containing the 2003 SARS outbreak. WHO was notified on 28 Feb 2003 of the spread to Hong Kong and Vietnam, and notified GOARN. The first members of a WHO/GOARN outbreak control team arrived in Hong Kong 14 Mar 2003, followed by another five-person team, which transitioned to Guangdong and thence to Beijing on 25 Mar 2003.

From as far back as 1952, WHO had established a **Global Influenza Surveillance And Response System (GISRS)** to deal with flu. China joined it in 1957 and its National Influenza Centres (NICs) and WHO Controlling Center of Reference and Research in China are within the CCDC's statutory board the NVIDC. The CCDC is in turn a member of GOARN, but its problem of communicating the new bug was probably internal rather than external. GISRS continues today as is a research and Information platform and constituent member of GOARN

[66] Chinese Communicable Diseases Control and Prevention (CDC) is and could have been originally a member. WIV only opened on 31 Jan 2015.

I have little doubt that the GOARN and GISIR played critical roles in bringing Covid-1 down so fast.

(Back to TOC)

MERS-Covid

The **Middle East Respiratory Syndrome** disease was an outbreak that took place mainly in the Middle East, in 2012, 2015 and 2018. It was caused by the MERS Coronavirus **(MERS-Covid**),

All three Coronavirus Covid viruses are human pathogens under the same genera Betacoronavirus, but MERS-Covid belongs to a different subgenera *Merbecovirus,* which includes *Pipistrellus,* the bat coronavirus *HKU*5, and *Tylonycteris* bat coronavirus HKU4,

The MERS-Covid virus is also enveloped, and is encoded in a positive-sense[67] single-stranded RNA genome. While belonging to a different subgenera, its constituent design and infectious characteristics are similar to that of the other SARS-Covid.

Typical MERS symptoms include fever, cough and shortness of breath. Pneumonia is common, but not always present. Gastrointestinal symptoms, including diarrhoea, have also been reported.

Approximately 35% of reported patients with MERS-Covid infection have died.

---

67 Positive-strand RNA viruses have genetic material that can function both as a genome and as messenger; it can be directly translated into protein in the host cell by host ribosomes.

The Pandemic

The first case took place in Jeddah, Saudi Arabia Jun 2012. In Nov 2012 a sample from the first confirmed case in Saudi Arabia was sent to a Coronavirus research centre in The Netherlands and a second case was proven in a lab in London in the same year.

In May 2013, the ICTV adopted the name, the Middle East Respiratory Syndrome Coronavirus (MERS-Covid).

By May 2013, 10 of the 22 people who died and 22 of 44 cases reported were in Saudi Arabia, and over 80% were male. This gender disparity was thought to be because most women in Saudi Arabia wore veils.

By 19 Jun 2013, MERS had infected at least 60 people, with cases reported also in Jordan, Qatar, the UAE, Tunisia, Germany, UK, France and Italy, with a death toll of 38.
In May 2014, WHO said global cases appeared to be on the rise, but the situation did not yet constitute a health emergency.

On 3 June 2014, Saudi Arabia revised the country's total cases of MERS to 688 cases after re-examining the data, and a total of 282 people had died from MERS. The numbers represented a jump of 113 cases and 92 deaths. Despite the jump in reported cases, the number of new cases was on the decline.

As of June 2015, there were 1,227 confirmed human cases of MERS, resulting in 449 deaths (37% mortality).[2

MERS-Covid is zoonotic virus and has been identified in dromedaries (camels) in several countries in the Middle East, Africa and South Asia. Current scientific evidence suggests that dromedary camels are a major reservoir host for MERS-CoV and an animal source of MERS infection in humans. Studies have shown that humans are infected through direct

or indirect contact with infected dromedary camels. However, the exact role of dromedaries in transmission of the virus to humans and the exact route(s) of transmission are unknown

It has been found that the virus does not pass easily from person to person, unless there is close contact. Most of the human infections have been attributed to infections in health care settings.

As of 2020 there was still **no cure or vaccine** for MERS-CoV.

The Role of Bats

The origins of the virus are not fully understood but, according to the analysis of different virus genomes, it is believed that it may have originated in bats and was transmitted to camels sometime in the distant past.

MERS-related viruses have reportedly been found in many bat families in Africa, the Americas, Asia, and Europe. Bat Covids are however typically host specific.

MERS-Covid outbreaks have been sporadic and scattered. WHO reports that there were 2,519 cases in all up to Jan 2020, of which 1,029 occurred in Saudi Arabia, and another 114 in nine other countries in the Middle East. South Korea had a boom of 184 cases in 2015.

WHO never declared MERS-Covid an epidemic or pandemic.

Observations

This was the second major Coronavirus penetration into the human world. We were better prepared. The international response was evident, although I did not see a major role by GOARN. There would not have been heavy presence on the ground of GISRS for the Middle East was not scheduled Influenza country.

Overall I it would appear that the outbreak was tame and the virus relatively still unskilled. They targeted the populations with nomadic traditions and one might suspect the migratory workers in the region, and they came close the world's largest annual gathering of people, the 2.5 million pilgrims who do the haj in Jul.

I have no reason to underplay their group-sensing, and not believe they could and would strike the latter one of these days – if we have not taken the necessary measures to forestall them. As presently operated, the outbreak notification and first response mechanisms of GISRS are too lambent and depend on the goodwill of the country of origin. Notice having now been given by MERS, we can expect both GOARN and the new GISAID to stand sentinel.

Three factors remain unresolved at the end of MERS. We have not found out how bats infect camels. We have not found out how camels infect humans. And we have not found out how bats infect humans. and still do not know how the virus was transmitted to humans.

(Back to TOC)

* *. *

PART THREE

A. The Covid-19 Pandemic

Hereon and in this document, unless otherwise stated –

.- “SARS-Covid-2” is the bug, and
.- “Covid -19” is the pandemic.

In this Part 3, we try to comprehend in some detail first what happened, and mankind’s preparedness and response.

This Part is accordingly divided into the following sub-parts:

PART 3A	The Covid-19 Pandemic
PART 3B	Country of Origin, Outbreak
PART 3C	WHO & Global Mobilisation
PART 3D	Covid-19 Tools (ACT - Accelerator)

The SARS-Covid-2 virus is a member of the Coronavirus family. It is responsible for the current horrendous **Severe Acute Respiratory Syndrome (SARS-Covid-19)** pandemic in humans.

For convenience purposes, I have placed the information component of this topic separately in Part 1 – Summary of Current Knowledge. (Read first).

The Pandemic

We have a Monster

In this day and age, the Coronavirus, in the form of the SARS-Covid-19 pandemic, has become a BEAST. It is a predator of proportions beyond the imaginings of the most ferocious computer games. We have is a Monster.

It is the most globally massive and sustained pandemic in modern times, with infections in every country of the world, and still on-going at an infernal rate.

Because it has happened in modern times of our tightly interlocked global economy and our dependence on massive movements of people and goods, the pandemic has brought the world to near standstill.

Rampage

The outbreak was officially notified to WHO on 31 Dec 2019. As at 22 Jun 2021[68], the tally globally is summarised in Table

Table 8

The Covid-19 Pandemic

Global Casualties Selected Data 2020-21*

Date	Cumulative No Infected	Cumulative No Deaths	Cumulative No Cured	No New Cases per day	No Cured per day
22 Jan	987	17			
14 Feb	67,773	1,672	8,197	14,180	
25 Mar	533,655	22,196	115,182	48,777	5,979
15 Apr	2,207,487	152,963	613,946	86,889	42,230
31 May	6,505,290	415,075	3,397,820	111,642	123,524
30 Jun	10,919,764	567,835	6,665,303	181,562	134,031
30 Sep	34,874,474	1,097,498	27,213,895	321,281	309.842
31 Dec	83,877,856	1,922,820	66,027,390	761,657	526,861
31 Mar	129,297,269	2,936,059	110,976,314	645,854	523,494
22 Jun	179,920,602	3,898,327	164,678,028	376,713	419,978
PEAKS					
7 Jan 21				843,055 (peak)	
20 Jan 21					631,871 (peak)
29 Apr 21				903,386 (peak)	
4 May 21					898,102 (peak)

*. -Data from https://www.worldometers.info/coronavirus/worldwide-pgraphs/#total-cases

We may observe that the situation was as follows:

,(a)- The total number of persons infected was nearly 180 million, and the total number who recovered was 165 million

.(b)- The total number of deaths was nearly 3.9 million, giving a gross mortality rate of 2.17%, with the total number remaining sick 1.1 million.

[68] Time of writing.

.(c) – There were two daily peaks of new cases, of 843,055 on 7 Jan 21 and 903,386 on 29 Apr 21, then droppingly to 376,713 on 22 Jun 21

.(d)- There were two daily peaks of cured/discharged persons, 631,871 on 20 Jan 21 and 898,102 on 4 May 21, dropping to 419,718 on 22 Jun 21.

.(e)- Overall, it may just be possible to discern the glimmer of a decrease in the rate of the overall infections curve.

For a closer look I have captured selected regional and country profiles to indicate the impact of the pandemic in various quarters:

Table 9

Covid-19 Pandemic (Selected)

Regional and Country Casualties (with Peak Data), Jun 2021*

WHO Region	**Date**	**Cumulat -ive No Infected**	**Cumulat -ive No Deaths**	**Peak No Infected per day**	**Peak Cases Date**
Americas	22 Jun 21	71,232,746	1,873,241	356,571	7 Jan 21
USA	23 Jun 21	33,243.529	597,372	250,135	13 Dec 20
Brazil	24 Jun 21	17,966,831	502,586	90,638,	2 Apr 21
Europe	22 Jun 21	55,473,875	1,176,552	58,913	15 Apr 21
France	24 Jun 21	5,651,293	109,924	69,989	1 Nov 20
Russia	24 Jun 21	5,368,513	130,895	29,018	25 Dec 20
UK	24 Jun 21	4,651,992	128,008	70,797	1 Jan 21
Italy	24 Jun 21	4,254,294	127,322	37,802	13 Nov 20
South East Asia	22 Jun 21	34,264,715	476,887	387,306	10 May 21

India	24 Jun 21	30,028,709	390,660	403,738	9 May 21
Indonesia	24 Jun 21	2,033,421	55,594	20,574	24 Jun 21
Eastern Mediter	22 Jun 21	10.793,326	213,897	59,627	9 Apr 21
Iran	24 Jun 21	3,117,336	83,217	58,913	15 Apr 21
Iraq	24 Jun	11,298,703	16,935	8,208	21 Apr21
Saudi Arabia	24 Jun 21	476,882	7,703	4,301	20 Jun 21
WHO Region	**Date**	**Cumulative No Infected**	**Cumulative No Deaths**	**Peak No Infected per day**	**Peak Cases Date**
Africa	22 Jun 21	3,852,707	92,719	30,698	7 Jan 21
South Africa	24 Jun 21	1.843,572	59,092	18,400	1 Jan 21
Zambia	24 Jun 21	133,659	1,744	3,367	24 Jun 21
Western Pacific	22 Jun 21	3,447,690	53,038	21,434	28 May 2
Philip-pines	24 Jun21	1,367.879	23,809	15,280	3 Apr 21
Japan	24 Jun21	787,650	14,496	6,076	7 Jan 21
Malaysia	24 Jun 21	705,762	4,554	7,857	28 May 21
China	24 Jun 21	117,758	5421	3,697	6 Feb 20
Singapore	24 Jun 21	62,448	35	942	26 Apr 20
Australia	24 Jun 21	30,366	910	602	1 Aug 20
Global**	24 Jun	178,842,997	3,880,698	300,491	

*. https://covid19.who.int/table?tableDay=yesterday

**. The Global Totals in Tables 5 and 6 differ slightly as they are from different sources, with no doubt different update routines.

As at 21-22 Jun 21, we may observe the following:

.(a)- Of the WHO Regions, the Americas were hardest hit with 39.2% of the infections and the Western Pacific the least hit with 1.9%.

.(b)- USA was the hardest hit country with 33,243.529 infections and 597,372 deaths.

.(c)- China (Country of Origin) had only 117,758 infections and 5421 deaths, while Japan had 787,650 infections and 14,496 deaths.

.(d)- The pandemic had two peaks. Generally the larger developed countries peaked in Dec 20 – Jan 21, with Italy first in Nov 20. The second wave peaked in Apr-May 21, covering countries in South East Asia, Middle East and Africa, in particular India which led the wave. Some, for example Indonesia, were still increasing in Jun 2021.

I have decided to take a close look at how it all began, how prepared we were and whether the responsible parties and entities played their parts to work the defence systems available in this advanced technological age.

(Back to TOC)

B. Country of Origin, Outbreak

Co-operative Responsibility

Under the existing International Health Regulations (IHR) 2005, each country is responsible for dealing with an outbreak within its borders, assisted as requested by the World Health Organisation (WHO). Where an outbreak crosses borders, it becomes a world problem. Then, WHO, as the UN Specialised Agency concerned, has the prime responsibility to combat the epidemic or pandemic. and leads and co-ordinates collective action. But it needs the consent of a country when acting within its borders.

It may be said that a country and WHO share a joint responsibility to see that an outbreak does not cross the border and start a world pandemic. To that extent, a country has a co-operative duty to notify WHO as soon as a threat exists. WHO in turn has the responsibility to monitor, assess, and confirm the situation, and if so to declare an emergent threat of concern. Thereon, it is incumbent on WHO to launch supportive actions externally and within the country.

In practice, most countries have a centre for disease control and prevention (CDC). The CDC will, in essence, have total command and operational responsibility to nail an outbreak and eradicate it, and to prevent a repeat. For most countries, the CDC (or its equivalent) will be designated the country's focal point for WHO.

The CDC will inevitably comprise divisions dealing with different diseases on the ground. Each will have departments and offices covering different aspects of prevention and control. In a large country, the CDC will have a backbone of CDC bureaus, offices and outposts at provincial, prefectureship, district and county levels, with hospitals,

screening and testing centres, diagnostic labs, and other facilities distributed under them.

A good CDC will have a good internal surveillance, MIS and response systems. It is NICs will be component-members of GISRS. These features enable the WHO to get to root of an infection or outbreak through the CDC.

A CDC will have higher level functions, ie policy making, planning, and performance review. It will also be concerned public education and social behaviour. WHO will be essentially advisory and supportive in these areas.

Large countries will have many institutes, universities, and independent agencies dealing with more in depth areas of investigation and research: genotyping the virus, studying how it mutates, and discovering its source, how it transited to the population, and any reservoirs around. These will be closely interlinked with the CDC and in practice work closely with the parallel infrastructures of WHO and related external agencies.

(Back to TOC)

Historical Perspective

The Country of Origin plays a crucial role in the identification, reporting and initial curtailment of an outbreak, in this case China. Therefore, understanding its previous experience, set-up, and performance capability is a major component of understanding Covi-19.

Historical Perspective

When the Peoples Republic of China (PRC) came into being. on 1 Oct 1949, its population was 570 million, almost wholly rural. It became a closed economy and society, cut off from the outside world. It was admitted into the UN on 25 Oct 1971.

After Chairman Mao died on 9 Sep 1976, China began marketising its economy from the early 1980s, initiating the current economic growth.

The following is extracted from a BBC report dated 28 Feb 2021[69] summarising the World Bank's latest review of China's social and economic progress

> "In 1990 there were more than 750 million people in China living below the international poverty line[70] - about two-thirds of the population.
>
> By 2012, that had fallen to fewer than 90 million, and by 2016 - the most recent year for which World Bank figures are available - it had fallen to 7.2 million people (0.5% of the population). https://www.bbc.com/news/56213271

At 1.44 billion, China's population is 18.5% of the world population in 2021.

China is now an upper-middle-income country, says the World Bank.[71] Its per capita GDP in 2020 was $10,401.8[72] compared to India at $1,900.7, Malaysia at $10,400.2, Singapore at $59,797.8, and USA at $63,543.6.

The CDC[73] Historical Perspective

Considering the tumultuous internal conditions, the lack of external communications, and its scale, China's record of fighting infectious diseases and health improvement over the "closed" years was remarkable. I make no excuse for quoting extensively from this rare and **excellent** study of 2011

---

69 https://www.bbc.com/news/56213271

70 The poverty line used by the World Bank is USD 1.90 a day. Poverty is defined by China as anyone in rural areas earning less than about $2.30 a day (adjusted for inflation).

71 https://data.worldbank.org/indicator/NY.GDP.PCAP.CD

72 $ = USD in this document.

73 CDC = "communicable disease control"

Communicable disease control in China: From Mao to now[74]
David Hipgrave, 1 Dec 2011

Abstract

The political turmoil and slow socioeconomic development in China between 1949 and 1978 obscure its impressive progress in population health during those years.

"China's progress on communicable disease control (CDC) in the 30 years after establishment of the People's Republic in 1949 is widely regarded as remarkable.

Life expectancy soared by around 30 years, infant mortality plummeted and smallpox, sexually transmitted diseases and many other infections were either eliminated or decreased massively in incidence, largely as a result of CDC.

Early efforts in public health included work on vaccination, environmental sanitation and hygiene (including the early introduction of composting of night-soil to reduce the concentration of intestinal parasites) and the development of organized CDC[75] programs. Incredibly, between 1950 and 1952, over 512 of China's 600 million people were vaccinated against smallpox, massively reducing case numbers; the last outbreak of smallpox in China occurred in 1960, 20 years before global eradication.

By 1957, more than two-thirds of China's then 2050 counties had an epidemic prevention station (EPS) or more specialized centres for the control of specific diseases (such as malaria, plague, schistosomiasis, leishmaniasis and brucellosis) modelled on those established in the Soviet Union earlier in the 20th century.

Their efforts included "patriotic health campaigns" focusing on ensuring a clean environment and safe drinking water, vector control, latrine construction and human waste disposal.

Other nascent disease control programs emerged. As a result, cases of typhus dropped by 95% in the 1950s, and there were

74 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3484775/
75 CDC = "communicable diseases control"

also major attempts to control gonorrhoea and syphilis,… first with imported and then domestically produced penicillin.

Vaccination and campaigns against diphtheria and tuberculosis (TB) also commenced in the 1950s. In the late 1950s, another campaign to “exterminate the four pests” (sparrows, rats, flies and mosquitoes) was avidly implemented, albeit with major negative results when the exploding locust population decimated crop harvests, contributing to famine from 1958-1960.
The 10-year Cultural Revolution from 1966 brought many hardships, but also clinical care and continuing public health programs to the masses through community-funded medical schemes and the establishment of community-based health workers.
“
in 1966 Mao launched the Cultural Revolution, throwing China into a ten-year period of political and economic chaos. One positive element of this period, however, was the establishment of a village level cooperative medical scheme (CMS) managed by “barefoot doctors”, a new cadre of community-level health worker who brought basic curative care, health education and a continuous rather than campaign-style public health approach to rural peasants

China’s barefoot doctors rose in number from around one million in 1970 to a peak of around 1.8 million in 1977. Many barefoot doctors were selected from, functioned in the context of, and were largely funded by local production brigades (roughly 1000-2000 people in a geographic area) or teams (200-400 people). These brigades had replaced the failed, larger communes established during the Great Leap years, and apart from their commitment to providing grain to the national coffers at fixed prices, were semi-autonomous.

The roles of the barefoot doctors and health aides included environmental sanitation, health education, disease screening, surveillance and control, basic clinical care or referral and family planning. CDC continued to benefit from management of water sources and disposal of human excreta (including through composting), improvements in wells, toilets, stables, cooking areas and the local environment, and specific disease control programs through reducing stagnant water, spraying and other measures to control flies, fleas and mosquitoes.

These people-focused approaches broke down with China's market reforms from 1980. Village doctors turned to private practice as community funding ceased, and the attention paid to rural public health declined.

CDC relied on vertical programs, some of them successful (such as elimination of lymphatic filariasis and child immunisation), but others (such as control of schistosomiasis and tuberculosis) demonstrating only intermittent progress. In addition, China's laissez-faire approach to public health placed it at great risk, as evidenced by the outbreak in 2003 of the Severe Acute Respiratory Syndrome.

Since then, major changes to disease reporting, the priority given to CDC including through major new domestic resources and reform of China's health system offer encouragement for CDC. While decentralized funding and varying quality diagnosis, reporting and treatment of infectious diseases remain major challenges, national priority on CDC in China is high."
(Slightly edited, and with some paragraph transpositions)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3484775/

Malaria Free

We might mention here that China has eradicated Malaria. WHO declared it free on 30 Jun 2021, after implementation of a model 10-year Action Plan.[76] .China used to report 30 million cases a year during the 1940s.

Earlier Viral Pandemics

It seems to be now established that the first Influenza pandemic (H1N1) originated in USA, was carried over into World War 1, and thence world-wide, including China.
This species has established itself since as an annual pandemic, again word-wide, with separate seasons in winter in the North and South, including China. The latter in fact has a third "double" season at mid year in the middle kingdoms.

[76] https://idpjournal.biomedcentral.com/articles/10.1186/s40249-021-00882-9

It would appear that China was the country of origin of the next two Influenza pandemics, the Asian Flu (H2N2) of 1957-58, and the Hong Kong Fu (H3N2) of 1968-9. . These were early days on both sides of the Cultural Revolution, and before China's entry into the international world. No much information is available for the "closed" period.

After re-joining the world system, the SARS-Covid pandemic of 2002-3 was the first pandemic, which I covered earlier.

China joins WHO .

China joined the UN and WHO on 25 Oct 1971. China has been placed in WHO's Western Pacific Region. The latter embraces nearly 1.9 billion people in 37 countries and territories. The Regional Office is located in Manila, Philippines and there are 15 country offices. The Region extends from the Pitcairn Islands to Mongolia, and includes Singapore**.**

WHO has Country Offices world-wide. Each office has a Representative (WR) and is staffed by experts and supporting staff, both foreign and local. Countries without a WHO office are covered by nearby field offices or by the appropriate regional office. The WR is responsible for execution of WHO's programmes for the country and accounting for the same.

The functions of WHO country offices include being the primary adviser to that country's government in matters of health and pharmaceutical policies.

WHO's China Representative is Dr Gauden Galea, since April 2018. The country office is based in Beijing.

(Back to TOC)

China's Responsibility Framework

In the reforms of 2013 the Ministry of Health was integrated into a new National Health and Family Planning Commission. The responsibilities of the latter included disease prevention and treatment, and epidemics, In 2018 the latter was integrated in a new Cabinet-level **National Health Commission** (NHC).

Chinese CDC

The Chinese Centre for Disease Control and Prevention **(CCDC)** is an independent agency[77] of the NHC, based in Beijing. First established in 1983, the CCDC focused national attention on the developing infectious threats and applying prevention and control measures. CCDC additionally promoted health through partnerships with provincial health departments and other organizations.

The CCDC organisation chart resembles the familiar military command set-up of line and support. It has a brace of headquarter divisions typical of a mega-organisation, 11 line units comprising centres and institutes and 10 support independent legal[78] entities:

. Headquarters
. 20 administrative and service divisions.
. Centers and Institutes
. 1 National Institute for Communicable Diseases Control Prevention
. 2 National Institute for Viral Diseases Control and Prevention
. 3 National Institute for Parasitic Diseases
. 4 National Center for AIDS/STD Control and Prevention
. 5 National Center for Chronic/Non-Communicable Diseases
. 6 National Institute for Nutrition and Health
. 7 National Institute for Environmental & Product Safety
. 8 National Institute for Occupational Health & Poison Control

---

77 Probably a "statutory board" in Singapore language.
78 Probably a "statutory board.

. 9 National Institute for Radiological Protection
.10 National Center for Rural Water Supply (Guidance)
.11.Centre for Women's Children's Health
. Independent Legal Entities
. 1 Division of Infectious Diseases
. 2 Office of Tobacco Control
. 3 National Center for Management of Hotline (12320)
. 4 Office of Epidemiology
. 5 The Public Health Emergency Center
. 6 National Center for TB Control and Prevention
. 7 Office of NCD Control and Community Health
. 8 National Immunisation Programme
, 9 National Center for Public Health Surveillance and Information
. 11 Center for Global Public Health

The CCDC's heavily inter-woven responsibilities are carried out by means of a tiered structure on the ground, comprising CDC Health Bureaus located at the province, prefecture, city and country levels, where they inter-mesh through the corresponding health authorities with the hospitals and monitoring centres, and through the latter right down to the township/village prevention and control units.

The National Institute for Viral Disease Control and Prevention **(NIVDC),** China's long-standing agency dealing with infectious diseases, was placed under the CCDC. See further on.

In Aug 2004, China took a major step forward with the revision of the Law on Prevention and Treatment of Infectious Diseases, This now mandated the reporting of 37 notifiable conditions, including immediate reporting of certain diagnoses. It replaced a system which had essentially become optional and mainly answerable to local government. As a result, CDC was now mainstreamed in China's health sector with both the curative and disease-control sectors responsible for prevention, and the reporting and management of infectious diseases.

The CCDC administers a number of laboratories across China, including the Bio-Safety Level 2 lab the **Wuhan Center for Disease Control** (not to be confused with the nearby Wuhan Institute of Virology). Their ongoing research includes screening and testing of emerging infectious diseases, key biological factors on AIDS transmission, and evaluation of the epidemic characteristic and prevention of SARS.

The CCDC and two of its institutes are members of the Global Virus Network (GVN), a coalition of leading virologists spanning 63 Centres, 11 Affiliates, and 35 countries working to advance knowledge of viruses and to develop drugs and vaccines.

The Division of Infectious Disease Prevention and Control (DID) is a technical department at the headquarters. DID coordinates the roles and responsibilities of national surveillance, early warning, outbreak investigation, and prevention and control response

The backbone of the upgraded national public health system was the **National Information System for Disease Control and Prevention (NISDCP)** operationalised in 2006. It is based on an on-line web-based National Disease Reporting System **(NDRS)** between the National and Provincial Health Commissions, which covers the entire population of China linking reporting nodes and users at all levels horizontally and vertically across the country.

National Administration of Disease Prevention and Control

On 13 May **2021**, China inaugurated a **National Administration of Disease Prevention and Control,** with five major functions including formulating policies for the prevention and control of infectious diseases.
The establishment of the national administration marked a key step toward deepening reform of the country's disease prevention and control system and enhance the country's

epidemic response capacity. The administration is a vice-ministerial level agency managed by the National Health Commission (NHC).

The administration is clearly aimed at strengthening the national framework at the policy, planning and implementation review levels. It will also steer the development of the disease prevention and control system, the epidemic monitoring and early warning system, and the scientific research system.

The administration is mandated to establish relevant institutions at the national, provincial, prefectural and county levels. while strengthening the leadership of the higher-level control agencies over the lower-level ones and improving their work coordination.

Finally, the administration is expected to set up a network of tiered and classified public health emergency response teams, developing new mechanisms for enhancing coordination between disease prevention and control agencies and hospitals, boosting scientific research in the field and improving the consultation system for decision making.

National Institute for Viral Disease Control and Prevention (NIVDC)

The National Institute for Viral Disease Control and Prevention **(NIVDC)** is an independent legal institution which belongs to CDC, with an excellent academic tradition and strong scientific research ability.

NIVDC has a long standing reputation in the field of medical virology, bearing four functions: emergency response, disease control and prevention, scientific research, and education and training.

NIVDC has several WHO Collaboration Centres and Laboratories, including:

.a WHO Influenza Collaboration Reference Center
.b WHO Western-Pacific Region (WPR) Polio Reference Laboratory
.c WHO WPR Measles and Rubella Reference Laboratory,
.d WHO WPR Japanese Encephalitis Reference Laboratory, and
e. WHO WPR Rotavirus Reference Laboratory, Chinese Center for

NIVDC has won many honours including the honours of national advanced group of Medical and Health, the national advanced group of Ebola epidemic prevention and control and the highest State Science and Technology Award in 2017.

Chinese Academy of Sciences

The Chinese Academy of Sciences (CAS) is the national academy for the natural sciences, which status it occupies together with the Chinese Academy of Engineering (CAE), the two being referred to together as the “The Academies”.

It functions as the national scientific think-tank and academic governing body, providing advisory and appraisal services. It is headquartered in Beijing, with branch institutes all over China. **It has also created hundreds of commercial enterprises,** Lenovo being one of the most famous.

It is the world's largest research organisation, comprising around 60,000 researchers working in 114 institutes.
The Chinese Academy of Sciences has been consistently ranked the No. 1 research institute in the world by Nature.

The Chinese Academy of Sciences has six academic divisions and 13 regional branches. It has over 100 institutes and two universities. These CAS branches and offices are located in 20 provinces and municipalities throughout China. CAS has invested in or created over 430 science- and technology-based enterprises in 11

industries, including eight companies listed on stock exchanges.

The Wuhan Branch has seven institutes, including the **Wuhan Institute of Virology** with its Bio-Safety Level 4 lab, not too far from the CDC's Bio-Safety Level 2 lab at the **Wuhan Center for Disease Control.**

[The National Space Science Center (NSSC) of the Chinese Academy of Sciences (CAS) has been responsible for China's space science satellite missions (including their three latest astronauts to the Tianhe module on 17 Jun 2021]

Wuhan Institute of Virology CAS (WIV)

Wuhan Institute of Virology (WIV) of the Chinese Academy of Sciences (CAS) was founded in 1956.

Currently, WIV consists of 4 research centres, namely the Center for Molecular Virology and Pathology, the Center for Emerging Infectious Diseases, the Center for Analytical Microbiology and Nanobiology and the Center for Microorganisms Resources and Bioinformatics.

Relying on its cluster of high-level biosafety laboratories, WIV focuses on basic and applied research in virology, immunology, biotechnology, etc.

Meanwhile, it strives to make breakthroughs in cutting-edge research on pathogens of emerging infectious diseases, and to enhance its ability to provide technological support for emergency response to emerging infectious diseases.

It has one of the only two[79] Bio-Safety Level 4 (BSL4) labs in China. It was built following the SARS-Covid epidemic of

[79] China's other biosafety level-4 lab (BSL-4) is located at the Harbin Veterinary Research Institute CAS, also launched 2018. It is for research involving large animals.

2002-03, in collaboration with the Jean Mérieux-Inserm Biosafety Level-4 Laboratory in Lyon, France. It came on-line in 2018. In addition WIW possesses 20 Level 3 (BSL3) and two Level 2 (BSL2) lab facilities

The institute is one of nine independent organisations in the Wuhan Branch of the CAS. **The institute is a lead centre for the study of coronaviruses. It has become a premier centre for the study of bats, with particular reference to their role in hosting and transmitting viruses.** WIV has been called a "world-class research institution that does world-class research in virology and immunology"[80]. WIV is a member of the Global Virus Network (GVN)[81].

(Back to TOC)

The Outbreak

Origins

In Nov 2019, the US National Center for Medical Intelligence was reported in the media to have informed the White House of the impending Covid-19 pandemic in Wuhan, China. I do not disbelieve either the report or the official denial. There have been assessments since that the virus was circulating among humans there from possibly as early as Oct 2019.

On 1 Dec 2019, the index case or first hospital patient with the symptoms was recorded.

On 8 Dec 2019, Wuhan Health Committee reported 41 people were confirmed positive with the sickness. Another six were diagnosed by 15 Dec 2019

---

[80] Richard H. Ebright, American molecular biologist. Professor of Chemistry and Chemical Biology at Rutgers University and Laboratory Director at the Waksman Institute of Microbiology

[81] Global Viral Network, see https://gvn.org/about/

On 16 Dec 2019, the preceding were logged in as the first cases of the pandemic in Wuhan (retrospectively on 20 Feb 2020).

On 24 Dec 2019, an unresolved sample was sent by Wuhan Central Hospital to Vision Medicals, in Guangzhou.

On 28 & 29 Dec 2019, the Hubei Provincial Hospital of Integrated Chinese and Western Medicine admitted seven cases. The hospital immediately alerted the Wuhan Jiangshan CDC, which took over six of the patients. The hospital also reported to the Wuhan Municipal Health Commission and the Hubei Province Health Committee.

On 30 Dec 2019, Wuhan Central Hospital received confirmation from Vision Medicals that their sample was the SARS coronavirus. There were seven cases at the hospital, all connected to the Huanan Seafood Wholesale Market.

On 30 Dec 2019, Wuhan Health Commission sent a hard-copy message to its affiliate institutions containing guidelines in confronting a possible outbreak of infectious pneumonia. Apparently there was mention of 27 cases. Apparently the message was also put on their or a website. This the first indication of the newly created National Health Commission (NHC), taking control of things.

The Chinese media (CCTV) picked up the news and so did social media (Weipo).Through its account on the latter, CCTV added that a team from the National Health Commission (NHC) would be visiting Wuhan soon.

The international media, Flu Tackers and Pro-MED mail picked up the news the same day, And **finally**, so did the WHO China, which relayed it to the Western Regional Office, and on to the US CDC.

On 31 Dec 2019, WHO was officially notified by the Wuhan Municipal Health Commission that there was an unidentified infectious outbreak in China. This again seemed done on behalf of the NHC.

Phylogenetic analyses would in due course estimate that SARS-CoV-2 first arose in October or November 2019, evolving from a coronavirus that infects wild bats and spreading to humans through an intermediary wildlife host.

While the first patient began to show symptoms as early as 1 Dec 2019, later research determined that a cluster of cases was not discovered until the end of December. Retrospective study would later indicate that 266 people had been infected before the beginning of 2020.

China's Initial Responses

On 3 Jan 2020, the Chinese National Institute of Viral Disease Control and Prevention (NIVDC) ruled out other known virus and **isolated the genetic sequence** of the novel β-genus coronaviruses (naming it '2019-nCoV') from specimens collected from patients in Wuhan, China, and three distinct strains were established.

Obviously now in full control, the National Health Commission (NHC) ordered institutions not to publish anything, send all samples to designated institutions or destroy them.

On the same day, Chinese officials informed the US at the White House of the outbreak, reportedly saying "this outbreak is a very big deal".

On 4 Jan 2020, the WHO China Office was briefed. US CDC formally offered to help.

On 7 Jan 2020, the NIVDC confirmed the novel coronavirus isolated on 3 Jan was the pathogenic cause of the viral pneumonia of unknown etiology (VPUE) cluster, and designated the disease as **a novel Coronavirus-infected pneumonia.** China announced the discovery of a new Coronavirus

On 9 Jan 21, WHO confirmed that the novel coronavirus had been isolated from one person who had been hospitalised. WHO reported that China had acted swiftly.

On 10 Jan 21The three genetic sequences of the isolated novel coronavirus, one from the CCDC, one from the Chinese Academy of Medical Sciences and one from Jinyintan Hospital in Wuhan, were posted to the Global Initiative on Sharing All Influenza Data (**GISAID**) portal. The gene sequencing data of the isolated 2019-nCoV was also posted on Virological.org by researchers from Fudan University, Shanghai.

The first patient outside Wuhan occurred on the above date , in Shenzhien, Guangdong.

On 11 Jan 2020, China shared the genetic sequences with WHO, and the Shanghai Public Health Clinic. Centre through the Wuhan Institute of Virology released the data to GenBank and Virology.org.

The first case outside China occurred on11 Jan 20, in Thailand.

12 Jan 2020, WHO said that "The Chinese government reports that there is no clear evidence that the virus passes easily from person to person".

On 14 January, The Wuhan Municipal Health Committee published a Q&A regarding the coronavirus, stating:

"current investigation hasn't found clear evidence of human to human transmission, however, the possibility of human to human transmission cannot be ruled out".

There were no new cases in Wuhan for two weeks and no lock-downs; only minimal measures.

On 17 Jan 2020, an epidemiological team from Beijing led by renowned Chinese scientist Zhong arrived in Wuhan and began an investigation into the epidemic. Officials reported 17 additional laboratory-confirmed cases, three of which were in critical condition. This brought the number of laboratory-confirmed cases in China to 62.

On 19 Jan 2020, the first confirmed cases were reported outside Wuhan, one in Guangdong and two in Beijing.

Wuhan reported 136 additional laboratory-confirmed cases, bringing the total number of laboratory-confirmed cases in China to 201. A new death was also reported in Wuhan, bringing the total number of fatalities in China to three.

On 20 Jan 2020, after two of their staff were infected, the NHC were able to confirm that the virus was now transmitting from human to human,

Public Health Emergency of International Concern (PHEIC)

Five attendees of a Singapore conference tested positive; one from Malaysia, two from S. Korea and two from Singapore. One attendee came from Wuhan. These cases were the first evidence that the coronavirus had spread through human to human contact outside China.

On 20-21 Jan 2020, WHO experts from its China and Western Pacific regional offices conducted a field visit to Wuhan. On

22 Jan 2020 the mission issued a statement saying that there was evidence of human to human transmission in Wuhan but more investigation was needed to understand the full extent of transmission.

On 21 Jan 20, the Communist Party's Central Political and Legal Commission called for the public to be kept informed. Deception, it warned, could "turn a controllable natural disaster into a man-made disaster".
[
On 22 Jan 20, the total number of laboratory-confirmed cases in China increased to 571 and the death toll to 17. Hong Kong reported its first case.

On 23 Jan 2020, city of Wuhan was placed on quarantine, no traffic in or out. By the end of the next day, the entire Hubei province had gone under a city-by-city quarantine, apart the forestry districts.

Zhou Xian-wang, the mayor of Wuhan, admitted that his team had not released information about the virus in a "timely" manner, resulting in over 5 million people having travelled out of the city before Wuhan was placed in quarantine. Zhou cited “party-reporting mechanisms", indicating that Wuhan needed authorization from the central government before they could make any announcement regarding the virus.
On 26 Jan 2020, CCDC started developing vaccines against the coronavirus

On 27 Jan 2020, Beijing suffered its second death.

On 28 Jan 2020, a senior WHO delegation visited China for further discussions

On 31 Jan 2020, WHO finally declared the virus was a Public Health Emergency of International Concern (**PHEIC)** and advised "all countries should be prepared for containment,

including active surveillance, early detection, isolation and case management, contact tracing and prevention of onward spread of 2019-nCoV infection, and to share full data with WHO."

As at that date there were 7,818 confirmed cases world-wide, with the majority of these in China and 82 cases reported in 18 countries outside China.

On 30 Jan 2020, cases had now been confirmed in all 31 provincial divisions of mainland China, with the first case in India.

On 10 Feb 2020, within 11 days of notification to WHO, China's deaths of 908 surpassed the 774 of SARS-Covid1 in 2002-03.

The Pandemic

On 6 Mar 2020, WHO issued COVID-19 Preparedness and Response Status for Countries, Territories, and Areas as at Mar 20. **On 11 Mar 20, WHO declared SARS-19 a pandemic**. Let me here simply update the total figures as at 9 Jul 2021, as I write this:

Table 10

SARS-Covid-19 Pandemic

Global Casualties Selected Data 9 Jul 2021*

Date	Cumulative No Infected	Cumulative No Deaths	Cumulative No Cured	No New Cases per day	No Cured per day
22 Jun 21	179,920,602	3,898,327	164,678,028	376,713	419,978
10 Jul 21	186,841.356	4,045,177	170,891,141	490,098	363,202

*. -Data from https://www.worldometers.info/coronavirus/worldwide-pgraphs/#total-cases

(Back to TOC)

C. WHO & Global Mobilisation

WHO Framework

The World Health Organisation (WHO), composed of 194 member states, was established in 1948. It is the UN Specialised Agency responsible for promoting human health, for "the attainment by all peoples of the highest possible level of health". A large part of this is defining the standards and norms of well-being, and advocating the same. At an intermediate level, it prescribes and regulates health behaviour for the common good. At the ground level, it is responsible for ensuring that the health of the world is not threatened by, among other things, infectious diseases.

WHO headquarters has an entire division responsible for Health Emergencies, with two sub-division dedicated to dealing with Emergency Preparedness and Emergency Response.

In the battle against communicable diseases, WHO has played a leading role in several public health achievements, most notably the eradication of small-pox and near eliminating polio. It has also featured similarly in the suppression of the major viral epidemics and pandemics including Influenza, HIV/AIDS, Ebola, and the early Coronaviruses. WHO has additionally waged long drawn out wars against Malaria, TB and Cholera.

Regions

WHO has six regional divisions, created to meet the special needs of each area. Each regional committee of WHO consists of all the Health Department heads in all the governments of the countries that constitute the region.

The regional committee is in charge of setting the guidelines for the implementation of the health and other policies of the WHO.

International Health Regulations (IHR)

The International Health Regulations (2005), the IHR was the first emphatic effort of the world community to establish an adequate legal framework for common action against the growing onslaught of global infectious diseases. It followed from the experiences of the SARS-Covid pandemic of 2002-3..

The IHR (2005) had as its purpose "to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade”

Adopted by the fifty-eighth session of the World Health Assembly (WHA) in 2005 in a thoroughly revised form compared with the previous version initially adopted in 1951, the IHR is legally binding under Articles 21 and 22 of the WHO's Constitution on member states. Two states not members of WHO (the Holy See and Liechtenstein) have also acceded to the Regulations.

When the IHR came into force in 2007, it was described as . "the result of experience gained, and lessons learned during the past 30 years."

The IHR embodies paradigm several shifts as compared to the predecessor regulations, especially:

. – (1) from a narrow list of only three diseases to a broad all-hazards approach, based on risk assessment and event-based surveillance

. -(2) from an exclusively state-based reporting and notification system to the use by the WHO Secretariat of non-governmental sources for surveillance and detection in addition to state-based reporting and notification;

. (3) from a passive to an active and structured mandate for WHO to alert the world to "public health emergencies of international concerns" and to issue of "Temporary Recommendations" (PHEICs)

. (4) from a rigid system of maximum measures that states may deploy to control outbreaks to a more flexible system based on an assessment of the overall context.

. (5) from non-existence of provisions regarding the internal capacity of states to prepare for and respond to outbreaks (e.g. laboratory capacity, referral and reporting mechanisms, effective logistical assistance) to legal obligations on states parties to establish so-called "core capacities" in the areas of disease surveillance and response.

In terms of compliance, the IHR relies on reports provided annually by states themselves. There is no independent audit.

The IHR outlines the criteria to determine whether or not a particular event constitutes a “public health emergency of international concern”. However, it provides no compulsory inspections.

All cases of the following four diseases must be automatically notified to WHO: smallpox; poliomyelitis due to wild-type poliovirus; SARS; and cases of human influenza caused by a new subtype.

Again, the IHR left it to the country to identify what the disease it was that was infecting them. Some would say, this was plain dumb.

Next, the IHR requires countries further:
- to designate a **National IHR Focal Point** for communications with WHO, and
.- to establish and maintain core capacities for surveillance and response, including at designated points of entry.

Again, the IHR failed to include the simple requirement that each country should inform everybody else and provide for cross enquiries and consultations. In a business like this, it is good for neighbours to know and help one another.

Ladtly, the IHR makes no mention about who pays for the international costs of fighting off a pandemic. In my review of the WHO budget (see furth on) I found WHO depended on charities to implement its regular programmes – not excluding implementing the IHR.

A set of international regulations which purports to be a contract to protect the world, but has no enforcement powers and depends on raising voluntary contributions from external charities is really no working agreement at all.

(Back to TOC)

WHO General Programme of Work 2019-23

Sustainable Development Goals+

In 2015, the UN charted its agenda for Transforming the World by 2030 through 17 Sustainable Development Goals[82]. WHO's domain lay in the following:

---

82 https://sustainabledevelopment.un.org/content/documents/21252030%20Agenda%20for%20Sustainable%20Development%20web.pdf

.Goal 3 - Ensure healthy lives and promote well-being for all at all ages.

.Goal 3.3 – By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases+

.Goad 3.d - Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks

GPW 13

On 25 May 2018 the WHA approved the 13th Genera Programmes of Work (GPW 13) of WHO for 2019-23. Structured to fulfil its commitments under UN's Sustainable Development Goals, GPW13 set out its programmes in three components:

.1 – One billion more people benefitting from Universal Health Coverage **(UHC)**
.2 - One billion more people better protected from **Health Emergencies,** and
.3 – One billion more people enjoying better **Health and Well-being**

Strategic Priorities

In Health Emergencies, which we may take to include outbreaks of infectious disease, WHO's strategic priorities under GPW13 are:

.1 – To build and sustain resilient national, regional and global capacities against epidemics and other health emergencies; and
.2 – To ensure that populations affected have rapid access to essential life-saving health services

Programmes

WHO's approach to health emergencies is described in the results framework of its programmes.

.1- ensure that populations affected by health emergencies have access to essential life-saving health services and public health interventions;

.2 - all countries are equipped to mitigate risk from high-threat infectious hazards;

.3- all countries assess and address critical gaps in preparedness for health emergencies and all-hazard risk management; and

.4 -national health emergency programmes are supported by a well-resourced and efficient WHO Health Emergencies Programme.

WHO Programme Budget 2020-21

Budget Allocation

WHO's Programme Budget for 2020-21 allocated a sum of $3,768.7 millions out of a budget of $5,840.4 millions for the Triple Millions Goals, sub-vented to the three goals by implementing level, as follows:

Table 11
WHO Programme Budget 2020-21
(USD 000s)

Goals	HQ	Regional Office	Country Offices	Total	%
1.Universal Health Coverage (UHC)	410.9	309.3	638.6	1,358.8	36%
2, Health Emergencies	223.2	202.4	463.3	888.8	24%
3. Better Health & Well-Being	124.9	112.1	194.0	431.1	11%
4. WHO direct Country Support	434.7	294.0	361.2	1,090.0	29%
5. Programme Total (3 Goals)I	**1,068.8**	**917.8**	**1657.1**	**3,768.7**	**100%**
%	28%	24.4%	44.0%	100%	
Others					
Polio Eradication Initiative (residual)				*863.0*	
Special Programmes				*208.7*	
Emergency Ops & Appeals				*1,000.0*	
Total (Others)				*2,071.7*	
5.Total Budget				**5,840.4**	

We may note that out of the programme budget of $3,768.7 millions, Health Emergencies have 24%, and that 44% of the latter allocation is placed with the Country Offices. The balance $2,071.3 is for extra-programme expenditure on (1) final phase of the Polio Campaign, (2) Emergency Ops and (3) other Special Programmes.

Revenue

A budget is meaningless without Revenue. This document did not have them. Happily, I found the Actual Revenue realised for the year annexed to the Audited Financial Statements for 2020[83], which indicates the sources of the funding, as follows:

Table 12
WHO Actual Revenue 2020
(USD 000s)

Revenue Source	General Fund $	%	Total WHO Revenue ($)	%
Country Assessed Contributions	465,946	11.2%	465,946	10.8%
Voluntary Contributions	3,655,390	87.9%	3,704,226	86.2%
Voluntary Contributions in kind and service (non-cash item,)	-		79,712	1.9%
Other Revenue	38.986	0.9%	49,450	1.2%
Total	4,160,322	100% (96.8%)	4,299,334	100%

WHO relies heavily (86.2%) on voluntary contributions **every year** from member states [over and above their assessed dues (10.8%)] and private donors ,for funding its operations. From a Wiki source[84], I ascertained that the highest donors in 2018-19 (grossing all applicable components) were: US (15.9%), the Bill & Melinda Gates

[83] https://cdn.who.int/media/docs/default-source/documents/about-us/accountability/a74_29-en.pdf?sfvrsn=13ad4db1_1&download=true
[84] https://en.wikipedia.org/wiki/World_Health_Organization

Foundation (9.4%), and UK (7.7%), GAVI, the Vaccine Alliance (6.6%), Germany (5.2%), and others (40.7%).

We may note that General Fund Revenue realised at $4,160.322 millions was less than the total Budget Provision of $5,840.4 millions, but more than the budgeted figure for the Triple Millions Goals of $3,768.7.

Budget Performance 2020

I was delighted to find that the Audited Statements of Accounts of WHO for the Financial Year 2020, issued on 31 Mar 21, was available. This enables us to see the actual expenditure against the earlier planned programmed figures

Table 13
WHO Budget Performance, 2020
(*USD millions)*

Programme	**Budget ($)**	**Expenditure ($)**	**Difference ($)**	**%**
UHC	1,358.8	557.0	801.7	41.0%
Health Emergencies	888.8	262.6	626.3	29.6%
Health and Well-being	431.1	108.2	322.9	25.0%
WHO country support	1,090.0	444.6	645.4	40,8%
3 Goals Prog	**3,768.7**	**1,372.4**	**2,396.3**	**36.4%**
Others				
Polio, emergency ops, special programmes	2,071.7	1691.0	380.8	81.6%
Total WHO Budget	**5,840.4**	**3,063.3**	**2,777.1**	**52.4%**

Allowing for it being the first of a four year programme cycle, I would say the organisation is sluggish at a 52.4% overall budget performance. Expenditure on the Triple Millions Goals

was just above one-third 36.4%), indicating perhaps over-budgeting. Expenditure on Others (including emergencies) was 81.6%. Bearing in mind that it was the first monstrous year of the SARS-Covid-19 pandemic, (which would not have been foreseen) even this percentage is not conspicuously above normal. There was no breakdown of the amounts spent on the latter.

It is sufficient for purposes of this review to note that, all-including, WHO's operating receipts totalled $4,299,334 and total adjusted expenses were $3,561,198, with a surplus of $824,473.

(Back to TOC)

WHO Initiatives

The WHO Health Emergencies Programme (WHE) was established in 2016 in the wake of the Ebola pandemic. The latter turned out to be a vital alert for Covid-19.

WHE Partners

WHO pulled together old and new technical and operational networks to create a new level of readiness after the disasters of Ebola.
are :

Global Outbreak Alert and Response Network (GOARN) – Established in 2000, it is a network of more than 250 technical institutions around the work that respond to public health emergencies through deploying personnel and resources to affected countries and sharing technical expertise and knowledge.

Global Health Cluster – a network of more than 900 partners that provide technical and operational support to national health and humanitarian crises.

Emergency Medical Teams Initiatives – supports organizations and Member States in strengthening their capacity and health systems through the deployment of emergency medical teams (EMTs) during outbreaks.

The WHE operated on a combination of core financing, a contingency fund for emergency response operations, and through ongoing appeals for funds. Historically, the programme has faced chronic budget and HR shortages, relying heavily on appeals and voluntary contributions to supplement the available budget.

R&D Blueprint

The West Africa Ebola epidemic saw the mobilisation of numerous actors around the world to find medical technologies to address the disease. Some brought results, such as the highly effective VSV-EBOV vaccine. In other cases there were large gaps in the way the global scientific and R&D community was organized to deal with an epidemic.

The R&D Blueprint, approved by the WHA in May 2016, is a WHO global strategy and preparedness plan that allows the rapid activation of research and development activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crises.

A broad global coalition of experts have contributed to the Blueprint, coming from the medical, scientific and regulatory backgrounds.

Global Coordination Mechanism (GCM)

The Blueprint established a Global Coordination Mechanism (GCM) to facilitate a regular dialogue among main stakeholders. Through the GCM, WHO collaborates with

partners engaged in similar activities and diseases. For example, there was a Memorandum of Understanding (MOU) between WHO and CEPI to collaborate on vaccine R&D for the Blueprint priority diseases. An MOU with GloPID R was also being prepared to facilitate collaboration with funders of research on emerging diseases.

The Blueprint facilitated the compilation and maintenance of an interactive list of key stakeholders (by areas or diseases of interest and current participation in collaborative networks) and a database of research preparedness resources to be integrated into the WHO Global Health R&D Observatory.

In addition, WHO prepared guidance documents for clinical research, etc in an epidemic context accompanied by practical checklists to facilitate use by researchers in the field.

R&D Roadmap

The R&D Blueprint uses a list of identified **priority diseases**. For each disease an R&D **roadmap** is created, followed by target product profiles. This is then used to guide the response to outbreaks in both urgent action and in developing ways to improve the global response for future epidemics.

Covid-19 Global Research Roadmap

The first point of departure for COVID-19 came on 10 January 2020, when the GCM for Research and Development to Prevent and Respond to Epidemics held its first teleconference, as did the Scientific Advisory Group for the R&D Blueprint. Those discussions led to the first global forum of international scientists on COVID-19, on 11–12 February 2020.
After assessing what was known at the time about the new virus, the more than 400 international experts

agreed on the critical thematic areas of research to prioritize, the mechanisms required to coordinate research to ensure no stone was left unturned, and the need for a framework to ensure that the most important research was funded efficiently.

These discussions were synthesized in the **COVID-19 Global Research Roadmap** that set out nine key to prioritize:
. -1 viral natural history, transmission and diagnostics;
. -2 virus origin, and management measures at the human-animal interface;
,- 3 epidemiological studies;
,- 4 clinical characterization and management;
,- 5 infection prevention and control, including protection of health care workers;
.- 6 candidate therapeutics;
.- 7 candidate vaccines;
.- 8 ethical considerations for research;

This Roadmap has governed the WHO-international response to Govid-a9.

(Back to TOC)

Strategic Preparedness and Response Plan (SPRP)

The first priority following a pandemic alert is to galvanise all countries into preparedness, and zap up their response ability.

SPRP 3 Feb 2020

WHO was notified by China of the outbreak of Covid on 31 Dec 2019, and declared that an international public health emergency of international concern existed one month later on 30 Jan 2020.

WHO released its initial **Strategic Preparedness and Response Plan (SPRP)** to all countries on 3 Feb 2020.

This contained a set of guidelines how to mobilise to meet the possible onslaught of the pandemic, and outlined the public health measures that the international community stood ready to provide countries.

The UN Crisis Management Team(UNCMT) with WHO in the chair was immediately established the following day, on 4 Feb 2020. This was the highest possible level of crisis alert in the UN system.

On 12 Feb 2020, WHO released its **Operational Planning Guidelines** to support development of National Action Plans. Simultaneously, it launched the COVID-19 Partners Platform to enable national authorities, UN-WHO Country Teams and partners to plan and allocate resources, identify funding gaps, and monitor progress against the National Action Plans.

UN Global Humanitarian Response Plan (GHRP),

On 25 March 2020, the UN Office for Co-ordination. Of Humanitarian Affairs (OCHA) issued its **COVID-19 Global Humanitarian Response Plan (GHRP),** and activated the UN Inter-Agency Standing Committee (IASC) to serve as the primary mechanism for inter-agency collaboration.

The Plan prioritises the humanitarian needs of the most vulnerable, including older people, people with disabilities, and women and girls. Given that the pandemic would heighten existing levels of discrimination, inequality and gender-based violence, the Plan included specific metrics to ensure that the vulnerabilities of these groups were addressed. This plan also included programmes that responded to the projected rapid growth in food insecurity.

In less than one year, more than 82 million COVID-19 cases and 1.8 million deaths were recorded. In that timeframe, out of the global COVID-19 totals, 30 per cent of COVID-19 cases and 39 per cent deaths were recorded in GHRP countries. The secondary effects were particularly serious. Disruptions to supply chains, etc pushed over 270 million people into acute food insecurity.

Health service disruptions also led to a 30 per cent reduction in the global coverage of essential nutrition services, leaving nearly seven million additional children at risk of suffering from acute malnutrition.

The economic contractions worldwide brought about the **first increase in extreme poverty since 1998.** Between 119 million and 124 million people could have fallen back into extreme poverty in 2020 due to COVID-19, with an additional increase of between 24 million and 39 million people in 2021, potentially bringing the number of new people living in extreme poverty to between 143 million and 163 million.

The GHRP was the humanitarian community's first event-specific global appeal. The plan originally appealed for $2 billion to respond to urgent needs in 54 countries. The GHRP was revised in May and July to 63 countries and the amount requested to $9.5 billion. As of 15 February 2021, reported funding for the GHRP had reached $3.73 billion.

The GHRP provided a global plan with indicators of progress. While improvements could be made in the future, the monthly reports provided a global, consistent and timely effort to demonstrate collective performance.

WHO Covid-19 Solidarity Response Fund

COVID-19 Solidarity Response Fund was a global fund for supporting the work of containing the Covid-19 pandemic. It was launched on 13 Mar 2020 by the UN Foundation and the Swiss Philanthropy Foundation. Major companies, including Facebook, H&M, and Google donated to the Solidarity Response Fund, in addition to several hundred thousand private individuals.

In the following months, several additional beneficiaries of the fund were added in order to work together, including UNICEF, the UNHCR (the UN Refugee Agency), and the UNRWA (UN Relief and Works Agency for Palestine Refugees in the Near East).

According to WHO's estimations, the requirement to respond to the pandemic until the end of 2020 was US$1.7 billion. As of December 7, 2020, 87.6% (US$1.52 b) of required amount had been collected.

SPRP Update 14 Apr 2020

The SPRP was updated in April.

The updated response strategy was organised around nine technical and operational response pillars[85], plus a tenth, the overarching global research and innovation pillar.

The strategy was designed to achieve three simple goals: (1) to control transmission of the virus, (2) to save lives, and (3) to protect the vulnerable.

There was no indication in this document of the big counter-offensive that was to come by the end of the month.

---

[85] As WHO lists these nine pillars in its **WHO Response to Covid-19: 2020 Report**, which I reflect further on, I do not list it here. See, https://www.who.int/publications/m/item/looking-back-at-a-year-that-changed-the-world-who-s-response-to-covid-19

(Back to TOC)

D - Access to COVID-19 Tools (ACT) Accelerator

The Three Pillars Strategy

That event, the **Access to COVID-19 Tools (ACT Accelerator)**, was duly launched at the end of that month (Apr 2020), at an event co-hosted by the Director-General of WHO, the President of France, the President of the European Commission (EU), and the Bill & Melinda Gates Foundation.

The ACT Accelerator was and is a global collaboration to accelerate development, production, and equitable access to COVID-19 tests, treatments, and vaccines.

It was set up in response to a call made by the G20 Leaders at their Mar 2020 meeting. The ACT Accelerator is not a decision-making body or a new organization. It is a **framework for collaboration.**

The participating global health organisations are:

.- World Health Organization (WHO),
.- Coalition for Epidemic Preparedness Innovations (CEPI),
.- Gavi, the Vaccine Alliance,
.- Global Fund to Fight AIDS, TB and Malaria (Global Fund),
.- Unitaid,
.- Foundation for Innovative New Diagnostics (FIND), t
.- Wellcome Trust,
.- World Bank Group, and
.- Bill & Melinda Gates Foundation.

The ACT Accelerator was and is the world's most comprehensive **end-to-end solution** to ending the **acute phase** (only) of the COVID-19 pandemic. It brings together governments, health organizations, scientists, businesses, civil society, and philanthropists to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines**.**

The ACT Accelerator comprises three components or "pillars":

.1- Diagnostics, co-led by FIND, Diagnostics for All and the Global Fund. This ACT aims to identify game-changing new diagnostics, and bring 500 million affordable, high quality **rapid diagnostic tests** to market by mid-2021, for populations in low- and middle-income countries.

I will say little more on this subject except to quote FIND's motto: "Testing is the first line of defence against outbreaks that are becoming increasingly severe and complex" In fact it has become abundantly clear to the world that it is essential to have adequate test kits to fight Covid-19 – and organise the immediate post-pandemic social processes.

.2- Therapeutics, led by Unitaid and Wellcome Trust This ACT seeks to develop, manufacture, procure and distribute 245 million treatments for populations in low-and middle-income countries within 12 months.

Currently, there are no broad-spectrum antivirals or immunotherapies available for the fight against emerging pathogens, and very few treatments approved for use against COVID-19. To effectively address COVID-19, the world will require multiple prevention and treatment options.

The programme is working to coordinate R&D efforts to help remove barriers and scale up interventions to drug development can be used as prophylactics or to treat mild and moderate forms of COVID-19.

The programme has an end-to-end focus, from drug in pipeline development through to manufacturing and scale up. As of Oct 20, ACT had already made investment grants of $21.6 million for Discovery, $50.4 million for Clinical, $2.8 million for Manufacturing , $9.4 million for Evidence and Data, and $14.5 for Diagnostics, totalling $98.6 million.

.3- Vaccines, led by CEPI, Gavi, the Vaccine Alliance and WHO. This ACT has been named **COVAX.** It seeks to ensure that vaccines are developed as rapidly as possible and manufactured at the right volumes – without compromising on safety – and delivered to those that need them most, including those that cannot not afford them. By early 2021, its goal is to secure 2 billion doses.

All participating countries, regardless of income levels, will have equal access to these vaccines once they are developed

Because the vaccine is so fundamental to the defeat of the virus, I capture the considerable work of this ACT in a separate section further on.

A complementary Health Systems Connector **pilla**r works across the above three pillars and is convened by the World Bank, Global Fund and WHO. It aims to strengthen the health systems and local community networks that are struggling to cope with COVID-19, and to unlock health system bottlenecks that might hamper the delivery and implementation of new and expanded COVID-19 tools.

The Access and Allocation Processes is led by WHO, which directs the ACT Accelerators' work on global access and allocation.
It also deals with regulatory processes (including the WHO **Prequalification** Programme. (The Prequalification Programme, set up in 2001, is a service provided by WHO to facilitate access to medicines that meet unified standards of quality, safety and efficacy for HIV/AIDS, malaria and tuberculosis.)

(Back to TOC)

COVAX

ACT Vaccines

This programme has been named **COVID-19 Vaccines Global Access**, abbreviated as **COVAX.** It is a worldwide initiative aimed at urgent and equitable access to COVID-19 vaccines. It is co-led by **Gavi,** the Vaccine Alliance, the Coalition for Epidemic Preparedness Innovations **(CEPI),** and WHO. Following its launch, UNICEF and Pan American Health Organisation (PAHO[86]) became delivery partners for COVAX.

Features of a Vaccine

Making a vaccine has unique features which make the conventional linear production processes too long, too costly and too risk laden. We may briefly itemise the critical stages to better understand the COVAX interventions and counter-measures:

.a-Identify the virus and its weaponry.
.b-Research the best defence, and prepare the vaccine
.c-Run trials with non-humans and with humans
.d-Comply with regulatory requirements to be. licensed
.e-Manufacture
.f Distribute

Even a decade ago, it could take up to 10 years to produce a vaccine. The estimated cost of one vaccine for any one of WHO's six EIOS at that time was $2.3-$3.6 billion.

---

[86] The Pan American Health Organisation (PAHO) is the specialised international health agency for the Americas. PAHO wears two institutional hats: it is the specialised health agency of the Inter-American System and the WHO Regional Office for the Americas.

COVAX Objectives

The objective of COVAX has been to intervene in the critical stages and target to get the vaccine out **within a year**. The concomitant objective has been to deliver the vaccine to all who most need it most, including those who cannot afford it.

The essence of COVAX is (a) massive mobilisation of demand in the form of pe-commitment by participating countries, (b) selection and support (which may include subsidy) of likely “vaccine candidates”, with pre-commitment to take delivery of eventual output at the agreed price, (c) rapid pre-qualification by WHO, (d) agreement among the countries to equitable sharing of the output, and (f) provision of funding to pay for the countries that cannot afford their share.

The initial target was to pre-qualify three candidate vaccines and deliver 1 billion doses by the end of 2021, which would supply 20% of the target population in the participating countries.

The Coalition for Epidemic Preparedness Innovations (CEPI), a private-public-philanthropic partnership was set up in 2017 to develop vaccines to stop future epidemics. As it turned out, its objective was to lay the groundwork for such a scheme in readiness for any threats from the EIOS[87]. The Vaccine Alliance, GAVI, a similar multi-party global initiative to increase access to immunisation in poor countries, was set up in 2000 and is doing outstanding and extraordinary work presently vaccinating half the children of the world. Together with WHO, these two partnerships play their respective, conjoint and overlapping roles in COVAX. By and large CEPI deals with developing and manufacturing the vaccine, and

[87] EIOS = WHO’s Epidemic Intelligence from Open Sources.

GAVI with equitable sharing of the vaccine with the 92 (out of the 150 odd) participating countries.[88]

COVAX Vaccine

The first component of the scheme was to invite vaccines, from among those already in the market and those in their trial and approval stages to those still under development, to apply to participate. The former group would be included as they qualified. The latter group would be evaluated and promising "vaccines candidates" selected for further support and assistance till they qualified. WHO stood ready to grant EULs[89] to the latter as they fulfilled its requirements, to proceed to manufacture. it would be with this potential manufacturing pool that COVAX would allocate its orders and negotiate price, based its control of assured demand. This supply is the "COVAX vaccine".

Built on the principles of speed, scale and equitable access, CEPI supports the research and development of a diverse portfolio of vaccine candidates based on a range of vaccine approaches. CEPI has invested in 12 vaccine candidates, ten of which are still in development. The aim is to advance COVID-19 vaccine candidates into clinical testing as quickly as possible, with the immediate goal to see three CEPI-supported COVID-19 vaccines through to licensure and available to priority populations.

---

[88] There are writeups on CEPI, GAVI and the other private-public partnerships involved in dealing with the Covid-19 pandemic, in Part 6.

[89] EUL = The WHO Emergency Use Listing Procedure (EUL) is a risk-based procedure for assessing and listing unlicensed vaccines, therapeutics and in vitro diagnostics with the ultimate aim of expediting the availability of these products to people affected by a public health emergency.

Centralised Labs Network

CEPI has established a **Centralised Labs Network** to enable the harmonisation of assessment of COVID-19 vaccine trial data from pre-clinical to Phase II testing. The seven labs located across multiple regions globally use the same testing reagents and follow common protocols to measure the immunogenicity of multiple COVID-19 vaccine candidates. The network is open for use to all COVID-19 vaccine developers (both CEPI-supported and non-CEPI-funded vaccine developers).

COVAX Marketplace

CEPI has created a COVAX Manufacturing Task Force to operate a **COVAX Marketplace,** to clear bottlenecks affecting the global supply chain leading to acute shortages of vital supplies which will prevent COVID-19 vaccine manufacturers from operating at full capacity, delaying production and contributing to inequity. Expanding manufacturing capacity requires managing intricate cross-border supply chains, frequently involving more than 100 components.

In this instance, manufacturers and suppliers have to triple their previous annual vaccine output, scaling up to produce an estimated 11 billion doses of vaccine, by the end of 2021. The innovative platform will match suppliers of critical inputs with vaccine manufacturers who urgently need them to produce vaccines for fair and equitable distribution through COVAX.

COVAX Facility

CEPI's central mechanism of the scheme is the COVAX Facility. Its function is to mobilise demand, and so give COMAX its bargaining power. Countries are invited to join the scheme by pre-committing to buy its vaccine requirement through COMAX up to their declared amount. As the supply rolls out, they agree to receive their quota equitably up to 20%

of their target population in the first instance. Countries may be self-financing or they may be loan or grant funded.

So far, 190 countries (soon to be 191, once the United States formally joins) are participating in the COVAX Facility. This includes most of the 92 countries that are eligible for donor-funded doses through the COVAX Advance Market Commitment (AMC)—an innovative financing mechanism through which the world's poorest countries will gain access to COVID-19 vaccines.

Even though self-financing participants can request for enough doses to vaccinate between 10-50% of their population, no country will receive enough doses to vaccinate more than 20% of its population until all countries in the financing group have been offered this amount. The only exception is those countries who have opted to receive fewer than 20%.

COVAX Advance Market Commitment (AMC)

Countries that cannot afford to pay may also participate in the COVAX Facility thought the Advance Market Commitment (AMC). Operated by GAVI. There were some 92 LMIC[90]s countries estimated to be unable to pay for their vaccine requirements to fight Covid-19. Under the AMC their participation is under-written by COVAX, ultimately paid for by ODA or humanitarian resources. These countries enjoy the same participation terms as the others for the COVAS vaccine.

The list of 92 AMC-eligible economies includes all economies with Gross National Income (GNI) per capita under $ 4,000 plus other World Bank International Development Association (IDA)-eligible economies.

---

[90] LMICs = Lower and Middle Income Countries

COVAX's success hinges on the receiving country's readiness to deliver the vaccine to the people. This includes putting legal and regulatory policies in place. Investments in infrastructure and workforce must also be scaled up quickly, from cold-chain expansion and health care staffing to identifying delivery routes and designing effective packaging. Community engagement strategies should include identifying target populations and raising awareness and acceptance. To boost these efforts, COVAX is providing essential resources for technical assistance and cold chain expansion to AMC-eligible countries.

Covid-19 ACT Funding

In Sep 2020, WHO released its estimates that the ACT Accelerator programme to cover requirements to the end of 2021 would require a bank roll of $38.1 billion, of which $16.0 billion would be for vaccines, and mostly pledged by governments (and the AMC) for purchase of supplies for their countries.

WHO provides a detailed (Funds)Tracker and the latest situation as at 12 Aug 2021 (today) is as follows in Table 14

Table 14
Covid-19 ACT Funds Tracker: Budget Gaps (adj 12 Mar 2021)
(USD billions)

Pillar	**Budget 20-21**	**Cost Adjust-ments**	**Contribu-tions**	**2021 Funding Gap**
Vaccines	16.0	-4.3	12.2	0.7
Therapeutics	6.6	-2.7	0.8	3.2
Diagnostics	6.0	+3.7	1.0	8.6
Health Systems	9.5	-1.6	0.6	7.2
Pending Allocation			3.1	-3.1
Total	38.1	-4.9	18.1	16.6

The following Table 15 shows the programme funding support by contributors

Table 15
Covid-19 ACT Funds Tracker: Receipts by Sources
Contributions as at 13 Aug 2021
(in USD millions)

Pillar	Public	Private	Multilateral
Vaccines	11,750	599	158
Therapeutics	364	367	27
Diagnostics	362	13	671
Health Systems	226	9	389
Pending Allocation	3,073		59
Total	15.775	989	1,304

NOTES: Largest contributors:
.1- Public(Country).US-$6,214m, Team Europe-$4,796m,Germany-$2,638.
.2- Private (Foundations). Bill-Melinda Gates- $420m, Gates Philanthropy-$119m, Wellcome Trust-$75m.
.3- Multilateral (Consortia). Global Fund-$458m, Diagnostics Consortium-$470, GAVI-$150m.

It should be pointed out that the contributions for Vaccines are mainly commitments to purchase supplies (to be paid to manufacturers) and therefore not subsidy funds. These contributions depend on the approved vaccines being available. As new supplies come on the market, the uptake via the COVAX Facility commitments will increase. The other components of the contributions can be regarded as pure subsidy, or as non-returnable human investment reflected in the lowered price of the product more rapidly available. The latter proportion now 58% of budget will therefore decrease, as the world's population gets vaccinated.

Lastly, it is fitting to recognise the outstanding role played by the Bill and Melinda Gates Foundation and Philanthropy who

contributed $539 million or 54.5% of the $989 million in private contributions. In the period 2016-2020, the Foundation had already separately contributed $1,552 million to GAVI for it world children immunisation programme, in addition to seeding money earlier made to start GAVI.. In my separate review of the WHO budget, I had noted that the Bill and Melinda Foundation funded up to 9.4% of the Voluntary Component of its budget, which in turn made up 86.4% of the total budget of the organisation.

COVAX exceeded its initial US$2 billion fundraising target for the AMC and is now making progress toward its US$5 billion goal for 2021

(Back to TOC)

PART FOUR

Combating Covid-19

Devastation

Personal Infection

The commonest threat of infection by the virus is through human-to-human transmission.

The viruses can live on wet surfaces and be transmitted from hand to hand via door knobs and lift buttons, In close crowded spaces, as in closed rooms and public transport, they can be aerosol and breathed in or transferred by contact.

The total experience of a Covid-19 infection is very like a very bad bout of Influenza, with congested lungs and very high fever, usually needing medical relief. The healthy adult without pre-conditions recovers in a fortnight or so. For older people, above 65 and with pre-conditions, infection can be fatal. Young children are also at risk.

The various people practices to fight the pandemic constitute the “Circuit Breaker”.

Scale of Infection

The real problem of (all) viruses is that they exist in the billions, attack a host cell in hordes (if not millions) at a time, and each virus replicates up to several copies of itself (let’s say 20) as fast as every 15 minutes, depending on the virus.

It takes only one virus to start an epidemic. In **two hours** one virus can replicate 128 million copies. And viruses do not die.

Even allowing 50% wastage, we are dealing with big numbers. Further, they can spread far and wide with the high mobility of people and things in what has become one world, literally.

The SARS- Covid-2 virus mutates very fast. It is said in every cycle of replication, there are some mutations. We are therefore constantly facing an enemy modified to trick the immune defence system.

A viral pandemic is like a hurricane, and does not go away until there is nothing else to feed it, in this case no one else to infect and replicate.

A virus needs a human cell to replicate. There are only three ways to stop a pandemic: (a) Stop all opportunity for human-to-human transmission (B) Prevent a person getting infected, and (C) Stopping a virus from replicating once inside.

Human Defence

Almost everyone knows the defensive actions to prevent human-to-human transmission. An infected person is a real menace. For completeness sake, and to capture the flavour of the “real bad” days of painful memory, Purely for the record, I list some of personal and country defences most people already practice and have suffered:

Table 16
Covid -19: Human Defences

Personal	Country
Personal . Wear a mask . Avoid personal contact . Avoid touching things . Wash and sanitise frequently Social . Maintain safe-distance . Avoid group gatherings . Avoid crowded places . Do not share utensils . Use your contact tracer tag . Carry your vacc certification Travelling . Stay at home . Work at home . Pray at home . Holiday at home . Shop on-line . Avoid travelling about.	Country Lock-Down Local Transport Region Transport State Transport Urban Lock-down Offices Factories Malls Schools Entertainment International Lock-down Airports Ports Railways Tourists Foreign Workers

Medical Defence

The lethal end of the Covid-19 fight is medical warfare. Humans have an immune system of many parts, which act to repel a pathogen on first arrival and if already inside to engage with it in different parts of the body. Our entire medical strategy is to boost this capability.

But, there is a prior step, and that is to identify the virus. This enables us to relate it to all that is already known about its family and genus, and our past dealings with them. If it is a mutation, it has to be properly tagged in relation to known knowledge. If it is a new family, genus or species, it will be

necessary to research its origin and transit path to human. The end product of this stage is to obtain the complete classification and genome of the virus.

We needed, further, to know its complete profile in order to interfere with or stop the virus at any or all of its stages of infection. Without sounding boring, this includes knowing its receptor targeting and surface docking apparatus, its methods of penetration of the epidermic layers, its unpacking, its replication process, and its final expulsion of progeny. Crucially, we needed to tag its antigens. The processes of discovery involved culture, manipulation, tests and observation.

Frenetic research was done in the first few months and shared freely. Thus, we knew early that Covid-2 is an enveloped Coronavirus with its genome encoded in a single strand RNA with positive sense.

Basically our standard medical defences, are three: (a) Tests (b) Vaccination, and (c) Anti-viral Drugs. Almost everyone today has experienced one or more of them. Some simple explanation helps.

National Regulatory Authorities (NRAs)

Internationally, candidate vaccines must clear the rigorous requirements before being granted approval for public release, including a series of successful trials. The same applies to therapeutic drugs, test kits and other devices, in differing degrees.

In principle, the National Regulatory (NRA) of a country exercises approval. WHO through its Prequalifying system exercises this approval authority for the world as a whole, but recognises some 35 of the NRAs as Stringent Country Regulatory Authorities (SRAs) as qualifying to do so. The US Food and Drug Administration (FDA), the British Medicines

and Healthcare Products Regulatory Agency (MHRA) and the German Federal Institute for Drugs and Medical Devices (BfAr are among these.

In Singapore, the NRA is the Health Science Authority (HSA), which licenses test kits, therapeutic drugs and vaccines.

(Back to TOC)

Tests

The test to find out if a person is infected is the first line of defence. There are three types of tests:

.(a) -Polymerase Chain Reaction (PCR)

PCR tests directly screen for the presence of viral RNA, which are detectable in the body even before antibodies form or symptoms are present. This means the tests can tell whether or not someone has the virus very early on in their illness.

During Covid-19 PCR testing, substances known as reverse transcriptase or DNA polymerase are added to a nasal sample in a lab. These substances work to make numerous copies of any viral RNA that may be present. This is so that enough copies of the RNA are present to signal a positive result and that an antigen has been found.

PCR gives a good indication of who is infected. But the sample has to be sent to a lab and takes a few days.

. (b) - Lateral Flow Tests (LFTs)

LFTs are similar to PCR tests, in that they're both types of antigen test, designed to pick up active Covid-19 infection rather than antibodies.. A nasal sample is placed on a small absorbent pad, which is then drawn along the pad coated in antibodies which bind to SARS-Cov-2 proteins. If these

proteins are present, this will show as a coloured line on the test, indicating infection.

The major benefit of LFTs over PCRs is that they do not need to be sent away for confirmation, and instead provide results within 15 to 30 minutes. However, what they gain in speed they sacrifice in accuracy

.(c) - Antibody (or serology) tests

An antibody test tells the proportion of the population that has been infected. It won't tell who is infected, because the antibodies are generated after a week or two, after which time the virus should have been cleared from the system. But it tells who has been infected and who should be immune to the virus.

Blood samples are used for antibody tests. Following infection, there will be a small amount of Covid-2 circulating in the blood but a significant and measurable antibody presence for the purpose.

It has been found that people who recover from even mild cases produce antibodies for at least five to seven months, and could do so for much longer. If there's a high enough level of people in the population who have immunity, it will stop the virus from circulating within the population, which is known as **herd immunity.**

Pool of Test Kits

The need for a test kit arises from the first case of infection. However the first defence of an uninfected person is vaccination. My case is probably typical. I received my first vaccination (Pfizer-BioNTech) in Apr 2021 and my second shot in May 2021 and I got my first tests (all three) when I visited a high risk location.

The first test kits to be available were in Germany in Jan 2020. South Korea and China focussed early on test development, and were exporting supplies to UK in Mar 2020, They were followed by the rest of the world in 2020 as their priorities with vaccines ease.

In parallel with countries completing their early vaccination targets, their demand for test kits grew proportionately, and accordingly the supply. I could not find out, but I imagine the 92 AMC LMIC countries who have to fulfil their 20% vaccination targets are as at mid-2021 equally desperately short of kits.

Singapore Situation

Perhaps, the global test kit pool is realistically reflected by the situation in Singapore. As at Aug 2021, the HSA has approved the following world-wide products:
.3 - Antibody (Serology) Tests;
.1 - PCR Based Molecular Tests;
.2 – Left Flow Tests (Antigen) Tests.

(Back to TOC)

Vaccines

The primary defence is vaccination. It suffices here to provide this quotation from the US CDC to introduce it:

> "Vaccines contain the same germs that cause the disease. But they have been either killed or weakened to the point that they don't make you sick. Some vaccines contain only a part of the disease germ.
>
> A vaccine stimulates your immune system to produce antibodies, exactly like it would if you were exposed to the disease. After getting vaccinated, you develop immunity to that disease, without having to get the disease first.

> This is what makes vaccines such powerful medicine. Unlike most medicines, which treat or cure diseases vaccines prevent them." (Slightly edited)
> https://www.cdc.gov/vaccines/vpd/vpd-vac-basics.html

Edward Jennings discovered the principle of vaccination in 1796, and Louis Pasteur developed the first live attenuated human vaccine against rabies in 1885. Live attenuated vaccines for humans were subsequently developed and became the chief defence against a number of the world's most deadly diseases over the years.

In the past, this took up to 10 years to develop a vaccine. In the panic of the early Covie-19 months, the major governments pumped vast sums into institutions and manufacturing agencies to kick-start research and development. Progress was quick. Soon, thanks to modern technology and the growing practice of sharing data, the lead time against Covid-2 has been cut to months, and we are provided with a wide range of options within one and a half years.

Types of Vaccines

There are basically four types of vaccines being developed for Covid-2:

.(a) – Whole Virus

Many vaccines use whole viruses to trigger an immune response. There are two main approaches. (A) Live attenuated vaccines use a weakened form of the virus that can still replicate without causing illness. (B) Inactivated vaccines use viruses whose genetic material has been destroyed so they cannot replicate, but can still trigger an immune response. Live attenuated ones may risk causing disease in people with weak immune systems. Inactivated virus vaccines can be given to people with compromised immune systems. Both might need cold storage.

.(b) – Protein Subunit, Recombinant, Conjugate

Subunit vaccines use pieces of the viurs- often fragments of protein - to trigger an immune response. Doing so minimises the risk of side effects, but it also means the immune response may be weaker. This is why they often require adjuvants, to help boost the immune response. An **adjuvant** is an ingredient used in some vaccines that helps create a stronger immune response. These subunit vaccines use specific pieces of the germ—like its protein, sugar, or capsid (a casing around the germ). Because these vaccines use only specific pieces of the germ, they give a very strong immune response targeted to key parts of the germ. But they can be used on almost everyone who needs them, including people with weakened immune systems and long-term health problems. One limitation is that you may need booster shots to get ongoing protection against diseases.

.(c) – Nucleic Acid (mRNA)

Nucleic acid vaccines use genetic material from the virus, either RNA or DNA, to provide cells with the instructions to make the antigen. In the case of COVID-19, this is usually the viral spike protein. Once this genetic material gets into human cells, it uses our cells' protein factories to make the antigen that will trigger an immune response.

The advantages of such vaccines are that they are easy to make, and cheap. Since the antigen is produced inside our own cells and in large quantities, the immune reaction should be strong. However, RNA vaccines need to be kept at ultra-low temperatures - -70 degrees Centigrade.

.(d) – Viral Vector

Viral vector vaccines also work by giving cells genetic instructions to produce antigens. But they differ from nucleic acid vaccines in that they use a harmless virus, different from

the one the vaccine is targeting, to deliver these instructions into the cell. One type of virus that has often been used as a vector is *adenovirus,* which causes the common cold.

As with nucleic acid vaccines, our own cellular machinery is hijacked to produce the antigen from those instructions, in order to trigger an immune response. Viral vector vaccines can mimic natural viral infection and therefore trigger a strong immune response.

Available Vaccine Pool

By Jan 2021, WHO reported there were 184 proposals in pre-clinical development and 108 at the clinical stage. WHO uses an Emergency Use Listing (EUL) facility to release vaccines for emergencies as quickly as possible. The FDA use its Emergency Use Authorization (EUA).

As at 6 Jul 2021,eight vaccines haven cleared for the market, and the another 15 are in the process of evaluation, see Table 17

Table 17
Vaccines Approved/Under Evaluation 6 Jul 2021

	Vaccine Manufacturer	**Country Nat Reg Authority**	**Type**	**Released**
1	Pfizer-BIONTECH	EU-USA EMA	Live. mRNA	31 Dec 2020
2	Astra-Zeneca Oxford	EU EMA	Recombinant	16 Apr 2021
3.	Astra-Zeneca Oxford	S Korea MFDS	Recombinant	15 Feb 2021
4	Serum Institute of India	India DCGI	Recombinant	15 Fef 2021
5	Johnson & Johnson	USA EMA	Recombinant	12 Mar 2021
6.	Moderna	USA EMA	Live mRNA	30 Apr 2021
7	Sinopharm /BIBP	China NMPA	Inactivated	7 May 2021

8	SINOVAC	China NMPA	Inactivated	1 Jun 2021
9	Gamaleya National Center (Sputnik V)	Russia NRA	Vector-based	On-going
10.	Astra-Zeneca Oxford	Japan MHLW/PMDA	Recombinant	On-going (July)
11.	Astra-Zeneca Oxford	Australia TGA	Recombinant	On-going (July)
12	CanSinoBIO	Canada, China NMPA	Recombinant	
13	Bharat Biotech	India DCGI	Inactivated	
14	NOVAVAX	Norway EMA	Recombinant	
15	Sinopharm WIBP	China NMPA	Inactivated	
16	UREVAC	EMA	Live. mRNA	
17	Sanofi Pasteur	EMA	Recombinant	
18	Vector State Research	Russia NRA	Peptide antigen	
19	Zfifei Longcom	China NMPA	Recombinant	
20	IMBCAMS	China NMPA	Inactivated	
21	Clover Bio pharmaceuticals	EMA	Recombinant	
22	BioCubaFarma	Cuba CECMED	Conjugated	

We may conclude this section to say that by 13 Jul 2021, some 3,505,007,924 vaccine doses had been administered, equivalent to 46 per 100 persons. Some 11 countries had more than 50% of the population fully vaccinated, while 90 others had less than 10%[91].

The last has come about because most high income countries put their own populations' priorities ahead of humanitarian

[91] https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html

concerns. While they participated in the COVAX Facility, they proceeded to pre-order the earliest approved supplies from manufacturers in their own countries, where necessary by restricting exports, or by offering top prices. Other countries who wished to secure essential first supplies also did the same. Singapore would have been one of them.

Singapore Situation

In Singapore, the HSA introduced a Pandemic Special Access Route (PSAR) to facilitate early access to critical novel vaccines, medicines and medical devices during a pandemic. The PSAR was only available for designated health products required for Coovid-19.

HSA's PSAR interim authorisation is similar to the emergency authorisation framework adopted by other regulatory jurisdictions as in Canada, US and the United Kingdom.

So far, HSA's authorised list has three vaccines, the Pfizer-BioNTech, the Moderna and the Sotrovimab Injection, the latter approved on 30 Jun 21.

Singapore has participated in the COVAX Facility as a Self-Financing Participant (SFP), booking for 288,000 does of Astra-Zeneca from SK Bioscience of South Korea, which went into Phase III clinical trials on 10 Aug 2021.

(Back to TOC)

Anti-Viral Drugs

There are two types of antiviral drugs.

.(a) New Covid-2 drugs

Drug development to produce preventative and therapeutic prescription medicine is a tortuous process, with pre-clinical

and clinical stages, followed by phases of trials with non-humans and finally humans, all phases tightly regulated by NRAs. It can take a decade and cost billions at the end.

The medical-pharmaceutic industry immediately saw the huge market potential of Covid-19. As early as March 2020, WHO, the EMA (European Medical Agency), FDA, and the Chinese government were collaborating with the research sectors and the medical-pharmaceutical industry to speed development not only of vaccines, but also of antiviral drugs and post-infection therapies. WHO recorded 419 drugs under clinical trials in Apr 2020.

Needless to say, the. regulatory authorities cut the red-tape, while funds and potential pre-orders were not in short supply from governments and non-governmental agencies.

But priority was given to vaccines. The lead time for antiviral and post-infections drugs would be a few years. There are therefore no new antiviral drugs for Covid-19 as of this writing.

.(b) - Re-purposing existing drugs

As the Covid-19 victims piled up in the hospitals, the doctors racked among their existing medicines for something to give them, something approved for a cognate disease. And, this they did, in the absence of no options.

Re-positioning or re-purposing existing drugs. ie using or adapting drugs developed for cognate diseases to alleviate Covid-19 immediately became the **front-line priority**. The candidate drugs needed to be quickly and massively tested with Covid patients and authorised, even before the vaccines on the **other front-line** were out.

In Mar 2020, in the same month it declared Coid-19 a pandemic, WHO initiated the “SOLIDARITY Trial”

programme. It became one of the largest international randomized trials for COVID-19 treatments, enrolling almost 12 000 patients in 500 hospital sites in over 30 countries. The Solidarity Trial evaluates the effect of drugs on three important outcomes: mortality, need for assisted ventilation and duration of hospital stay. Drugs may be added and removed based on emerging evidence. WHO cautions against physicians and medical associations recommending or administering unproven treatments to patients with COVID-19 or people self-medicating with them.

Earlier in Feb 2020, a series of four trials, subsequently named Adaptive COVID-19 Treatment Trial 1-4 (ACTTs-1-4) was initiated by the US National Institute of Allergy and Infectious Diseases ((NIAID). It became progressively more refined, combining and separating different groups of different age groups, in different stages of infection and with different symptoms, and testing with various combinations of drugs. The study has been a multi-centre trial conducted in up to approximately 100 sites globally, with adaptive re-combinations of drugs, each change accompanied by a revised sample of patients. ACTT 4 was launched in Nov 2020. With each set of trials, the results were used by the FDA to grant Emergency Use Authorizations (EUA) for individual drugs.

Other agencies in different countries up took the trial process. We might mention the RECOVERY Trial. Founded in Mar 2020 by UK Research and Innovation (UKRI)'s Medical Research Council and the National Institute of Health Research (NIHR), it is led by the University of Oxford. Its work has expanded internationally, eg Indonesia and Nepal, and at last count totalled 40,789 participants in184 active sites. The French version, co-ordinated by their National Institute of Health and Medical Research (Inserm) is called DISCOVERY, also started in Mar 2020.

I have not checked, but I get the impression that manufacturers are charged a tidy sum (at least at cost, if not

more for priority) for trials of their candidate products, in anticipation of mega sales returns if successful. It is neat risking-taking on their part, with our medical boys recovering much need moneys for humanitarian expansion, while the Covid patients have only their lives on the table - to gain and everything to lose. It is, in this case highly opportune capitalism.

Available Pool of Anti-Viral Drugs

It is not practicable to follow the trial results of the different agencies. For the curious, I list some of the better known drugs that have been endorsed by the FDA[92]
for use:

[92] https://www.health.harvard.edu/diseases-and-conditions/treatments-for-covid-19

Table 18
Antiviral Drugs with FDA's EUA

	Drug	**Remarks**
1.	Remdesivir	Only FDA drug with full approval for Covid-19
2	Baricitinib (	EUA. In combination with Remdesivir
3.	Dexamethasone	No EUA. But it has become preferred treatment for Covid019 patients.
4	Tocilizumab (Monoclonal antibody)	EUA. For the treatment of hospitalised adults and children ages 2 years and older, who are receiving systemic corticosteroids such as dexamethasone, and who require supplemental oxygen, mechanical ventilation, or a heart-lung bypass machine.
5	Other Monoclonal antibodies .1 Casirivimab and Imdevimab (REGN-COV) .2- A combination of bamlanivimab and etesevimab, made by Eli Lilly; and ,3 -Sotrovimab, made by GlaxoSmithKline.	All with EUAs. Monoclonal antibodies are manmade versions of the antibodies that our bodies naturally make to fight invaders, such as the SARS-CoV-2 virus. All three of the FDA-authorized therapies attack the coronavirus's spike protein, making it more difficult for the virus to attach to and enter human cells. These treatments are not currently authorized for hospitalized COVID-19 patients or those receiving oxygen therapy.

Hydroxychloroquine is primarily used to treat malaria and several inflammatory diseases, including lupus and rheumatoid arthritis. It is inexpensive and readily available.

However, the NIH treatment guidelines recommend against the use of hydroxychloroquine for COVID-19, in both hospitalized and non-hospitalized patients.

In June 2021, the US government announced that it will invest more than $3 billion to develop antiviral medications to treat COVID-19 and to prepare for future pandemic threats.

While COVID-19 vaccines remain the central to protection, antiviral medications may be important for people whose bodies do not mount a strong response to the vaccine, who experience breakthrough infections, and for those who are unvaccinated.

.(c) - Convalescent Plama

When people recover from COVID-19, their blood contains antibodies that their bodies produced to fight the coronavirus and help them get well. Antibodies are found in plasma, a component of blood.

Convalescent plasma — literally plasma from recovered patients — has been used for more than 100 years to treat a variety of illnesses from measles to polio, chickenpox, and SARS. It is widely believed to be safe.

In August 2020, the FDA issued an emergency use authorization (EUA) for convalescent plasma in patients hospitalized with COVID-19.
However, a meta-analysis of four peer-reviewed and published randomized clinical trials, published in JAMA[93], had less-promising results. The trials included in the analysis included 1060 patients with COVID-19 who received either convalescent plasma, a placebo, or standard treatment. Compared to placebo and standard treatment, convalescent

[93] Journal of the American Medical Association.

plasma did not significantly improve risk of death, length of hospital stay, or the need for a ventilator.

Singapore Situation

The information on Singapore is not clear. Presumably, doctors are free to use (re-purpose) all approved drugs on the market if considered efficative in their medical opinion, and the public would commit no crime trying out something.

On 10 Jun 20, HSA approved the use of Gilead Sciences Inc's antiviral drug Remdesivir for the treatment of severely ill patients with COVID-19 infection. The approval would allow treatment of adult patients if they had low blood oxygen levels, required supplemental oxygen or intensive breathing support.

On 30 June 2021, HSA granted approval for Sotrovimab, a monoclonal antibody by GlaxoSmithKline Pte Ltd (GSK) and Vir Biotechnology. It was approved by the FDA earlier in May. This allowed the therapy for the treatment of mild-to-moderate COVID-19 in patients aged 18 years and older, who did not require oxygen supplementation and were not at risk for progression to severe COVID-19.

* * *

(Back to TOC)

PART FIVE

Score-Lines

Covid Variants

Viruses (including the SARS-Covid-2) are easily and highly-mutative**.**

They can and will reconstitute or adapt a working part wherever and whenever these encounter an obstacle, so as to continue with their purpose . And the latter is inflexible – to capture a living cell and replicate.

Viruses do not engage one-on-one, but operate by mass invasion and rapid repeated replications. Thus, as successive waves of virions are exposed to varying adverse conditions, they make incremental adaptations, from one mutation to the next.The net result is a. high level of success in achieving a brace of mutations to overcome an obstacle. Further they seem able to co-ordinate and complement incremental and progressive changes across the herd, and across continents.

When a virus has consolidated a set of changes to create a significant new personality, we call it a Variant. The latter can in turn form Clades or families of the variant.

GISAID, the international shared data base of viral genomes, which has over 2.4 million samples of Covid-2, reports over 6,000 mutations among them. WHO has classified 10 Variants, four Variants of Concern (cause havoc) and six Variants of Interest (not fully evaluated) as follows

Table 19
SARS Covid-2 Variants

Serial	Variant of Concern	Earliest documented
1	Alpha	United Kingdom , Sep 2020
2	Beta	South Africa, May 2020
3	Gamma	Brazil, Nov 2020
4	Delta	India, Oct 2020
	Variant of Interest	
5	Epsilon	USA, Mar 2020
6	Zeta	Brazil, Apr 2020
7	Theta	Philippines, Jan 2021
8	Iota	USA, Nov 2020
9	Kappa	India, Oct 2020

The Delta Variant which started in India continues to cause chaos throughout Asia, Australia and New Zealand even as of today, including a major new wave in China.

Infections Tally Update

The tally of infections as at 21 Aug 2021 world-wide is

Table 20
Covid-19: Global Casualties Selected Data 20 Aug 21*

Date	Cumulative No Infected	Cumulative No Deaths	Cumulative No Cured	No New Cases per day	No Cured per day
22 Jun 21	179,920,602	3,898,327	164,678,028	376,713	419,978
10 Jul 21	186,841.356	4,045,177	170,891,141	490,098	363,202
20 Aug 21	211,509,710	4,427,918	189,257,310	683,637	5112,221

*. -Data from https://www.worldometers.info/coronavirus/worldwide-pgraphs/#total-cases

As 20 Aug 21, the number of new cases exceeds the number cured. New infections hit an **all-time** peak of 898,098 per day on 4. May 2021, mainly through Variant Delta.

Herd Immunity

A virus community ceases to multiply when there is no one left to infect. The pandemic ceases when there are no new infections. In the absence of vaccinations, that means extinction. The converse is that if everyone is safely vaccinated, the pandemic will also cease, but we shall have survived. Those in the know calculate that a 60% level of (a single) vaccination of the adult population will provide a defensible herd immunity . This is the current world's first target.

As at 2021, the world population was 7.9 billion, of which some 74% or 5.8 billion were 15 years and above. The latter may be considered the minimal herd. Some 60% of this would be 3.5 billion people. We might use the following matrix as a frame of reference:

Tgt Pop (billion)	Coverage (%)	One Shot (billion)	Two shots (billion)
5.8	60%	3.5	7.0
5.8	70%	4.1	8.2
5.8	100%	5.8	11.6
7.9	60%	4,7	9.4
7.9	70%	5.6	11.2
7.9	100%	7.9	15.8

Seven billion doses would in fact be just right to immunise the 60% of the minimal target population with two shots, and I would use that as the yardstick.

Individual countries will aim for 100% coverage, with double or triple shots depending on the Variant and the type of vaccine.

However, I would set the first level of global security when the LMICs hit 60%.with two shots. Although the LMICs are more isolated, it is a matter of equity they receive the same minimum protection from the first.

(Back to TOC)

Vaccine Front

COVAX AMC Summit Donor Commitments.

On 2 Jun 21, Japan hosted the One World Protected COVAX AMC Summit. In addition to the $7.402 billion previously committed[94], the summit realised a further $2.423 billion in additional donations, giving a total of $9.825 billion. GAVI gives in line by line detail the information at https://www.gavi.org/sites/default/files/covid/covax/COVAX-AMC-Donors-Table.pdf

It is interesting that $1.153 billions of this sum was donated through the mechanism of, the International Finance Facility for Immunisation **(IFFIm**)[95]. The summit also saw further donations of nearly $0.8 billion for AMC logistics.

On a simple analysis of the above, COVAX AMC with $9.825 billion in commitments has enough funds to do a 60% two-shot coverage of the world, including children, at a price of $10.00 per shot, or other combinations thereof.

For our purposes, it is tactical to aim first for a 60% two-shot world cover excluding children. The magic figure is 7 billion doses.

---

[94] I believe, correctly I think, that commitments of SFP (Self Financing Participation) funds under the Facility are excluded, or the situation is worsened to that extent.

[95] It issues **Vaccine Bonds** (for GAVI's children immunization programme) converting short- and medium-term donor pledges into financial instruments, "frontloading" cash for immediate needs.

Global Procurement

The Duke Global Health and Innovation Center has a Launch and Speedometer website[96], which maintains a watch on Covid-19 vaccine manufacturing and procurement..

It reports that countries have purchased vaccine doses from a wide pool of candidates to cover their populations. As on 20 Aug 21, confirmed purchases cover 11.9 billion doses, with another 6 billion doses currently under negotiation or reserved as optional expansions of existing deals. The latter include candidate vaccines still in progress to approval.

This suggests that the world is now funded to pay for the 7 billion doses, and more. It also indicates that the manufacturing capacity is likely in due course to support a 100% coverage of the world population at 2 shots.

Procurement Distribution

The distribution of the above procurement by income levels is however skewered, see Table 20

Table 21
Vaccine Procurement by Income Levels, 21 Aug 2021

	Countries	Procurement (doses)	%
1	High Income	6,795,129,421	42.0
2	Upper Middle income	2,515,613,849	15.6
3	Lower Middle Income	3.238.535,976	20.0
4	Low Income	348,978,812	2,2
5	COVAX/Other Global Entities	3,265,028,571	20,2
	Total	16, 161,000,000	100.0

96 https://launchandscalefaster.org/COVID-19

Some 82.2% of the world population, or 6.5 billion, live in the LMICs, including Indian, China and Russia. They have only 22% of the vaccines procured. Even with the 20.2% controlled by COVAX, they have less than half the vaccine supply.

Fortunately, COVAX has secured enough funds to achieve the targeted herd immunity levels in the LMICs. When the last of the latter receive their supplies at 60% times 2 shots, the world will have equal minimum global cover.

Global Timing

The second problem is timing. The present objective is to achieve global immunity by Mar 2022. Keeping the dateline firm must be the crucial objective. If there is delay, the deliveries to countries not yet covered must be given precedence.

The first vaccinations became available from 30 Dec 2020. The early batches were largely pre-contracted. The COVAX supplies became available and started being delivered to the AMC countries only in Feb 2021. As at 20 Aug 2021, some 4,562,256,778[97] vaccine doses had been administered according to WHO. This is 64% to target. However the distribution is poor, see coverage by selected countries in Table 22

[97] This is 78.6% of world's population of 5,8 billion above 15 years of age.

Table 22
Vaccinations by Selected Countries as at 19 Aug 2021
(millions)

Country (Selected)	Doses/ 100 residents	% One dose	% Fully vaccina-ted (x2)	Doses Supplied (million)
1.UAE	179.8	84.5	74.5	17,6
2.Malta	157.1	81.6	81.2	0.8
4.Singapore	149.9	79.9	73.1	8.5
9.Canada	138.8	73.3	65.4	52.2
15 UK	133.0	71.1	61.9	88.8
36.USA	108.1	60.1	51.0	355
46 Malaysia	93.5	55.	37.8	29.9
57.Brazil	82.3	59.1	25.2	173.7
69 Australia	63.9	41.1	22.8	16.2
83 Russia	52.0	28.8	23.2	75.0
95 India	41.5	32.3	9.2	566
103 Indonesia	31.9	20.7	11.2	86.4
111 Zimbabwe	24.7	15.2	9.5	3.6
122 South Africa	17.4	13.3	7.9	10.2
130 Namibia	10.8	7.5	3.2	268.6k
131 Vanuatu	10.4	9.8	0.6	31.0k
143 Gabon	5.9	3.4		127.8k
150 Afghanistan	4.8	2.0		1.8
160 Ethiopia	2.1			2.3
169 Papua NG	1.3	1.0		113.5k
178 Haiti	0.2	0.2	0.003	20.3k
180 DR Congo	0.1	0.09		86.9k
184 Eritrea + 2 others	-	-		-

From the source table, only 36 countries (out of 180) had vaccinated 60% or more of the population with one dose. Among these, 20 countries had 60% or more fully vaccinated (twice). On the other hand, 79 countries had received supplies of only 30% of the population or less, of which 66 had received 20% or less, of which and 3 nothing yet. The problem area is the shortfall to LMICs. Only 1.4% of people in low-income countries have received at least one dose.

LMICs Supply

As of 24 Aug 21, COVAX had shipped over 215 million COVID-19 vaccines to 138 participants. There is a long way to go.[98]

Orders have to date been placed by COVAX for 320,064,420 doses of vaccine. This will be more than enough for the balance requirements of the LMICs

Of the above orders, 227,664,000 doses are from the Serum Institute (Sii) of India and 91,200,000 from SK Biosciences of South Korea, both for the Astra Zeneca vaccine, and another 1,200,420 doses will come from Pfizer-BioNTech.

Apart from the higher income countries grabbing the greater share of the vaccines, the supply position has been aggravated by India's output being diverted to fight the Delta Variant locally. Any similar withdrawal for local emergencies by South Korea, China and Russia (or to move to higher cover Immunity ahead of other LMICs) will similarly delay the supplies to the other LMICs. These three countries currently produce the major proportion of approved vaccines.

Parallel Supply

It is gratifying that there are parallel moves to create supply.

On 16 July 2021, the African Union's (AU)'s African Vaccine Acquisition Trust (AVAT), COVAX and the US announced the donation of 25 million Johnson & Johnson to 49 African countries. The Afreximbank at the same time put in place a $2 billion Advance Procurement Commitment (APC) Guarantee to obtain 400 million more doses of the Johnson & Johnson COVID-19 vaccine, providing a total of 620 million doses to Africa by the end of 2021. The vaccines will be in part sourced

98 https://www.gavi.org/covax-vaccine-roll-out

from licensed production in South Africa and distributed by COVAX ,with the goal to vaccinate 60% of the population.

Similarly, Mexico and Argentina have an agreement with Astra-Zeneca to produce the vaccine for the eventual distribution of 250 million doses to Latin America (excluding Brazil).

As of 6 April 21, India has made donations of 10 million doses to about 44 countries.

Pakistan has reportedly made a deal with Cansino, which allows for bulk vaccine imports amounting to 3 million doses.

To the extent, the parallel supplies approved, the higher the overall immunity levels can be reached

Other Resource Mobilisation

The are a host of supply and logistics requirements, many critical, to ensure immunity vaccines in time. One set relate to various trials and regulatory compliances. One set to relate to the absolute world shortage of all everything, from test chemicals to packaging components. Thirdly, there are special requirements like cold chain transport and storage.

The UN COVID-19 Supply Task Force was set up to coordinate the supply of essential Personal Protective Equipment (**PPE) and medical oxygen** to low- and middle-income countries, to protect frontline workers and over-stretching of health systems and resources.

(Back to TOC)

Country Mobilisation

The first priority of WHO was country mobilisation under the SPRPs of Feb and Apr 2020. There are three elements of need: (a). preparing the country for the surveillance, identification and first responses to a virus outbreak, (b) social preparation of the population, and (c) equipping and training the country to deal with a pandemic, including the delivery of vaccines when they arrived. Separate funding was required for all this, in addition to funding the cost of the vaccines.

The neatest way to view countries' response by the end of 2020 is to look at their fulfilment of WHO's nine pillars of action. Even if tedious, I include the following Table 23 which gives a slightly closer focus on fighting the pandemic at ground level.

Table 23
Collective Country Response by end 2020 - The Nine Pillars of Action[99]

No	Pillar of Response	End 2020 WHO Assessment %
1	Country/area-level coordination, planning and monitoring	99% to 47%
2.	Risk communication and community engagement	97% to 81.%
3.	Surveillance, rapid response teams and case Investigation	100% to 30%
4.	Points of Entry (PoE)	72% to 35%
5.	National Laboratories	100% to 85%
6.	Infection prevention and control (IPC)	83% to 39%
7.	Operational Support and Logistics	52%
8.	Maintaining essential health services and systems	45% to 46%
9.	Cross-cutting issues	80% to 28%
10.	Case Management	89%

It looks like the countries had by and large got off the ground. I should have thought so. As at year-end 2020, the total infected per country (/150) averaged 559,157 and the total still active averaged 105,766. I would say they had been roundly invaded and the enemy were in their backyard.

[99] See Annex A of WHO's Response to Covid-19 dd 16 Feb 2021,at https://www.who.int/publications/m/item/looking-back-at-a-year-that-changed-the-world-who-s-response-to-covid-19

Financing the War

Vaccines Costs

I have earlier dealt in detail how the Medical Defence costs, especially Vaccines, have been financed, both the components to collectivise demand and to stimulate manufacture. Essentially COMAX has been a success, albeit with distribution problems. It remains to be seen whether LMICs will get herd immunity or the virus launches off on another (fourth) spike.

COVID-19 Solidarity Response Fund

In my review of the WHO budget, I pointed out that the organisation depended substantially, up to 86.4% in fact, on **annual voluntary** contributions for the larger proportion of even its "non-pandemic" work.

I did not see vast reserves held for handling pandemics, which as a result invariably required special humanitarian calls.

WHO wasted no time in launching the **COVID-19 Solidarity Response Fund** on 13 Mar 2020, Excluding vaccines costs, much funding was needed for country mobilisation and confronting the humanitarian issues of the pandemic.

I could find no statement of donations and expenses from this Fund for 2020, except the following from a WHO website[100]:

[100] https://www.who.int/news/item/15-03-2021-covid-19-solidarity-response-fund-marks-first-anniversary-and-appeals-for-continued-support

> "The fund has raised more than US$ 242 million from more than 661 000 individuals, corporations, and other organizations to support WHO and partners' global COVID-1
> An additional US$ 1.96 billion is needed for WHO in 2021 to continue coordinating global pandemic response, more than 60% will go towards requirements for the Access to COVID-19 tools, including diagnostics, treatments and vaccines."

Contributions to the SPRP

According to WHO's estimations, the requirement to respond to the Covid-19 pandemic to until the end of 2020 was $1.74 billion. As of 7 Dec 2020, 87.6% ($1.52 billion) of the required amount had been collected.

There was the further remark in the text of the 2020 Report that the latter sum ($1.52 billion) was collected from over 70 donors and included the $242 million donated to the COVID-19 Solidarity Response Fund.

I found the above information in conflict with data in Annex B of the Report. The latter gives a list of 113 (I counted) donors who made "Contributions to the SPRP" which totalled $1,539.53 million (we can ignore the small discrepancy with the $1.52 billion given earlier.). Further the list included a contribution from the "Covid-19 Solidarity Response Fund" of $84.07 million, which led me to look for the balance ($242 - 84.07) purportly collected.

It seems that the Covid-19 Solidarity Response Fund **failed** to finance the SPRP**.** I did not find that WHO ran any other fund-collecting drive for contributions to the SPRP.

Therefore, unless I am mistaken, WHO deployed funds from its "normal" Voluntary Contributions for its Programme Budget 2020. There was in fact some $3.7 billion in various allocations available and re-directable towards Covid-19.

My count showed a total of 113 contributors to the $1.539.553 in the Report. The 16 largest ($20 million and above) were:

Table 24
Largest Contributors to SPRP Fund. 2020
(USD millions)

No	Contributor	$
1	Germany	434.00
2	European Commission	135.76
3	United Kingdom	127.68
4	World Bank	65.56
5	Kuwait	60.00
6	Iran	51.97
7	Japan	50.47
8	USA	36.57
9	UNDP	33.45
10	Saudi Arabia	32.00
11	China	25.10
12	King Salman Aid/Relief Center	23.00
13	UN OCHA	21.78
14	Canada	20.92
15	UN Central Emergency Response Fund	20.91
16	Yemen (Islamic Dev Bank)	20.00

The above 16 donors contributed $3,230.25 millions or 15.4% of the total contribution for the pandemic. The UN brotherhood made sure WHO had seed-money by dumping in $141.70 millions of their moneys to kick-start WHO's operations.

I conclude my financial remarks by saying again that all this was also a one-off. It is no way to run a prolonged pandemic war.

* * *

(Back to TOC)

PART SIX

Global Partners

One reason we entertain reasonable hope of beating Covid-19 is that many sectors of the world community (including governments) were far-seeing and had made preliminary moves, whether in planning, research, surveillance or humanitarian services. When the crises came, they reacted spontaneously, rallied round WHO, worked together and shared their resources unreservedly.

They greatly enlarged the services the world has come to depend on from our historic NGOs, such as the Red Cross and Médecins Sans Frontières/Doctors Without Borders (MSF), etc

My review abounds in mention of these parties. I say it here without reservation: without their voluntary involvement, we would not make it as the world is presently organised.

I would like to briefly highlight their contributions. There are four groups: (a) the scientific-academic community (b) the charity foundations, (c) the humanitarian organisations and (d) the collaborative partnerships and networks.

If I were to single out three, they would be the Bill and Melinda Gates Foundation (BMGF), GAVI, the Vaccine Alliance and CEPI.

Scientific Collaboration

ICTV

"Taxonomy, the discipline of classifying and naming things, is the bedrock of all the sciences}." (ICTV)

The first attempts to introduce order into the bewildering variety of viruses took place by the scientists at the International Congress of Microbiology held in Moscow in 1966. A committee was created, later called the **International Committee on Taxonomy of Viruses (ICTV)** and was given the task of developing a single, universal taxonomic scheme for all the viruses infecting animals (vertebrates, invertebrates and protozoa), plants (higher plants and algae), fungi, bacteria and archaea. The ICTV is governed by the International Union of Microbiological Societies (IUMS).

The first Taxonomy of Viruses was published in 1971, comprising 290 species in 43 genus and. 2 families. The latest (35th) revision of 2020 comprised 9,110 species, in 2,224 genus, 189 families, and 59 orders.

Science made a great leap when we became able to discover the DNA of a virus. Through genome analysis we are able to determine its evolutionary history, family relationships, and ancestry back to early mutations.

ICTV is supported by a grant from the Wellcome Trust; contributions from the Virology Division of the International Union of Microbiological Societies, the American Society of Virology, and the Microbiology Society, among others.

The microbiologists and virologists of the world deserve our deepest thanks for their initiative in giving us the ICTV, and maintaining it on a voluntary basis.

NCBI

> "Understanding nature's mute but elegant language of living cells is the quest of modern molecular biology. From an alphabet of only four letters representing the chemical subunits of DNA emerges a syntax of life processes whose most complex expression is man. "
> https://www.ncbi.nlm.nih.gov/home/about/mission/

The **National Center for Biotechnology Information (NCBI**) was established in Nov 1988, as a division of the National Library of Medicine (NLM) at the US National Institute of Health (NIH).

The NCBI has been charged with creating automated systems for storing and analysing knowledge about molecular biology, biochemistry, and genetics; facilitating the use of such databases; coordinating efforts to gather biotechnology information both nationally and internationally; and performing research into advanced methods for analysing the structure and function of biologically important molecules.

The NCBI houses a wide range of non-computerised data-base resources, the latter including subdivisions into genomes, genes, and proteins. These three areas are in turn supported by five holdings of specialised resources, namely Taxonomy, **GenBank**, RefSeq, BioProject and BioSample, with common access tools.

The NIH and NCBI are funded by the US government under the Department of Health and Human Services (MHHS).

Two of the most important components of the US antiviral war machine are its Centers for Diseases Control and Prevention (CDC) and the National Institute of Allergies and Infectious Diseases (NIAIA). Both depend on the NCBI in their research work

Many developed countries share their scientific data in the same and different ways. As just one other example, the Federal German Genebank of Agricultural and Horticultural Crop Species is among the largest collection of its kind worldwide.

GenBank.

The GenBank database of NCBI is designed to provide and encourage access within the scientific community to the most up-to-date and comprehensive DNA sequence information. Therefore, NCBI places no restrictions on the use or distribution of the GenBank data.

GenBank is part of the **International Nucleotide Sequence Database Collaboration**, which comprises the DNA DataBank of Japan (DDBJ), the European Nucleotide Archive (ENA), and GenBank at NCBI. These three organisations exchange data on an hourly basis.

The GenBank also encourages **Metagenomics**. The analysis of metagenomic data provides a way to identify new organisms and isolate complete genomes from unculturable species that are present within an environmental sample.

GVN

The **Global Virus Network** (GVN) was co-founded in 2011 by Robert Gallo (of AIDS fame)), of the Institute of Human Virology at the University of Maryland School of Medicine, William Hall, of University College Dublin and the late Reinhard Kurth, of the Robert Koch Institute. . It is a coalition comprised of leading virologists spanning 63 Centers, 11 Affiliates, and 35 countries worldwide, all working to advance knowledge about how viruses make us sick and to develop drugs and vaccines to prevent illness and death. No single institution in the world has expertise in all viral areas. GVN brings the best medical virologists together to leverage individual strengths and to focus global teams of scientists on

key scientific problems. The power of GVN lies in its global reach, the depth of its science, and its commitment to solving viral challenges facing the human population. No other entity exists like the GVN.

GISAID

GISAID was established originally as the **Global Initiative on Sharing Avian Influenza Data** in 2006. Pre-existing it was the GISRS(see further on), which still serves as the surveillance and early warning system and information platform in the war against influenza.

GISAID however was a non-governmental initiative among leading scientists to provide hot-line communications and open-access to genomic data-bases on avian influenza. It has continued to do so for the influenza, coronaviruses, etc viruses in all the pandemics since.

GISAID was recognized for its importance by the G20 health ministers in 2017, and in 2020 WHO called the data-science initiative "a game changer"

On 10 Jan 20, the first complete SARS-CoV-2 genetic sequences were released by the Chinese Center for Disease Control an Prevention (CCDC) and shared through GISAID.

By mid-April 2021, GISAID's **SARS-CoV-2 database** reached over 1,200,000 submissions, a testament to the hard work of researchers in over 170 different countries. Only three months later, the number of uploaded SARS-CoV-2 sequences had doubled again to over 2.4 million. This contributed to the rapid development of our vaccines within one year.

GISAID officially launched in May 2008 at the WHA, as a publicly-accessible database converting it from the original “consortium” requiring membership.

Unlike public-domain databases such as GenBank, users of GISAID must have their identity confirmed and agree to its Database Access Agreement.

Among other things, it attempts to address the issues surrounding intellectual property. This is the stumbling block which can and does crucially delay public availability of research findings. GISAID's procedures require that those who access the EpiFlu database (name delightfully not changed!) consult the countries of origin of genetic sequences and the researchers who discovered the sequences. As a result, the GISAID license has changed the field of viral sequence data analysis.

GISAID has not only vitally provided the platform for Covid-19, but represents a model for sharing research in our future collaborative mechanisms.

GOARN

The **Global Outbreak Alert and Response Network (GOARN**) is a network composed today of over 250 technical and public health institutions, laboratories, NGOs, and other collaborating organizations that work to respond to threatening epidemics on a quick action basis.

GOARN was established under the auspices of WHO, originally with 67 Members in 2000.

The WHO does not have resources on standby to adequately help prevent and respond to outbreaks all around the world. GOARN was therefore formed to mobilise assistance on an immediate response basis, globally and covering all epidemics.

At the same time, the network’s guiding principles were to standardize "epidemiological, laboratory, clinical management, research, communication, logistics, support,

security, evacuation, and communication systems", and coordinate international resources to support local efforts by GOARN partners to combat outbreaks.

The WHO does not directly fund GOARN. Instead, funds from GOARN members and other are raised and used on a one-off basis to support a response. GOARN is effective at operating from a fairly small budget. It's forte is it can mobilise a team quickly.

GOARN has responded to over 120 occurrences in 85 countries and has deployed over 2,300 experts into the field.

GOARN was among the first to send a team to China on first reports of Covid-19 to investigate the virus.

(Back to TOC)

Foundations

Bill and Melinda Gates Foundation (BMGF)

Originally founded in 1994 as the William H. Gates Foundation, it became the **Bill & Melinda Gates Foundation (BMGF)** by merger with the Gates Learning Foundation, in 2000. As of 2018, Bill and Melinda Gates had donated around US$36 billion to the foundation
It is reported as of 2020 to be the second largest charitable foundation in the world, holding $49.8 billion in assets.

The primary goals of the foundation are to enhance healthcare and reduce extreme poverty across the world, and to expand educational opportunities and access to information technology in the U.S..

In October 2006, the Bill & Melinda Gates Foundation was split into two entities: the Bill & Melinda Gates Foundation Trust, which manages the endowment assets and the Bill & Melinda Gates Foundation, which "... conducts all operations and grant-making work, and it is the entity from which all grants are made".

As of April 2014, the foundation was organised into the following programme areas:

- Global Development Division
- Global Health Division
- United States Division
- Global Policy & Advocacy Division
- Global Growth & Opportunity Division.

The trust section manages the investment assets and transfers proceeds to the foundation as necessary to achieve the foundation's charitable goals.

The foundation expended a sum of US$21,485.0 millions in the five years up to 2015 in the healthcare sector, of which $5,586.4 went to Infectious diseases control, $1,456.1 millions went to Malaria and $1,308.0 went to STD including HIV. In terms of receiving organisations, GAVI received $3,152.8 millions and WHO received $1,535.1 millions.

Wellcome Trust

The **Wellcome Trust** is a charitable foundation focused on health research based in London, UK. It was established in 1936 with legacies from the pharmaceutical magnate Henry Wellcome, to fund research to improve human and animal health. The aim of the trust is to "support science to solve the urgent health challenges facing everyone."

It had a financial endowment value of $37.0 billion in 2020 (GBP 29.1 millions), making it the fourth wealthiest charitable

organisation in the world. It is UK's largest provider of non-governmental funding for scientific research, and one of the largest in the world. According to their annual report, the Wellcome Trust spent $1.4 billions (GBP 1.1 billions) on charitable activities across their 2019- 202 financial year

In 1995, the trust divested itself of any interest in pharmaceuticals by selling all remaining stock to Glaxo

The trust is a major charitable foundation supporting WHO against the Covid-19 pandemic.

(Back to TOC)

Private-Public Partnerships

CEPI

The **Coalition for Epidemic Preparedness Innovations (CEPI)** is a partnership between public, private, philanthropic, and civil organisations launched to develop vaccines to stop future epidemics.

It works to accelerate the development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for people during outbreaks.

The concept originated in an idea by three eminent virologists in Jul 2015 of "Establishing a Global Vaccine-Development Fund". The concept was discussed at the World Economic Forum (WEF) in 2016 as a solution to the problems encountered in developing and distributing a vaccine for the West African Ebola virus pandemic. CEPI was formally launched in 2017 at the World Economic Forum in Davos.

It was co-founded and co-funded with $460 million from the Bill and Melinda Gates Foundation, the Wellcome Trust, and a

consortium of nations, viz India, Germany, Japan and Norway; the European Union (2019) and Britain (2020). CEPI is headquartered in Oslo.

CEPI's creation was co-funded by the pharmaceutical industry, including GlaxoSmithKline, whose CEO said "People do not realise that there's no spare capacity in the world's vaccine production system today". **Gates said that a key goal was to reduce the time to develop vaccines from 10 years to less than 12 months.**

CEPI's task is to build the scientific and technological infrastructure for developing vaccines quickly. CEPI's priorities would include to establish technical and regulatory pathways, develop manufacturing solutions for vaccine candidates nearing completion, and create stockpiles of vaccine candidates for production for use in emergency situations.

The initial targets were the six WHO identified EIDs.[101] viruses. However, from early on, CEPI strategies included provision for dealing with WHO's **Disease X** – that unknown new virus that would sweep the world if not anticipated.

In October 2018, CEPI scientists estimated that the costs of developing at least one vaccine for each of the EID diseases that could escalate into global humanitarian crises was between $2.8 billion and $3.7 billion.

By Feb 2020, CEPI had raised a total of $760 million, with additional donations from the governments of Australia, Belgium, Canada, and the $K.

---

101 An emerging infectious disease (EID) is an infectious disease whose incidence has increased recently (in the past 20 years),and could increase in the near future.

In March 2020, the British government pledged $287 million in funding to CEPI to specifically focus on a vaccine for the coronavirus; making Britain CEPI's largest individual donor.

CEPI was poised to join battle with WHO and the rest of the world against Covid-19 that had just broken out. **CEPI might be thought of as the front-end of COVAX.**

CEPI's critical contribution is the research. If successful, it (or some other agency) can sub-contract production to a manufacturer, allowing him rights and patents in respect of his proprietary components, including brand name. The manufacturer may or may not be permitted to fulfil any national obligations. CEPI may even manufacture in more than one country. Depending on its subsidy policy, there could be one world price, or different prices depending on whether for the medical authorities or the public and or country. CEPI is in a position to conduct much of this is lateral operations and not sequentially, and so bring out the vaccine fast,

CEPI looks to establishing rapid response platforms. These refer to systems that use the same basic components as a backbone, but can be adapted against different pathogens by inserting new genetic or protein sequences. Platform manufacturing can be set up for rapid use against novel pathogens. Over time, as regulatory authorities gain experience with such platforms. and will likely become comfortable about rapidly moving new vaccines into clinical trials. This has been the case with influenza vaccines, which are developed every year on an existing platform.

CEPI is the primary party behind the **COVAX Facility** scheme and the success in bringing to us the supply of vaccines and therapeutic drugs against Covid-19 within one year.

GAVI, The Vaccine Alliance

GAVI, officially **Gavi, the Vaccine Alliance,** is a public-private a major global health initiative with the goal of **increasing access to immunisation in poor countries.**

GAVI was created in 2000 as a successor to Children's Vaccine Initiative, which had been launched in 1990. Gavi has helped immunise over 760 million children, preventing over 13 million deaths worldwide, helping increase diphtheria vaccine coverage in supported countries to 81% in 2019, contributing to reducing child mortality by half.

GAVI supports the immunisation of almost half the world's children, giving it power to negotiate better prices for the world's poorest countries and remove the commercial risks that manufacturers faced in serving this market. It also provides funding to strengthen health systems and train health workers across the developing world.

One author described GAVI's approach to public health as business-oriented and technology-focused, using market-oriented measures, and seeking quantifiable results.

In their 5-year cycle, 2016–2020 ,GAVI received $9.3 billion, with UK providing around $2.32 billion, the Bill and Melinda Gates Foundation ($1.55 billion and US and Norway close behind.

For their cycle, 2021 to 2025, $8.8 billion has been raised. This included $2.0 billion from the UK, $1.6 billion from the Gates Foundation, and $1.0 billion from Norway. This round of funding will mean that 300 million more children in lower-income countries will be immunized. including measles, polio and diphtheria by the end of 2025. Additionally, the funding will support health systems to withstand the impact of coronavirus and maintain the infrastructure necessary to roll out a future COVID-19 vaccine on a global scale.

Gavi's impact draws on the strengths of its core partners, WHO, UNICEF, the World Bank and the Bill & Melinda Gates Foundation.

Because of these market shaping efforts, the cost of fully immunising a child with all 11 WHO-recommended childhood vaccines now costs about US$ 28 in Gavi-supported countries, compared with approximately US$ 1,200 in the US. At the same time, the pool of manufacturers producing prequalified Gavi-supported vaccines has grown from 5 in 2001 (with 1 in Africa) to 17 in 2019 (with 11 in Africa, Asia and Latin America).

Gavi partners CEPI in COVAX scheme, in particular the **COVAX AMC** component, focussing on ensuring the equitable supply of vaccines to the LMICs.

IFFIm

The **International Finance Facility for Immunisation** (**IFFI**m) was created out of the need **by Gavi** for the huge funds required for its immunisation work on a continuing basis. Working with the World Bank and some 10 long term donors, the idea was born to issue **Vaccine Bonds** within the IFFIm scheme which would be managed by the World Bank. The scheme was launched in 2006.

IFFIm has become a role model for Socially Responsible Investment (ISRIs) in global development, which faces constant funding challenges and unpredictability.

Vaccine Bonds provide investors with a unique opportunity to realise an attractive and secure rate of return and diversify their portfolios while helping save young lives. It's not a donation, it's an investment. IFFIm has been so successful, it has changed the face of global development funding.

IFFIm's unique financing model is built upon social responsible partnerships. IFFIm receives long term, legally

binding pledges from donor countries and, with the World Bank acting as Treasury Manager, turns these pledges into bonds. The money raised via Vaccine Bonds provides immediate funding for Gavi, the Vaccine Alliance. Since, 2000 Gavi has dramatically improved access to new and underused vaccines for children living in the world's poorest countries.

IFFIm accelerates the delivery of vaccines by making the money from long term government donor pledges available immediately. Through this funding mechanism, known as "frontloading,"

Vaccine Bonds lead to funding that is more predictable, enabling public health officials to plan vaccination campaigns well in advance.

In order to ensure investors of its ability to pay back interest and principal, IFFIm only raises bonds against a percentage of their overall pledge. IFFIm uses the remainder as a reserve to make sure that there will always be more than sufficient funds to pay bondholders when the bonds mature.

Donors' annual payments to IFFIm—or proceeds from new bond issues—go toward repayment to bondholders. For example, with a 5-year bond, at the end of 5 years, IFFIm would have paid interest, and will return the full principal.

At the end of the donor payment period and after all bonds are redeemed, IFFIm can transfer to Gavi any outstanding reserve—that was earlier set aside as reserve or to purchase more vaccines.

I notice that out of the $2.423 billion committed at the COVAX Donor's Summit in Jun 2021, $1.153 or 47,6% was through the IFFIm, by US, UK, Sweden and Norway.

(Back to TOC)

Other Collaborations and Partnerships

GLOPID-R

In 2013, the heads of international (biomedical) research funding organisations agreed to create an initiative to facilitate **collaboration between funders** in the field of new and re-emerging epidemics. The European Commission and the international funders launched the **'Global Research Collaboration for Infectious Disease Preparedness'** (GloPID-R)

Until then there has been no platform for scientists and research funders to identify the best research solutions and channel the necessary funds rapidly. The alliance was welcomed by G7 leaders in their "Vision for Global Health" published in May 2016.

Some 29 major research funders are represented in GloPID-R today. GloPID-R does not fund projects directly but rather coordinates and shares information among the funding organizations. That way, research funders can jointly or separately target funds to specific infectious disease research programs. They also stay updated on each other's research results and keep alert to emerging epidemics.

Thanks to this cross-sharing of information, members of the GloPID-R network were immediately able to coordinate in response to the emergence of COVID-19, to identify and bolster existing relevant funded in this area but also rapidly launch emergency calls to support new, urgent scientific priorities.

GloPID-R was the gestation environment that gave birth to WHO's first **Strategic Preparedness and Response Programme** (SPRP) of Feb 2020 and all that came after.

GLOBAL FUND

Formed in 2002, the Global Fund to Fight AIDS, Tuberculosis and Malaria (or simply the **Global Fund**) was an independent international partnership organisation that aims to "attract, leverage and invest additional resources to end the epidemics of HIV/AIDS, Tuberculosis and Malaria. At that time, these were the monster pandemics.

The Global Fund is a financing mechanism rather than an implementing agency. Programmes are implemented by in-country partners such as ministries of health. Implementation is overseen country-level committees of stakeholders that need to include, according to Global Fund requirements, a broad spectrum of representatives from government, NGOs, faith-based organizations, the private sector, and people living with the diseases.

Since the Global Fund was created in 2002, public sector contributions have constituted 95 percent of all financing raised. From 2002 to July 2019, more than 60 donor governments pledged $51.2 billion and paid up $45.8 billion. The largest contributors have been the US, France, UK, Germany and Japan.

It became apparent that a pure funding mechanism could not work on its own, and it began relying on other agencies, notably WHO, to support countries in designing and drafting their applications and in supporting implementation. As a result, the organisation is most accurately described as a financial supplement to the existing global health architecture rather than as a separate approach.

The Global Fund Strategy 2017-2022: Investing to End Epidemics outlines the partnership’s bold agenda for 2017-2022 based on an ambitious vision to end the epidemics.

Financial contributions from governments are critical to ending the epidemics and to strengthening systems for health. More than 80 countries have made or pledged contributions to the Global Fund to accelerate the fight against the three diseases.

The Global Fund is an WHO partner in the latter's COVID-19 Tools (ACT) Accelerator Programme **– for Diagnostics.**

FIND, Diagnostics For All

FIND **is a** global alliance for diagnostics was founded in 2003. It is a non-governmental non-profit organisation which seeks to ensure equitable access to reliable diagnosis around the world. It connects countries and communities, funders, decision-makers, healthcare providers and developers to spur diagnostic innovation and make testing an integral part of sustainable, resilient health systems.

It is widely supported by governmental, humanitarian institutions and funds, and the private sector.

FIND's raison d'etre is:. Testing is the first line of defence against outbreaks that are becoming increasingly severe and complex.

The following list of "what we do" heading explains their activities: Universal Health Care (UHC) and health emergencies; Roadmaps -diseases and diagnostic systems; Technology review and support; Target product profiles,; Biobank services; Accessible Pricing; Reports and. guidance.

FIND is WHO's partner under Covid-19 (ACT) Accelerator programme for **Diagnostics.**

UNITAID

Unitaid is a global health initiative, founded in 2006, that works with partners to bring about innovations to prevent, diagnose and treat major diseases in low- and middle-income countries, with an emphasis on tuberculosis, malaria, and HIV/AIDS and its deadly co-infections at the time .

The organization funds the final stages of research and development of new drugs, diagnostics and disease-prevention tools, helps produce data supporting guidelines for their use, and works to allow more affordable generic medicines to enter the marketplace in low- and middle-income countries.

Hosted by WHO in Geneva, Unitaid was established by the governments of Brazil, Chile, France, Norway and the United Kingdom.[4]

As of 2019, Unitaid manages a portfolio of 48 grants worth around $1.3 billion. Unitaid's main donors are France, the United Kingdom, Norway, the Bill and Melinda Gates Foundation, Brazil, Spain, South Korea, and Chile.
The single main source of income is an airline ticket tax currently in effect in ten countries: Cameroon, Chile, Congo, France, Guinea, Madagascar, Mali, Mauritius, Niger, South Korea and France.

Norway allocates part of its tax on carbon dioxide emissions from aviation to Unitaid, and the United Kingdom contributes through multi-year commitments.

Unitaid and partners have brought new, affordable HIV medicines to people in Africa in three years, three times faster than for previous generations of antiretrovirals.
Unitaid and partners have revolutionised childhood TB treatment with quality paediatric medicines that are affordable and taste good.

Unitaid and its partners are finding new ways to manage and mitigate mosquitoes' resistance to insecticide with the first long-lasting insecticides recommended by WHO in 40 years

Unitaid and partners have succeeded in introducing quality-assured, affordable self-testing kits across Africa in the space of three years. Fifty-nine countries now have policies on HIV self-testing.

In 2010, Unitaid created and invested in the Medicine Patent Pool (MPP) to negotiate voluntary licenses for HIV medicines. MPP helped bring about the widespread use of tenofovir for HIV treatment, which resulted in a savings of $195 million in drug costs between 2012 and 2015

Unitaid is a WHO partner in the **COVAX scheme.**

GPHIN

The Global Public Health Intelligence Network is an **AI-based** surveillance system initiated and run by Health Canada and the WHO. It currently analyses more than 20,000 online news reports in nine languages daily.

The value of informal sources is to increase the timeliness of disease outbreak detection and provide detailed epidemiological information in the early warning and preparedness.

Their integration is formalised through the so-called epidemic intelligence (EI) process.

Due to the growing volume, variety and velocity of digital information, a wealth of unstructured open-source data is generated daily, mainly as spoken or written communication. Unstructured open-source data contains pertinent information about emerging threats that can be processed to extract

structured data from the background noise to aid in early threat detection.

EIOS

The **Epidemic Intelligence from Open Sources (EIOS**) initiative is a unique collaboration between various public health stakeholders around the globe. It brings together new and existing initiatives, networks and systems to create a unified all-hazards, “One Health” approach to **early detection,** verification, assessment and communication of public health threats using publicly available information.

Creating a community of practice for public health intelligence (PHI) that includes countries, international organisations, research institutes and other partners and collaborators is at the heart of the initiative; saving lives through early detection of threats and subsequent intervention its ultimate goal.

The EIOS community of practice is supported by an evolving EIOS system, which not only connects other systems and actors – including ProMED, and the Global Public Health Intelligence Network (GPHIN) – but also promotes and catalyses new and innovative collaborative development. The EIOS system builds on a long-standing collaboration between WHO and the Joint Research Centre (JRC) of the European Commission (EC) ve to bring together PHI efforts. It is aimed at consolidating a wide array of endeavours and platforms to build and link robust, harmonised and standardised PHI systems and frameworks across organisations and jurisdictions.

In Sep 2017, WHO accepted leadership of EIOS under the Health Emergencies Programme (WHE) with a governance structure involving multiple stakeholders..

The **WHO Corona Virus (COVID-19) Dashboard**[102]**,** an outstanding collective product of the EOIS and other systems, allows for visualisation of the progress of the outbreak in real time. The application currently displays data from WHO, Johns Hopkins University, the European Centre for Disease Prevention and Control and Worldometer[103] and automatically checks for updates every five minutes.

The **Google COVID-19 News Map** is another of the applications to visualise he information coming through EIOS. It displays the headlines and snippets of the ten most recent articles that the system has identified.

The EOIS systems are key **surveillance systems** of the future.

(Back to TOC)

Surveillance and Early Warning Networks

GISRS

WHO's **Global Influenza Surveillance and Response System (GISRS)** was the first system set up, in 1952, before the information age. It is a **country based** partnership, and is today a fully matured system guarding against Influenza. Needless to say these days, other information also flow through it as relevant into the EOIS

The mission of GISRS is function as (a) a global mechanism of surveillance, preparedness and response for seasonal, pandemic and zoonotic influenza; (b) a global platform for monitoring influenza epidemiology and disease; and (c) a global alert network for novel influenza viruses and other

102 https://covid19.who.int

103 https://www.worldometers.info/coronavirus/worldwide-graphs/#total-cases

respiratory pathogens. GISRS currently comprises 145 centres in 114 WHO Member States:

National Influenza Centres (NICs) collect virus specimens in their country and perform preliminary analysis. They ship representative clinical specimens and isolated viruses to WHO CCs for advanced antigenic and genetic analysis.

The results form the basis for WHO's recommendations on the composition of influenza vaccine each year, as well as relevant risk assessment activities of WHO.

NICs are national institutions designated by national Ministries of Health and recognized by WHO. They form the backbone of the WHO's Global Influenza Surveillance and Response System (GISRS).

Currently there are six WHO Collaborating Centres (CCs) and four Essential Regulatory Laboratories within GISRS, including one in China and one in Russia.

In fact H5 Laboratories, capable of researching across human-animal divide, were added to some of them when the new avian Influenza H5N1 Variant threatened around 2004.

Today, GISRS is the mature "resident" system of WHO spanning all countries. While its tools are specialised against influenza, they can be deployed to deal first line with other epidemics.

Today, GISRS can be thought of as a common information and resource platform for both GOARN and GISAID.

* * *

(Back to TOC)

PART SEVEN

Concluding Observations

The Pandemic

Virus

That viruses do not die is a definitional problem in biology. In fact, a virus is created with a life-cycle to replicate, and in doing so to allow itself to be destroyed. It is the prototype of the kamikaze. Viruses leave a trail of fragments or fossils.

The problem arises because a virus can only replicate in a living cell. More, it is constitutionally hard-wired to hunt, invade, infect, and replicate in a living cell. It is a predator. Ultimately it **kills** the infected cell - to which we take great objection.

The second fact is that, when active, a virus replicates many times a day and exponentially. And, thirdly, if not active, it lasts forever until it can replicate. The result is that there are zillions of them around hunting us.

Several species specialise in human cells. We are their walking targets.

Finally viruses possess highly mutative skills. For this reason, they breach the natural human immunological defence systems regularly. Once they penetrate into our cells, there is little we can do. Our primary defence is vaccination, which jacks up our immune system to stop them getting in.

Our next biggest threat is an infected person. Human-to-human transmission is the main danger. The only protection

we have against ourselves is social distancing. Before a vaccine is available, it is the only defence.

It is a great blessing that once a person has been infected, he or she is immune. Once everybody is immune, we are safe. Our ultimate defence against a pandemic therefore Is **herd immunity.** The virus gets around this by creating Variants. It becomes a continuous high-noon of who can draw faster, Variant o Vaccine. So far I saw proof of the belief that viruses get weaker as they replicate.

The Outbreaks

The SARS Covid1 outbreak in 2003 was clamped down in four months. No vaccine was available. It was done by social distancing, Chinese style. There would not have been time for herd immunity,

The Spanish Flu (Influenza A H1N1) in 1918-1920 petered off after 500 million people were infected and 18 million died, while the rest of the world survived by a combination of international and local social distancing and herd immunity.

Since then it has been a cat and mouse game. The first Influenza vaccine was developed in 1945. The virus has evolved several times, hopping between man and birds, with four big pandemics. Meanwhile, the virus has gone seasonal world-wide. We in turn are down to a flu jab every year to keep ahead. It is a stalemate. Influenza still ranks as one of the biggest annual killers, at 1.23 persons per minute.

It was the ferocity of the Ebola Viral Disease (EVD) that shook the world. First encountered in 1976, it caused two epidemics, in West Africa in 2013-6 and in the Congo in 2018-20. It hit populations at the lowest levels of income and defence. Social distancing did not apply, for it was not human-to-human transferred. The virus was acquired by eating the bushmeat of infected monkeys. There was no vaccine, and there were no drugs. The devastation was phenomenal, with death rates

running at about 20%-50% and over. In each case, the epidemic ceased, I am not aware specifically how, but undoubtedly with a combination of the efforts of the people, international help and possibly herd immunity. That the countries were not in the main communication streams probably helped containment. In 2019, the FDA approved a vaccine on trial.

No vaccine has yet been found for HIV/AIDS, which pandemic began in 1981 and is still on-going. Some 75 millions have been infected and some 37.6 millions have died . In 1996, a definitive anti-viral drug-cocktail HAART became available. It halted the virus' subversion of the immune-deficiency defences, but not cured the person. As a result, there are another 37.4 million people living today with AIDS. The annual infection rate is still 1.5 million. There are now some 30 drugs to help them.

In the SARS-Covid-19 pandemic, we have come up with a dozen vaccinations inside a year and a half. The virus on the other hand has come up with four "Variants of Note", with another five "Variants of Interest", and promise more. Unless we do something about it, we shall at best be in the same situation as with Influenza – with one new vaccination every year for every new Variant.

Covid-19 has wracked its own havoc. The world economy has had to be in lock-down. The pandemic hit 222 countries almost simultaneously, and 3% of the world population (excluding China) were infected before the first vaccine was ready. We were taken by surprise by its virulence, said to be 10 times more than its suspected parent – and suspected to have been the result of lab experiments.

As it is, we must take risks and re-open the world economy bit by bit. And it will take another two years to reach global herd immunity. The LMICs will be the last covered and the worst hit.

Overcrowded World

An increasing number of virus arrivals are now zoonotic. Man's rapid encroachment into the natural world puts further squeeze on our fellow earthlings, including viruses, and makes cross-overs easier.

One senses that we have two overcrowding species trying to occupy the same space. There is a similar situation in the oceans, where viruses are killing bacteria, turning them into bacteriophages, critically affecting our oxygen supply. There have also been pandemics in the plant and animal kingdoms, some potentially capable of undermining the human food chain.

The net result is that the world is under a viral threat across the biosphere. Here I am concerned with the human biome. The threat is accentuated by the speed and scale at which a virus can generate a pandemic in modern times. Sooner or later, they will get us if we do not do something. Although I have not seen specific literature, I have found myself believing viruses have caused species extinctions before in history, perhaps even regularly.

Coming back to the present, the overall death rate of Covid-19 was around 2.31% as at Aug 2021. We will not all die from it, only the old folks, who seem to be falling like ten pins. Someone had better focus on keeping the latter alive. . Let me make my position clear. As long as one person is left behind to die, the war is not over. Everyone must be allowed to live out his or her old age.

The real threat to our common survival is in the shut-down of the economic systems for too long, disruption to the food and other chains of supply, and the endangering of the eco-system. We have to beat the virus.

(Back to TOC)

How We Performed Globally

On the Prepared Side

While our response has been patchy in places, the world overall has confronted Covid-19 with great heroism, and in some respects with outstanding credit to our humanity.

On the prepared side, we must give first place to WHO's Global Influenza Surveillance and Response System (**GISRS),** established in 1952. It is a fully matured country-based early warning system with 146 National Influenza Centres (NICs) in 114 countries, and 70 years' experience fighting the flu. The system was immediately deployed to track the Covid-19 virus. The first reports of atypical outbreaks came through this system from China – as Influenza.

In 2000, even before the SARS-Covid1 pandemic, WHO and partners had established the Global Outbreak Alert and. Response Network **(GOARN).** Voluntarily funded and operating on an assignment basis, it is a network of more than 200 partners ready to respond to and identify infectious disease outbreaks worldwide. GOARN teams were among the first in the field in China in both SARS-COVID1 and SARS-Covid 19.

And in 2008, the. World Health Assembly (WHA) endorsed creation of GISAID. Originally proposed by some 70 leading scientists as a consortium titled Global Initiative on Sharing Avian Influenza Data (**GISAID),** the acronym stuck although it became the mechanism for open-access sharing of genomic data of all viral pathogens. Its formula took account of property rights, basically overcoming this intractable obstacle. It was the "game-changer" that facilitated the rapid sharing of research information on emerging viruses. It was the foundation that enabled the uninhibited flow of genetic research that was to follow.

In 2016, WHA approved an **R&D Blueprint**, prepared by a broad coalition of medical, scientific, and regulatory experts, a plan for the rapid activation of research and vaccine development during epidemics.

It was driven by a Global Co-Ordination Mechanism **(GCM),** which facilitated collaboration by researchers and donors dealing in the same disease. For each disease an **R&D roadmap** was created, followed by target product profiles. Needless to say, this was vital infrastructure for the coming work.

On the Response Side

The first point of departure for COVID-19 came on 10 Jan 20, when the GCM to Prevent and Respond to Epidemics held its first teleconference, as did the Scientific Advisory Group for the R&D Blueprint. Those discussions were synthesised in a **Covid-19 Roadmap** and led to the first global forum of international scientists on COVID-19, on 11–12 February 2020.

On 3 Feb 20, WHO issued the Strategic Preparedness and Response Plan **(SPRP)** to guide all countries how to prepare for the anticipated pandemic. It was updated on 14 Apr 20.

And finally on 26 Apr 20, WHO and its principal partners launched the **Access to Covid-19 Tools (ACT) Accelerator** programme, with three “pillars” or targets: (1) Diagnostics. (2) Therapeutics and (3) Vaccines. The last became the **COVAX** programme.

Before Covid-19, it took up to 10 years to develop a vaccine. But, this time, they took only a year. It has been an outstanding feat of voluntary collaborative endeavour by a united world community of scientists, financiers, administrators and humanitarians.

The COVAX Facility, the COVAX Marketplace and COVAX Advanced Market Commitment (AMC) feature have been triumphs of modern ingenuity. The invention of Vaccine Bonds (IFFims) has been another "game changer" of long term impact.

As I do the final edit of this Part, on 27 Sep 21, we have no less than 12 vaccines in production round the world, of which the largest outputs will be from China, India and Russia, all COVAX approved. ART Home Test kits are today freely available around the world.

The main constraint is getting the vaccines to the LMIC countries, where 82.2% of the world live. The COVAX.AMC scheme to finance them has again been an ingenious mechanism, It pools donor funds as a bargaining advantage to secure early supplies for them, lack of which would drag the pandemic on further.

The another difficulty has arisen because countries have had to prioritise their own populations as the pandemic failed to decline. They have gone for total herd vaccination with two or more shots. And they have pre-empted their domestic production for their needs. India is an interesting case in point. The world largest LMIC, it is also at present the largest manufacturer of vaccines for COVAX. It was forced to divert its output locally to combat its horrendous second pandemic – contributing to the world shortfall. If the same happens to China or Russia, the other two big manufacturers, the (other) LMICs will end up further short.

The problem is not supply. We are vaccinating at 29.4 million does a day world-wide. We have in fact so far vaccinated the equivalent of 39.9% of the total world population. The problem is priority. The rich countries are cornering the supply for their populations. And, as soon we can, we shall need to up the world herd percentage to 100% and include children, and then go to two shots, and then boosters. Meanwhile, we need to detonate the virus' standard processes of producing Variants.

The present world **herd humidity** was originally set at a first level of 60% (without children) across the globe by end- 2021, with a target of 2 billion shots for the LMICs. WHO has announced a 30% shortfall of the latter. Our present global dateline is Mar 2022.

WHO

WHO has my full respect. From the preceding, they were as prepared as could be. In my view, WHO showed both foresight and competence over the battlefield.

Further WHO has led the world credibly. It has been able to provide the overall leadership necessary across the political, professional, technical and humanitarian horizons of this crisis, notwithstanding a perhaps undue circumspection towards China. Most importantly, it has been able to marshal the private partnership community.

At the same time, WHO was born out of the UN politics of post-World War 2. It has inherent weaknesses for its role in the 21st Century, or fighting virus pandemics if nothing else. The IHR is as functional far as it can go, and it is not enough. I touch on some issues under Direction of Change.

Score-lines

Today, on 29 Sep 2021, as I write, the world total infections stands at 234,085,545, with total deaths at 4,793,682.The total still actively infected on the same date was at 18,404,896. We have just turned the third and highest daily global peak of 19,124,897 which occurred on 5 Sep 21. The world vaccination coverage was about 48.6%

With easing of social distancing to open up the economy, the Singapore total infections had gone up from 64,453 two months ago to an all-time peak of 94,043 on 29 Sep 21.The daily new cases was 2,268 and death 93, as compared to

around 12 and zero respectively six month before. There are indications we shall cross the 150,000 mark, with corresponding deaths as the virus focuses on the old folk. Some 84% of the population has been vaccinated, the vast majority twice. There were 16,643 active cases, and climbing. The. government is now lamely talking about “living with covid as endemic”.

And finally, as an example of a lower-end LMIC, Ethiopia has had 344.322 cases in all and 5,534 deaths, with 28,081 active cases currently. Only 2.5% of the population of 118, 618,470 have been vaccinated

(Back to TOC)

Country of Origin’s Performance

The present pandemic has taught us how important the Country of Origin is. In this section we examine how China performed in this role. Because information about China is hard to find assembled in one place, I have re-summarised, and included here detail not earlier available.

Important new documents became available in August and September 2021 relating to the GOF/Accidental- Leak Theory of the origin of Covid-19. This has enabled me to devote a whole section (following this) to examining the subject and drawing my conclusions.

China’s Initial Response

Credit must be given to China in that they identified and sequenced the genome of the virus and released the information on GISAID within 10 days of notification of the outbreak. I have no doubt that, in accordance with the compulsions that drive the Chinese psychic, it was essential that they demonstrate their scientific equality in this

achievement. They did so. How they came to be in the position to do so is explored further on.

There is however a lot of dissatisfaction whether China took too long to carry out the preliminary investigations of the outbreak before notifying WHO.

We may ignore the original reports of atypical influenza in Nov 19. But, from the first index case of 1 Dec19 to notification to WHO on 31 Dec 19 there had been a build-up of cases, bringing the total number to 41 on 8 Dec 19.

On 24 Dec 19, a local hospital sent a sample to a private lab in Guangdong for analysis, which confirmed on 30 Dec 19 that it was the SARS Coronavirus I. wonder why the hospital did not go to WIV which at that point was the most knowledgeable party on the subject.

It took another 27 cases for the panic set in. An alert put out by the Wuhan Health Commission to affiliate institutions on 30 Dec 19 was picked up by the media – and apparently WHO China. WHO was officially informed the next day of an unidentified infectious outbreak.

My conclusion is that there was a fumble by the local health people. They did take too long to consult and raise the alarm. It is not clear to me whether the political boys had taken control yet before the cat got out of the bag.

Identification of the Virus

The proper authorities took control thereafter. On 3 Jan 20, the NIVDC isolated its genetic sequence and on 7 Jan identified the virus. On 10 Jan 20, with NHC approval, three genetic sequences of the novel coronavirus, one from the NIVDC, one from the Chinese Academy of Medical Sciences and one from Jinyintan Hospital in Wuhan were

posted on to the Global Initiative on Sharing All Influenza Data (GISAID) portal.

On 11 Jan 20, China formally shared the genetic sequences with WHO, and the Shanghai Public Health Clinic Centre through the Wuhan Institute of Virology released the data to GenBank and Virology.org.

With these steps, China established its status as a credible and independently able Country of Origin. Later it will be shown that they had had almost 18 years of prior research in this area

Wuhan, Eye of the Pandemic.

It is normal for the Country of Origin to be the first and worst hit. China's experience has been somewhat different.

On 14 Jan 20, The Wuhan Municipal Health Committee stated: "current investigation hasn't found clear evidence of human to human transmission, however, the possibility of human to human transmission cannot be ruled out".

By mid-Jan 20, the Lunar New Year travel rush was on, and the world's largest annual human migration got underway, with 5 million people leaving Wuhan to return home or pass through on their journeys.

On 18 Jan 20, some 40,000s of Wuhan families took part in a mass Lunar New Year banquet hosted by the city. Many became infected.

On 19 Jan 20, the first confirmed cases were reported outside Wuhan, one in Guangdong and two in Beijing. Wuhan reported 136 additional laboratory-confirmed cases, bringing the total number of laboratory-confirmed cases in China to 201.

On 22 Jan 20, the total number of laboratory-confirmed cases in China increased to 571 and the death toll to 17. Hong Kong reported its first case. The panic was on.

The eye or vortex was Wuhan. Once it got out into Hubei, it would become a hurricane and hit the whole country of 1.4 billion people.

Hubei is about the size of UK without Scotland. It has the same population of 56 millions and a similar urban-industrial-communications environment, with Wuhan itself corresponding to London. Whereas Britain is surrounded by its the seas, Hubei lies in the centre of China, surrounded by rest of the Chinese, and that would be 20% of the world population.

Wuhan-Hubei had to be locked-down. WHO commended China on its mighty resolve, but had never contemplated action on such a scale.

To quote the official report of the pandemic, it was "the largest medical assistance operation since the founding of the PRC.[104]"

World's First Lockdown

On 23 Jan 2020, the city of Wuhan was placed on quarantine, no traffic in or out. By the end of the next day, the entire Hubei province had gone under a city-by-city quarantine, apart from the forestry districts.

On 23-24 Jan 20, some 16 multi-million cities with a total of 56 million people went under the world's first "lock-down".

A shutdown on this scale required powerful leadership. President Xi Jinping took personal control., He set the mood for the country clearly: " Hubei and Wuhan are the decisive

[104] http://en.nhc.gov.cn/2020-06/08/c_80724.htm

battlegrounds. Victory in Wuhan would ensure victory in Hubei, and ultimately victory across the country. No effort would be spared in saving lives".

The second requirement is a people capable of such compliance. Wuhan carried out two rounds of community-based mass screenings of its 4.21 million households, leaving no person or household unchecked

Thirdly a shutdown like this required a large "hinterland" of resources and much centralised muscle to mobilise the same. Here I quote just one example from the same report of action taken (edited):

> The government …mobilized 40,000 construction workers and several thousand sets of machinery and equipment to build two hospitals. The construction of the 1,000-bed Huoshenshan Hospital was completed in just 10 days, and that of the 1,600-bed Leishenshan Hospital in just 12 days. In 10 short days, 16 temporary treatment centers providing over 14,000 beds were built.[105"]
> White Paper - "Fighting Covid-19: China in Action
> State Council Information Office
> 7 Jun 2020.

Within the country's tight controls, prefectures and cities exercised the lockdown provisions according to need. The same applied in the rest of China. I have no details, but my impression at least much of the trunk traffic was closed.

WHO's China Representative made this meaningful remark: "One area that China has been very effective in has been implementing a differentiated, location-specific response to limiting transmission, so that public health measures are tailored to the differing realities on the ground. Measures in Wuhan, for example, were very different than those

---

105 ibid

implemented in other places such as Shanghai or Chengdu.[106]"

By 12 Feb 20, total daily infection cases reached a peak of 13,332 in Hubei, and 15,152 altogether in China.(
By 18 Feb 20, however, the daily number nation-wide of the newly cured and discharged patients exceeded that of new cases, and the number of confirmed cases began to drop.

By 19 Feb 20, for the first time in Wuhan, newly cured and discharged cases outnumbered newly confirmed ones.

By 21 Feb 20, most provinces and equivalent administrative units started to downgrade their public health emergency response level in light of the local situation, and gradually lifted traffic restrictions.

By 24 Feb 20, all provincial trunk highways had reopened, and order was restored to the transport networks with the exception of those in Hubei and Beijing

By 6 Mar 20, The daily domestic cases on the Chinese mainland dropped below 100, and fell further to single digits on 11 March 20.

On 25 Mar 20, Hubei lifted outbound traffic restrictions and removed all health checkpoints on highways across the province except in Wuhan.

By midnight on April 16, the total number of confirmed cases in Wuhan had been revised up by 325 to 50,333, and the number of deaths up by 1,290 to 3,869.

On 8 Apr 20, Wuhan lifted its 76-day outbound traffic restrictions; and local work and daily life began to return to normal.

---

106 https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/4/

Thereafter, the Worldmeter website gives us these figures for China, with Italy for comparison.

Table 25
Covid-19: China Casualty Statistics, 2020-21[107]

Date 2020-21	Cumulative Total Cases	Cumulative Total Deaths	Italy: Cumulative Total Cases
22 Jan	571	17	0
20 Feb	75,465	2,236	4
20 Mar	81.008	3,255	47,044
20 Apr	82,747	4,632	181,216
20 May	82,965	4,634	227,358
20 Jan	88,557	4,635	2,424,450
20 Jun	91.587	4,636	4,252,493
20 Sep	95,738	4,636	4,638,513

Total cases in China soared to 81,008 by Mar 20 and plateaued off. It appears that they halted the pandemic across the whole country in **four months**, just as they did SARS-Covid1 in 2003, with a small resurgence this last quarter. Only four people died of Covid in China in the last 18 months. I put the figures for Italy alongside, illustrating what was the more typical experience world-wide.

On 29 Feb 20, the WHO-China Joint Mission on Covid-19 released a report which said, “In the face of a previously unknown virus, China has rolled out perhaps the most ambitious, agile and aggressive disease containment effort in history… As striking has been the uncompromising rigor of

107 https://www.worldometers.info/coronavirus/country/china/

strategy application that proved to be a hallmark in every setting and context where it was examined… Achieving China's exceptional coverage with and adherence to these containment measures has only been possible due to the deep commitment of the Chinese people to collective action in the face of this common threat."[108]

It is clear to me that the ability of a country to repeat the feat will be directly proportional to its totalitarian powers to command and regiment the country.

If the Variants of Covid-2 get a foothold on Chinese soil, the country may face the same problems of the virus going endemic as in the rest of the world. There is evidence this is about to happen.

Herd Immunity

China achieved a spectacular triumph in snuffing out the eye of the pandemic in Hubei by 26 Apr 20, only to realise that the rest of China still had no herd immunity.

Starting first with imported vaccines, they proceeded to vaccinate the population in parallel, starting with the high risk groups. The big scramble was to get as many vaccinated as possible before the Lunar New Year 2021.

Its own production became available from mid-2021. Bloomberg reported that as of 27 Sep 21, China had administered at least 2,211,452,000 doses of COVID vaccines. Assuming every person gets 2 doses, that was enough to have vaccinated about 79.1% of the country's population. That is another feat.

---

108 http://en.nhc.gov.cn/2020-06/08/c_80724.htm

- Vaccinations

Like the rest of the world, China rushed to produce a vaccine for Covid-19. Apparently, the near elimination of the virus also caused a scramble among their vaccine developers for suitable testing groups in developing countries. Because this option was more difficult to carry out and the results to evaluate by regulatory authorities, China's vaccines came on the world market later.

Nevertheless, as of today, China has the following vaccinations with approved EULs (Emergency Use Licenses) by WHO and therefore among other things purchasable through COMAX:

.1 - **BBIBP-CorV**, by the Beijing Institute of Biological Products and the state-owned **Sinopharm**, has emerged as China's leading Covid-19 vaccine, both within the country and abroad. In Sep 2021, Sinopharm had reached an annual production capacity of 7 billion doses.

.2 – **Coronavac,** by **Sinovac,** has emerged as one of China's leading vaccines, with a billion doses as of August 2021.

As at mid-year 2021, China had another 17 candidate vaccines in the trial stages.

The Global Times reported on 13 Aug 21 that China was able to produce 5 billion doses of COVID-19 vaccines per year and only needed half of them to vaccinate its 1.4 billion people. This meant China was able to provide the world with a large amount of vaccines.

In the face of growing "vaccine nationalism", earlier on 5 Aug 21 at the China-hosted Forum on International Co-operation on Covid-19 Vaccines, they announced that would China provide the world with 2 billion doses of COVID-19 vaccines this year and donate $100 million to COVAX.

One commentator describes the above as “vaccine geopolitics”. As both Chinese vaccines use Inactivated Virus technology, one main advantage of theirs is that their vaccines can be stored in a standard refrigerator at 2-8 degrees Celsius, more suitable for developing countries. The other, of course, is that price of Chinese vaccines can be set lower in negotiation, as quasi-aid or as an incentive, without too much market constraints.

Not to be left behind, China's first mRNA COVID-19 vaccine production plant will become operational in Oct 2021. The facility will produce 200 million doses of mRNA vaccine annually. The plant will produce the mRNA vaccine – A**RCo**V – jointly developed by the People's Liberation Army (PLA) Academy of Military Sciences, Suzhou Abogen Biosciences, and Walvax Biotechnology.

Among those still in trials is **CanSinoBIO,** which shot uses a modified common cold virus known as adenovirus type-5 (Ad5) to carry genetic material from the coronavirus protein into the body.

China has come out of the Covi-19 pandemic as the top vaccine producer of the world. A Country of Origin need not be able to make its own vaccines, but must have access to what it needs to halt the initial onslaught.

Overall performance

In terms of the initial set of actions required of a Country of Origin, China isolated the virus, identified the virus, sequenced its genome, and informed the world. The grouse against is that it took too long to before notifying the world of the outbreak.

In terms of internal pandemic control, it did exceptionally well.

It squashed the spread domestically, prepared it own vaccines, and has near achieved herd immunity. The deaths totalled has been a mere 4,636 during most of 2021.

In terms of vaccines, China's successes may become a significant factor in saving us from this pandemic.

What is apparent now is that at a point when the Wuhan Grant researches had reached GOF breakthroughs with the potential of creating a new enhanced pathogen (an ePPP in fact), China exercised what might be termed its right to call off its institutions and abort the project. I date this as happening 2.00 am on 12 Sep 2019. What had been shared, was shared. China secured and kept the rest, including the records, samples and other stuff not shared.

On the face of it, any country (say USA or Singapore) would be justified if such a pandemic threat was being developed within its boundaries by a foreign-financed contractor. In a sane world, that country would take it to the UN or WHO. At present, the latter two lacked anything like the resources (labs) or authority to handle a crisis at this level. In the absence of the latter avenue, it would not be farfetched for others to suspect that the pre-empting country would fiddle with the research material to explore other benefits.

In this case, the US in effect accused China of proceeding further with the Wuhan researches on its own, coming up with the SARS-Covid 2, and allowing it to escape; and demanding the latest Wuhan records and samples, so that the origin of the virus could be unquestionably determined. It becoming a political issue, China has just refused. It managed the joint WHO-Chinese mission so that it found nothing except what China wanted it to see. China has steadfastly refused to countenance or allow any independent investigation.

However, in the interests of international clarity and for my own satisfaction, in the next section I explore these

allegations further and try to form my own conclusions on establishable facts.

(Back to TOC)

Wuhan GOF and Accident-Leak Allegations

Unfortunately we live in a world of big powers dominated by distrust. I have no illusions they are not continually looking for new weapons, of which the virus as a bio-weapon is an obvious possibility.

I am further far from naïve to believe that individuals in the science community, whether encouraged by profit-hungry corporations, pressured by their governments or driven by self-interest, have not, with the best of intentions, ventured across the line into dangerous research, such as gain of function (GOF). The framework of international controls and surveillance in this area is weak. Further, such activity will be kept well out of detection. If China or any other country is so engaged, I do not think we can know about it – unless there is a “spill”.

This leaves only accidents in genuine research. At the scientific level, things can be more open, and mistakes can be admitted and even shared. It is in fact in the best scientific ethic to let people know in advance and document such activity, often venturing into it collectively for safety.

Where scientists are under political control, the latter may instruct concealment when an accident results in a potential weapon. If they are people interested in weaponry, they may deny it and remove the evidence. There is nothing to do, except try to investigate the facts. It changes nothing. Politicians will make a meal out of it.

Research at Wuhan

It is alleged that not only was there an accidental leak or escape of the virus from a Wuhan lab , but that its pathogenicity or infectiousness had been enhanced by Gain of Function (GOF) experimentation by the Chinese.

.(a) US-China Virus Research

At one stage in the previous decade, there was growing technological exchange and co-operation among China and the rest of the world. Lenovo, for instance, the world's leading supercomputer manufacturer today, was started by sale of a whole IBM division in 2014. The Wuhan Bio Safety L4 Lab was built and completed by 2018 in collaboration with the French Centre International de Recherche en Infectiologie of Lyon.

NIH had itself funded at least 60 scientific projects at the Wuhan institute over the past decade, according to the analysis of scientific papers done by The Australian (a newspaper) in conjunction with US bipartisan taxpayer watchdog group White Coat Waste Project, according to information released by the paper on 5 Sep 21 [109].(I assume this includes the sub-grants of the EHA-Wuhan grant.) The same source reported that USAID, the federal aid agency, funded at least 16 projects (10 of which were jointly funded with the NIH), the Department of Health and Human Services funded three, the Department of Defence, the Department of Energy, and the China-US Collaborative Program on Emerging and Re-emerging Infectious Diseases each funded one project in conjunction with the Wuhan institute.

---

[109] https://www.theaustralian.com.au/world/fauci-led-push-for-research-at-wuhan-institute-of-virology/news-story/31024790d0a83bb6398f40b9dc712b18

The relevant NIH website confirms that 80 grants (actually subventions of parent grants) were made to Raszak and or EHA from 2012 onwards for wildlife-virus work.

I could not determine whether the US was, as a matter o homeland safety, deliberately carrying out dangerous viral research off-shore. It was beyond me to study the overall pattern of US research, necessary to conclude on this. Factually, most of the recent viral eruptions had begun in the developing world. These countries are characterised by limited human protection and technical resources, and therefore attract external assistance. Much of the first-line work has to be done at the points of origin. The zoonotic frontier became the primary focus. The SARS Covid 1 pandemic in China and the revelation of its large bat viral reservoirs inevitably attracted most foreign attention. On the face of it, the facts support the altruistic posture of the US's interest in research in China.

.(b) Emerging Pandemic Threats (EPT)

PREDICT was the major percussor of the Wuhan Grant project[110]. It was funded by USAID under its Emerging Pandemic Threats (EPT) programme. It was a 10-year programme initiated in 2009. It objectives were (1) modelling hotspots for disease emergence, (2) conducting surveillance in wildlife for new emerging zoonoses.(3) strengthening the global capacity at country level for detection and discovery of zoonotic viruses with pandemic potential.

This programme was the main action front against Influenza and Ebola, originally in Africa. Inevitably, the bat-coronavirus frontier became its major investigative concern with Asia coming into focus, including . Bangladesh, India, Thailand, Malaysia, Indonesia and China..

[110] For editorial convenience, I use "Wuhan Grant" to mean the NIH_NIAID grant awarded to EcoHealth Alliance (EHA) in 2014.

PREDICT operated on five-year funding cycles, receiving about $200 million over its decade in operation. The programme partners included EcoHealth Alliance (EHA); which had a 10-year grant of $8 million from USAID.

The programme was ended in March 2020 by the Trump Administration. At that point, it was involved in some 30 countries, including China. However, on 1 April 20, following the declaration of the current pandemic, USAID granted $2.26 million to the programme for a six-month emergency extension, to support the "detection of the new virus". I could not tell if President was aware of this.

China became the major location of research following the discovery of bats carrying the Coronavirus that caused the SARS-Covid1 pandemic in 2003. This became particularly so after six miners were infected in a copper mine in Yunnan in 2012, which caves were found also to abound with these bats. Work on this front was led by the Wuhan Institute of Virology (WIV).

It would appear that, at that stage, the Chinese government maintained an open attitude to (if not encouraged) foreign interest, participation and funding in this research. Researchers, both Chinese and foreigners (and. jointly), could freely publish their findings in the international professional journals and pass their samples to each other. China, of course, had much to gain by the build-up of infrastructure, databases and expertise. There would come a time they would close up.

The US government, no doubt for strategic as well as humanitarian reasons , had been supporting pandemic research for many years through its multiple agencies. It would have taken the keenest interest in the research activity at Wuhan.

.(c) EcoHealth Alliance (EHA)

It seemed perfectly expected therefore that, when in 2013 EcoHealth Alliance (EHA) applied for a research grant to "Understand the risk of bat coronavirus emergence", the US National Institute of Health (NIH) should go on to approve it (R01AI110964).The targeted bats were in Wuhan. There would not be another such opportunity available.

EcoHealth Alliance Inc (EHA) Is a US-based NGO with the mission of protecting people, animals, and the environment from Emerging Infectious Diseases (EIDs)..

Founded as the Wildlife Preservation Trust International in 1971, it became The Wildlife Trust in 1999 and EHA in 2010. EHA today promotes 'conservation medicine" or eco-system health.
EHA's funding comes mostly from U.S. federal agencies such as Defence, Homeland Security, USAID and NIH. Wikipedia has this to say of EHA ," The organization has administered more than $100 million in US federal grants to fund overseas laboratory experiments"[111].

Dr Peter Raszak was originally a researcher with the group. He became CEO when EHA was formed. He has become renowned as a "disease ecologist", with distinguished professional and academic recognition, an impressive consultancy record (including the WHO), and a high media profile.

At the point that the National Institute of Allergic and Infectious Diseases (NIAID), the relevant agency of the NIH, made the Wuhan Grant (in 2014), Dr Peter Raszak had already had a collaboration with the research staff of WIV (Dr Shi Sheng Li, among others) going back to 2002. He actually worked in the field to explore the Yunnan bat caves and collect samples. It is not clear under what terms he

111 https://en.wikipedia.org/wiki/Peter_Daszak

participated in this work, perhaps within PREDICT. It must nevertheless be supposed that he was familiar with the whole development history, assets and shortcomings of the institute, and it staff. More than that, he must have known much if not all of the research (and results) going on.

One may conclude that because of his international eminence and his research record in China, Dr Raszak was a “persona grata” “bearing gifts”. He brought funds as well as expertise.

.(d) NIH-NIAID Grant Terms

The following is about as clear a statement of the Wuhan Grant project as one might get, extracted from NIAD’s original approval.[112]:

> “This project is a multi-institutional collaboration led by EcoHealth Alliance, New York (Raszak, PI), which will subcontract funds to two institutions: the East China Normal University (Dr S Zhang) and the Wuhan Institute of Virology (Dr Z Shi), which are both foreign institutions. Dr Raszak has over 15 years previous experience managing collaborative projects.”

The Terms of Award of the grant are explicit. The grant is made to the grantee (and no one else), and the grantee is responsible for full compliance with the conditions of award. Among these a grantee must submit a report of work completed at the end of each year, together with an application for renewal or extension for the next year’s tranche, updated with all new relevant detail. If at any point in time any research work was in danger of violating any condition or guideline (GOF rules in particular), the grantee must stop it and refer the case back for approval. Another fundamental requirement was that the grantee must submit a data sharing plan and comply with several requirements for

112 https://theintercept.com/document/2021/09/08/understanding-the-risk-of-bat-coronavirus-emergence/

publishing and making available to the world scientific community the results and outputs of the project

It was clear that the NIH-NIAID knew and approved that the location of the research was China, and that EHA would "sub-contract" work to institutions in that country, with whom they also otherwise "collaborated" on the project. As far as I can see, notwithstanding whether an activity was a "sub-contract" or a "collaboration", all the grant conditions applied, and the responsibility for compliance would rest with the grantee, unless the partners contravened the grantee's orders.

It might be noted that, as the Wuhan Grant project was essentially a private multinational operation in China, it was subject to local law and government overseership. It may be supposed that China was agreeable to the project. In China, such institutional participation can only happen with government consent.

Using the NGO-institutions set-up was a neat arrangement to keep the two countries disentangled. Under these arrangements, EHA would be responsible for any non-compliances or illegalities on both sides.

I further see that both sides would have anticipated the use of the Bio Safety L4 Lab if the research drifted into dangerous territory. I have no doubt, both US and China were perfectly aware (perhaps hoping) that something unexpected might be discovered (useable to their advantage).

It might be further noted that when the EHA grant was made and during its currency, the following were in operation or due to come into force:

.- NIH Genomic Data Sharing Policy, 27 August 2014[113]

[113] https://grants.nih.gov/grants/guide/notice-files/not-od-14-124.html

.- Statement on Protecting the Integrity of U.S. Biomedical Research, August 23, 2018[114], and finally
.- Final NIH Policy for Data Management and Sharing, coming into force on 25 January 2023[115]

Suffice it to be said that there was no fuss up by NIH-NIAID about EHA non-compliance. So, I will go no further into this.

But it does seem to mean that the NIH-NIAID were being supplied with or had access to the results and outputs of the project, and possibly were in possession of the databases and samples or had access to them - up to when China fully closed down WIV.

It must be supposed that China was also comfortable with these sharing policies. We may suppose that through their institutions they would have the same access as NIH-NIAID, maybe more. All said and done, the viruses, the wildlife and the infected people "belonged" to them. No doubt they would have been kept informed of what was going on.

The remaining question is whether EHA had (has) a complete set. During the height of the leak controversy, they did not come forward to declare or clarify their holdings – as one might expect of an organisation with nothing to hide. Yet when I read their applications or self-descriptions, I find they projected their strength to be their accumulated knowledge, skills, technical tools and databases, to make them one of the best resourced outfits for their work. This suggested they kept a set of the outputs of each of their projects. More, this might include the operations, processes, techniques and working records (including test failures, etc) related to the data and end-products released to the public domain.

---

114 https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-protecting-integrity-us-biomedical-research

115 https://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm

I also noticed that neither did NIH-NIAID rush out to make available to Congress all their holdings and documentations, despite furious cries by the latter for information. In fact the independent newspaper, **Interceptor**, had to take out a court order under the Freedom of Information Act before NIAID released the Wuhan Grant dossier[116]. That is how I could complete my investigations.

.(e) The Wuhan Grant

My searches revealed that the NIH-NIAID grant (R01AI110964) was awarded on 27 May 14 to EHA for the project "Understanding the Risk of Bat Coronavirus Emergence"[117], in the sum of $3.25 million over five years. Of the grant, $3.10 was paid out before abrupt termination by President Trump in Apr 2020. WIV was paid $598,500 and the Wuhan University Medical School (in the original application the second institute named was East China Normal University, Shanghai) was paid $201,217, 21.3% in all, for sub-grants.

Thanks to the newspaper, I was able to see NIH's record[118] of EHA's original application-grant, from which I quote in full the Abstract of the project:

> "This project will examine the risk of future coronavirus (CoV) emergence from wildlife using in-depth field investigations across the human-wildlife interface in China, molecular characterization of novel CoVs and host receptor binding domain genes, mathematical models of transmission and evolution, and in vitro and in vivo laboratory studies of host range. Zoonotic CoVs are a significant threat to global health, as demonstrated with the emergence of pandemic severe acute respiratory syndrome coronavirus (SARS-CoV) in China in 2002, and the recent and

116 https://theintercept.com/2021/09/09/covid-origins-gain-of-function-research/

117 https://theintercept.com/document/2021/09/08/understanding-the-risk-of-bat-coronavirus-emergence/

118 https://grantome.com/grant/NIH/R01-AI110964-04#panel-institution

ongoing emergence of Middle East Respiratory Syndrome (MERS-CoV). Bats appear to be the natural reservoir of these viruses, and hundreds of novel bat-CoVs have been discovered in the last two decades. Bats, and other wildlife species, are hunted, traded, butchered and consumed across Asia, creating a large scale human-wildlife interface, and high risk of future emergence of novel CoVs.

This project aims to understand what factors increase the risk of the next CoV emerging in people by studying CoV diversity in a critical zoonotic reservoir (bats), at sites of high risk for emergence (wildlife markets) in an emerging disease hotspot (China). The three specific aims of this project are to:
1. Assess CoV spillover potential at high risk human-wildlife interfaces in China. This will include quantifying he nature and frequency of contact people have with bats and other wildlife; serological and molecular screening of people working in wet markets and highly exposed to wildlife; screening wild-caught and market sampled bats from 30+ species for CoVs using molecular assays; and genomic characterization and isolation of novel CoVs.
2. Develop predictive models of bat CoV emergence risk and host range. A combined **modelling** approach will include phylogenetic analyses of host receptors and novel CoV genes (including functional receptor binding domains); a fused ecological and evolutionary model to predict host-range and viral sharing; and mathematical matrix models to examine evolutionary and transmission dynamics.
3. Test predictions of CoV inter-species transmission. Predictive models of host range (i.e. emergence potential) will be tested experimentally using reverse genetics, pseudovirus and receptor binding assays, and virus infection experiments across a range of cell cultures from different species and humanized mice.
Public Health Relevance
Most emerging human viruses come from wildlife, and these represent a significant threat to global public health and biosecurity - as demonstrated by the SARS coronavirus pandemic of 2002-03 and an ongoing SARS-like epidemic in the Middle East. This project seeks to understand what factors allow animal Coronaviruses to evolve and jump into the human population by studying virus diversity in a critical group of animals (bats), a sites of high risk for emergence (wildlife markets) in an emerging disease hotspot (China).

https://grantome.com/grant/NIH/R01-AI110964-04#panel-institution

It is clear the project was fully defined, and that it would take place in China.

(Back to TOC)

(f) GOF/Leak Origin of SARS-Covid2 virus

The Wuhan Grant's end-date was 30 Jun 20, but President Trump terminated it around 24 Apr 20. Technically, the project was still on when the pandemic was declared on 11 Mar 20.

Therefore, it could be said that, whatever might subsequently be ascribed to WIV as the antecedent cause, EHA were tangentially responsible. However, from the narrative of events, it seemed to me that the local health and governmental authorities took full charge of WIV (and hence the workings of the project) well before even the first reference case. I saw no EHA presence in the sequence of activities related to the outbreak. The local authorities handled all the initial outbreak cases exclusively.

When the Covid-19 pandemic broke out, the fundamental need was to identify the origin of the virus and the path it took to human infection. The closest (available) original bat-coronavirus (WIV1) did not have the necessary infectious faculties. These must therefore have been lab-acquired later. The latter virus must then have been accidentally leaked.

The furor arose because the latest Wuhan lab records were not available. China had withdrew them completely from 12 Sep 19. One set of accusations suggested that the final GOF modifications were made by the Chinese after they took over. The other set suggested the Chinese allowed the leak to happen due to inadequate biosecurity. The political slant was that Chia was responsible for the pandemic.

.(g) Enlarged Wuhan Inquiry

Somewhere during Apr 2020, President Trump accused China of being responsible for the leak of the Covid19 virus.

Following an Interim Report in Jun 2020, the US Congress House Foreign Affairs Committee Minority Staff on 21 Sep 20 submitted its Final Report on the Origins of the COVID-19 Global Pandemic, (@ the McCaul Report). It captured in detail the grounds on which the US alleged cover-up actions of China and the "mis-steps " of WHO over the GOF experiments and the leak.

The same House Committee Minority Staff continued their investigation and tabled an **Addendum Report** on 1 Aug 21. New information had come to light painting an enlarged and more detailed picture of what had been happening. This section draws from that report[119].

From as early as. 2002, the Wuhan Institute of Virology (WIV) dedicated its energies to studying coronaviruses from bats. They were led by Dr Shi Sheng-li, a principal researcher, who became known as "Bat-Woman", and who went on to hold held several key positions. WIV became the leading bat-coronavirus study institute in the world.

One other person deeply interested in pandemics was Dr Peter Raszak, (then) principal researcher of EcoHealth Alliance's (EHA's) predecessor. He was active in Wuhan as early as 2002. He teamed up with Dr Shi from that date over the following 16 years. I need to quote that Addendum here:

> "(Together, they) led dozens of expeditions to caves full of bats, to collect samples and analyze them. They have identified more than 500 novel coronaviruses, including roughly 50 related to SARS or MERS, and they have repeatedly engaged in gain-of-

[119] https://gop-foreignaffairs.house.gov/wp-content/uploads/2021/08/ORIGINS-OF-COVID-19-REPORT.pdf

function research on coronaviruses designed to make them more infectious in humans.

As discussed below, the vast majority of the most relevant scientific publications that have emerged from the WIV regarding coronaviruses was conducted with funding provided by the US via Peter Daszak through EHA"[120]

Dr Shi was listed Key Person No 1 in EHA's application for the grant. A few cases from published reports listed in the Addendum indicate how far things were going:

,(a) In 2007, researchers created multiple chimeric viruses by inserting different sequences of the SARS-CoV spike protein into the spike protein of the SARS-like viruses. being examined. One of these chimeric viruses was able to enter cells through the human ACE2[121]

.(b) In 2013, researchers isolated a wild SARS-like coronavirus that binds to ACE2, and proved that bat coronaviruses are capable of infecting humans directly, without having to pass through an intermediate host.

.(c) In 2015, Dr Ralf Baric (of U of Northern Carolina, Chapel Hill), another US collaborator of EHA, created a chimeric virus (at Chapel Hill) from a Yunnan cave sample, which was then shown to bind to ACE2 in humans, **replicate** "efficiently" in primary human airways cells, and withstand antibodies and vaccines. He also proved that one could engineer a virus without leaving a trace.

. (d) In 2016 WIV researchers created a **reverse genetics system** and used it to genetically modify WIV1, the live coronavirus that was successfully isolated in 2013. They

---

120 Ibid

121 ACE2 = angiotensin converting enzyme 2, which is a protein found in human receptors on the surface of cells and tissues throughout the human body,

created multiple versions of this virus by deleting or adding genetic information to the virus' RNA.

.(e) In 2017, WIV researchers isolated a third coronavirus and created eight separate chimeric viruses. Two of these chimeric viruses and one natural virus, Rs4874, all replicated within hACE2 expressing cells.

All the WIV research was done in BSL-2 and BSL3 labs, before the Wuhan National Bio-Safety Lab 4 (BSL-4) became operational in Jan 2018.

All the above researches were co-funded by China.

.(h) Research under the Wuhan Grant

The EHA project only commenced on 27 May 2014, and was scheduled to extend for two five-year periods (2014-2024). It was renewed yearly and extended up to 31 May 20, until stopped by President Trump effective 24 Apr 2020.

The Wuhan Grant project therefore ended there. I note from **USAspending.gov** that the last disbursement made to EHA was on 13 Jul 20, and to WIV on 31 May 19. The latter looked like the last piece of sub-contract paid for.

I could not find what work EHA did in the last year of the Wuhan Grant, in fact whether the Chinese extended facilities for them to do so. The Chinese effectively took down the WIV databases on 12 Sep 2019. We may take that as the date of the termination of the grant project in the field.

It should also be noted that a substantial part of the discovery work had been done before the grant project, from 2002 to 2013.

Therefore, if any, **the Wuhan grant project only contributed to the first GOF stages in the (supposed)**

gestation of the SARS-Covid2 virus, and was not involved in the leak.

.(i) China Takes Over

In 2015, China announced reforms that made science and innovation a key element of modernising its armed forces. And in 2016, its Science and Technology Commission, which decided research funding, became one of 15 newly formed military 'sections'. The reforms also put the Academy of Military Medical Sciences, the PLA's main military strategy institution, in charge of nine other research institutions.

At some stage, CPC/PLA personnel began to take control of WIV, in particular the new Wuhan Bio-Safety 4L. The Chinese authorities also progressively enlarged their own research activities:

.(a) In 2018 the Chinese Academy of Sciences launched a new special project titled "Pathogen Host Adaption and Immune Intervention." One of the five subprojects was titled "Research on Virus Traceability, Cross-Species Transmission, and Pathogenic Mechanism" .

.(b) Next was a new Strategic Priority Research Programme, run by Dr Shi, that was actively manufacturing chimeric viruses in BSL-2 and BSL-3 conditions and seeking out novel viruses. A second Chinese grant was awarded to another researcher to test novel coronaviruses against human immune systems.

One can only surmise that China was extending the work begun under the Wuhan project. It is more than likely that they began using the new Bio-Safety L4.

As I said before, when it became evident that the Wuhan Grant was making GOF breakthroughs with the potential of creating a new enhanced pathogen, China exercised what might be termed its right to call off its institutions and abort the

project.. What had been shared, was shared. China secured and kept the rest, including the records, samples and all other stuff not shared. I date the fact step as happening at 2.00 am on 12 Sep 2019

Leak Allegations

.(a) Initial Allegations

At the beginning of the controversy, the allegations revolved around the outbreak in the Wuhan Huanan Seafood Wholesale Market and the suspected accidental leak of the virus while the samples were being investigated by researchers.

In Jan 2020, WHO commissioned a study on the origins of the virus jointly by WHO and Chinese experts. In March 2020, the published findings of this study determined that the virus most likely had a zoonotic origin in bats, possibly transmitted through an intermediate host. It also stated that a laboratory origin for the virus was "extremely unlikely. We might note with some surprise that Dr Peter Raszak was a member of the mission, selected by WHO. On 30 Mar 20, WHO director-general said it was "premature" for the WHO's report to rule out a potential link between a laboratory leak and the pandemic. He called on China to provide 'raw data' and lab audits in a second phase of investigations. China refused a second phase.

.(b) Alternative Accidental-Leak Hypothesis

One remarkable finding of the US Congress' Foreign Affairs Committee Minority Staff in their Addendum[122] was that **the leak most likely took place earlier, in Sep 2019.**

[122] https://gop-foreignaffairs.house.gov/wp-content/uploads/2021/08/ORIGINS-OF-COVID-19-REPORT.pdf

On 12 Sep 19, WIV's research databases were suddenly taken off line. The authorities had been tendering to repair the hazardous waste disposal system and the central air conditioning at the new BSL4 Lab. There were rumours of an accidental viral release, and there was heightened activity at the surrounding hospitals.

The Addendum hypothesised that the authorities' concern at that point was low, not knowing then of the existence of SARS-CoV-2 or that it could spread via human-to-human transmission and by asymptotic people. And there was no mass infection. The decision was made to allow the 2019 Military World Games at Wuhan city to continue, but no spectators were allowed to attend the games. Reports have it that dozens of athletes and some of the 236,000 volunteers became infected, spreading the virus in the city. An untold number of athletes and volunteers could have become infected. The athletes returned to their home countries in late October, carrying SARS-CoV-2 across the world. I quote the report's hypothesis:

> "It is the opinion of Committee Minority Staff, based on the preponderance of available information; the documented efforts to obfuscate, hide, and destroy evidence; and the lack of physical evidence to the contrary; that SARS-CoV-2 was accidentally released from a Wuhan Institute of Virology laboratory sometime prior to September 12, 2019. The virus, which may be natural in origin or the result of genetic manipulation, was likely collected in the identified cave in Yunnan province, PRC, sometime between 2012 and 2015. Its release was due to poor lab safety standards and practices, exacerbated by dangerous gain-of-function research being conducted at inadequate biosafety levels, including BSL-2. The virus was then spread throughout central Wuhan, likely via the Wuhan Metro, in the weeks prior to the Military World Games. Those games became an international vector, spreading the virus to multiple continents around the world. "

The same US Congress' Foreign Affairs Committee Minority Staff recommended: "Peter Daszak must be subpoenaed to

appear before the House Foreign Affairs Committee and Senate Foreign Relations Committee as material witness to this investigation. Committee Minority Staff attempted, on multiple occasions, to contact Daszak with a list of questions relevant to its report. He never responded. “

My assessment is that if there had been a leak during the 2019 World Military Games the scenario would have been different. The games according to Wiki, were held from 18-28 Oct 19 and involved 9,308 athletes from over 109 countries competing in 327 events in 27 sports in umpteen venues. They lived in an “olympic village”. If it was a SARS-Covid 2 leak, the pandemic would indeed have begun there.

The report cites post-games cases of illness in four countries. If there was serious concern for this possibility, every one of the athletes (minus the 553 from China) could have been traced and checked out. US had 172 participants. Country reports would also have surfaced. Nothing. I find no grounds for entertaining this hypothesis. I am surprised, while the report states the alternative hypotheses as its conclusion, it made no follow up to check out the athletes. Just one case of a SARS-Covid2 infection among them, backed by a sample specimen, in one those countries, would have been proof.

As it is Wuhan went on merrily for another two months before the real outbreak. If there had been an accidental leak in early Sep 2019, the virus could have been a weaker one, judging by the lack of any convincing infection scenario .

If there was an accidental leak, it is more likely to have been later in Nov-Dec 2019, by which time the present virulent form had time to fully develop (or be developed). It may indeed then have done the jump on its own without a leak.

.(c) US Intelligence Community Report

On 26 May 21, President Biden directed the US Intelligence Community (IC), believed to comprise 19 agency members,

to comprehensively and decisively determine the source of the Covid-19 virus, and submit their combined conclusions in 90 days, see extract from the White House statement:

> "I have now asked the Intelligence Community to redouble their efforts to collect and analyze information that could bring us closer to a definitive conclusion, and to report back to me in 90 days. As part of that report, I have asked for areas of further inquiry that may be required, including specific questions for China. I have also asked that this effort include work by our National Labs and other agencies of our government to augment the Intelligence Community's efforts. And I have asked the Intelligence Community to keep Congress fully apprised of its work."[123]

The report was duly present on 27 Aug 21 by the Director of National Intelligence, and an Extract was made public[124]. I quote it in full because it is brief enough being a summary:

> "After examining all available intelligence reporting and other information, though, the IC remains divided on the most likely origin of COVID-19. All agencies assess that two hypotheses are plausible: natural exposure to an infected animal and a laboratory-associated incident.
>
> • Four IC elements and the National Intelligence Council assess with low confidence that the initial SARS-CoV-2 infection was most likely caused by natural exposure to an animal infected with it or a close progenitor virus—a virus that probably would be more than 99 percent similar to SARS-CoV-2. These analysts give weight to China's officials' lack of foreknowledge, the numerous vectors for natural exposure, and other factors.
>
> • One IC element assesses with moderate confidence that the first human infection with SARS-CoV-2 most likely was the result of a laboratory-associated incident, probably involving

---

123 https://www.whitehouse.gov/briefing-room/statements-releases/2021/05/26/statement-by-president-joe-biden-on-the-investigation-into-the-origins-of-covid-19/

124 https://www.dni.gov/files/ODNI/documents/assessments/Unclassified-Summary-of-Assessment-on-COVID-19-Origins.pdf

experimentation, animal handling, or sampling by the Wuhan Institute of Virology. These analysts give weight to the inherently risky nature of work on coronaviruses.

- Analysts at three IC elements remain unable to coalesce around either explanation without additional information, with some analysts favoring natural origin, others a laboratory origin, and some seeing the hypotheses as equally likely.

- Variations in analytic views largely stem from differences in how agencies weigh intelligence reporting and scientific publications, and intelligence and scientific gaps.
The IC judges they will be unable to provide a more definitive explanation for the origin of COVID-19 unless new information allows them to determine the specific pathway for initial natural contact with an animal or to determine that a laboratory in Wuhan was handling SARS- CoV-2 or a close progenitor virus before COVID-19 emerged.

- The IC—and the global scientific community—lacks clinical samples or a complete understanding of epidemiological data from the earliest COVID-19 cases. If we obtain information on the earliest cases that identified a location of interest or occupational exposure, it may alter our evaluation of hypotheses.

China's cooperation most likely would be needed to reach a conclusive assessment of the origins of COVID-19. Beijing, however, continues to hinder the global investigation, resist sharing information and blame other countries, including the United States. These actions reflect, in part, China's government's own uncertainty about where an investigation could lead as well as its frustration the international community is using the issue to exert political pressure on China."

It may be noted that IC report came out about four weeks after the Addendum. There is no evidence (from the Extract) that the IC were offered or saw the Addendum material or conclusions.

Perhaps the contents of the Addendum were made known to the IC, but they decided not to notice it on two grounds: (a) the alternative leak hypothesis, which was within their terms

of reference, was unsupported by evidence, and (b) the GOF findings, although strong in evidence, were outside their terms of reference.

Gain of Function (GOF) Research.

.(a) HHS PE3CO Framework

On 14 Oct 2014, the Obama Administration imposed a moratorium (or pause) on approving new Gain-of-Function (GOF) research, with existing projects to fall in line. The Wuhan Grant was affected.

The consultations following resulted two landmark documents: (1) White House's Recommended Policy Guidance for Review Mechanisms for Potential Pandemic Pathogens Care and Oversight issued on 7 Dec 17, and (2) Health and Human Services Dep's Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens **(HHS PE3CO Framework)** issued on 19 Dec 17, on which date the moratorium was lifted. The Wuhan project was affected.

These documents define GOF as follows:

.- A potential pandemic pathogen (PPP) is a pathogen that is likely highly transmissible and cause significant morbidity and/or mortality in humans.

.- An enhanced PPP is defined as an (**ePPP)** resulting from the enhancement of the transmissibility and/or virulence of a pathogen.

.- To the extent that transmissibility and/or virulence of PPPs are modified in the following categories of studies, the resulting pathogens are **not considered to be enhanced PPPs:**

. 1 Surveillance activities, including sampling and sequencing; and

.2 Activities associated with developing and producing vaccines, such as generation of high growth strains.
I am satisfied from the Addendum that the WIV researchers had taken their work to advanced levels of virus manipulation, to the point they were creating chimeral viruses that could and did infect human tissue. In my view this is Gain of Function (GOF) research *per se.* I will leave it to the professionals to judge if in the context of the Wuhan project these would come under the exclusions of (being ePPPs) under the PE3CO framework. If so, they would be allowable. NIAID thought so.

.(b) Wuhan Grant vis-à-vis PE3CO

In May 2020, Dr Anthony Fauci, Director, NIAID testified before Congress: "The NIH has not ever and does not now fund gain-of-function research in the Wuhan Institute of Virology." An NIAID spokesperson has clarified to the **Interceptor**[125]**,** an independent newspaper that did an expose on the subject, on 10 Sep 21, that the agency had in fact reviewed the EHA's work and approved the research, yearly, as not constituting ePPP or GOF.

To my mind, it was not so much whether it was ePPP, as whether the work was excluded under the PE3CO. It is clear NIDAID considered it excluded.

The newspaper covered the views of a wide range of professionals, who both agreed and disagreed with NIAID.

Dr Anthony Fauci had said somewhere (and I paraphrase) that there was nothing in the molecular makeup of the one (the last developed EHA virus, which sample he must therefore have had) that could result in the other (SARSs-Covid2). I have not seen any response to this.

---

125 https://theintercept.com/2021/09/09/covid-origins-gain-of-function-research/. The Intercepter had obtained the Wuhan grant documents by a court injunction under the Freedom of Information Act.

.Assessment

.(a) GOF research

The most relevant document in this matter is the Health and Human Services Dep's Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens **(HHS PE3CO Framework)** issued under the Trump Administration on 19 Dec 17. It clearly defined a potential pandemic pathogen **(PPP)** as a pathogen that is likely to be highly transmissible and cause significant morbidity, and an enhanced PPP as an (**ePPP)** resulting from the enhancement of the transmissibility and/or virulence of a pathogen. The latter, which was GOF research, was forbidden. However, to the extent that transmissibility and/or virulence of PPPs are modified in the following categories of studies, the resulting pathogens are excepted and **not considered to be enhanced PPPs:**

. 1 Surveillance activities, including sampling and sequencing; and

.2 Activities associated with developing and producing vaccines, such as generation of high growth strains.

I am clear from the evidence in the Addendum that before the Chinese takeover the Wuhan Grant was already engaged in GOF (ePPP) work. Dr Fauci has maintained it did not, but in my view purely by virtue of the exception clause. One might call this prevarication. It will not escape even the casual observer that the PE3CO was promulgated near the. end of the Wuhan Grant, *ex-post facto* one might say, and might have been conveniently worded to exclude it; nor indeed that the Chinese took note of it and immediately moved to take over Wuhan in the months following.

I myself would like to see a detailed comparative (lay intelligible) itemisation of the constituents and functions of the working parts of the last lab-enhanced Wuhan

virus or chimera available against an original SAR-Covid2, highlighting the sameness and differences.

This table should aim to clarify whether the original (i) could have hopped over as it was, or (ii) it needed to be further enhanced or modified (and exactly how, ie what is missing or should be taken away) to become a SARS-Covi2 virus. I would further want clarification (iii) whether it was at all possible for (ii) above to have been done at WIV subsequently to create the SARS-Covid2, and (iv) finally, whether we could reverse-engineer to make the last Wuhan virus available from an original SARS-Covid 2.

I would expect the above to take into account **three** things highlighted by Addendum:

. (1) SARS-CoV-2 has a highly unusual affinity for binding to human ACE2 receptors over other hosts.

.(2) The SARS- CoV-2 binds more than 10 times more tightly to human ACE2 than the virus that caused SARS-Covid1.

.(3) These facts provide evidence that SARS-CoV-2 is uniquely well adapted to humans, suggesting a post-zoonotic and non-zoonotic source of the outbreak

Pending the above clarifications, my working hypothesis would be: until we have unquestionable evidence of an alternative evolutionary path from a Coronavirus in a bat to the SARS-Covid2 in a human, including the cross-over bridge, **all outside a lab**, the SARS-Covid2 is most likely to have been given these capabilities in the lab at Wuhan than to have evolved them spontaneously.

.(b) GOF/Leak - What Could Have Happened?

On the balance of the evidence adduced, my tentative views on the GOF- Accident-Leak theory are:

. A Did WIV have a new more virulent Coronavirus in Sep 19? No. If they did, it was not so virulent.

. B Did WIV have a new more virulent Coronavirus by Nov-Dec 19,? More likely. Possibly a near variant to the SARS-Covid2, if not the latter daddy itself.

. C Was it more likely to have evolved spontaneously or been lab-fabricated? The latter.

.D Did it come from the Wuhan lab? Yes. It was the only place with such a virulent bug.

.E. Was there an accidental leak WIV? We cannot know without the records.

.F Was there a spontaneous jump from WIV? We cannot now know without the records.

.(c) Missing Information

Ultimately, it has not been possible for me to clear the NIH-NIAID from these possibilities: that they were in full possession of all relevant information and samples of virus experiments at Wuhan up to and until the Chinese clamp-down, and that these could show direct lineage of their work to the SARs Covid-2 , with or without further Chinese manipulation. It has not escaped me either that the US investigative committees and intelligence agencies studiously skirted examination and reporting of this point. It is possible, the evidence could also have been destroyed. The additional facts that the EHA stayed from similar disclosure of their holdings, have not been investigated and have not been called before Congress further suggest blanketing of the possible culpability of NIH-NIAID, if not the US.

I am sure it has not escaped the parties involved that the best and probably the only way to prove that China produced the final version of SARS Covid 19 is to prove that the Wuhan under EHA-NIAID did not do it . That they have not done so

weighs against them, one possibility being they are unable to. It would be surprising if President Trump had not asked about and been fully briefed on the exact activities of NIH-NIAID in China.

Finally I notice that the I**ntercept** did not include any mention in their application for release of information about the databases, research records and samples. I cannot think their reporter was so dumb, and am entitled to speculate whether there was voluntary or involuntary compromise involved.

.(d) Bottom-line

My bottom-line is: **first we must still try to ascertain whether or not SARS-Covid2 came out of Wuhan.**

Unfortunately, we are mired in political cross-accusations. If China developed the virus and it escaped, they are not going to tell us. If they did not, and tell us, many will not believe.

At the same time, there is a reasonable possibility that the next pandemic may break in China. We do not want to be in the same position as now.

We must take it out of the realm of politics. Limited as it is, WHO must pre-empt the lead. Let all parties involved in the Wuhan Grant and WIV make available what information is available. One approach is as I suggest in (a) above. Whatever the final dispositions of the countries, WHO must get on with the job and conclude this matter as quickly as possible. **The frightful thing would be if we found out that the SARS-Covid 2 virus could not have originated in the WIV labs.**

For then, we must still face the most important question in the world: where the hell did it come from? Not in China, the Country of Origin?

Finally, the world needs to set up an effective international framework This has to be by enlarging the functionality of WHO and adoption of an enforceable set of IHRs. I touch on this under Directions of Change.

(Back to TOC)

International Collaboration

One reason we entertain reasonable hope of beating Covid-19 is that many sectors of the world community (including governments) were far-seeing and had made preliminary moves, whether in planning, research, surveillance or humanitarian services. When the crises came, they reacted spontaneously, rallied round WHO, worked together and shared their resources unreservedly.

They greatly enlarged the services the world has come to depend on from our historic NGOs, such as the Red Cross and Médecins Sans Frontières/Doctors Without Borders (MSF), etc

My review abounds in mention of the invaluable work of these parties. I say it here without reservation: without their voluntary involvement, we would not make it as the world is presently organised.

I have included an entire Part to highlighting their contributions. There are four groups: (a) the scientific-academic community (b) the charity foundations, (c) the humanitarian organisations and (d) the collaborative partnerships.

The scientific community had deepened their research, shared their resources, and set up various information networks and databanks. The humanitarian community developed massive vaccine delivery and other health

services for the LMICs, recognising their vulnerability. And the donor community directed vast sums to all sectors.

If I were to single out three, they would be the Bill and Melinda Gates Foundation (BMGF), GAVI, the Vaccine Alliance and CEPI.

Our global international framework is still weak and much fractured. Whatever improvements we do make following this pandemic, let us always have and foster the enormous idealism, energies and resources of our private humanitarian partnerships and their belief in One World.

Needless to say that there are many wealthy and not so wealthy countries who, realising our needs, made massive contributions in cash and technical assistance. Three quarters of WHO's budget relies on their voluntary contributions over and above their obligated due, and on private foundation contributions. There is much good in the world worth preserving.

Mostly importantly, let us salute the scientific and. technical communities. Most of them work and share their work unselfishly and unrecognised. Without scientists we would not have molecular biology and DNA sequencing.. Without the technical boys (and girls) we would not have the computer, the internet, and the cryonic electronic microscope. Without these, Covid-2 would have annihilated us ere now.

(Back to TOC)

Directions of Change

Research

I come straight to my most important point. Whatever else we do, we must now immediately mobilise and launch into the most comprehensive and thorough programme of research to find out all there is to know and **build a complete picture** about viruses, the virus world, what some call the "virosphere", and what I have referred to as the unknown "third universe"..

Much as we know, we are far short of complete knowledge. We have no idea what life-form they are, how many, of what kinds, what they do when not infecting us, their life-cycle, or indeed where they are

On the other, we know equally little of the benefits of having them around, and their place in the ecosystem. we know nothing of the part they have played in the history of the world's evolution. Perhaps in killing off some species, they have enabled others (us?) to thrive. Perhaps, periodically, they have played a Malthusian role. We certainly do not know whether or to what extent the world could survive without them.

Right now, we mainly know the pathogens and a narrow spectrum around these families. Even then, whether in the human domain or in the plant domain, we know little else. We are soon out of our depth in the oceans.

At the same time, we are told that viruses impregnate all living things, the waters and the land. They fill the air around us, but to what height we do not know.. There are more viruses in us than cells, but of what kinds and what they do we do not know. We have found them in. our brains. We know that some have replicated In our germlines. Some 8% of our genome

are inherited from viruses. What this means, we do not yet know.

The enhanced science of palaeontology has begun to reveal new vistas about the evolutionary and historic events of our viruses. In fact there is a new branch called “paleovirology”. We already know that viruses began alongside the first microbes 4 billion years ago, and may in fact have been the evolutionary waste-products of the later.

They have been around the Milky Way on the galactic plane 17 times. We emerged less than 200,000 years and are at the starting point of the first cusp. They have survived five earth extinction events and 11 glaciations. We surfaced in their world, not they in ours.

Other than by physical destruction, viruses do not “die”. They are dormant when not hunting. We have no idea how long viruses remain dormant. We do not know whether they evolve in that state and circle back, or only mutate and evolve when resisted by a living cell. I am not sure we even know and can predict how they mutate, only that that they do - after the fact .

On the other hand, if dormant viruses endure indefinitely, and a few zillions are replicated and added every hour, there must be an accumulation of unimaginable proportions, somewhere and growing - perhaps to overflowing? This could be a pressure point for the increasing scales of their invasion of our universes.

I fear we could be on a collision course. Mankind is swarming. We need to know whether viruses are swarming. If they are we need to know their swarming history, and which of them are about to do so. In fact it would be good to know when they are next coming. And we had better be able to take evasive or decisive action.

Even if some or all of my premises are wrong, it is time to get all the facts and put the whole picture together. Even the

Egyptians knew more about the celestial bodies in their time than we do about the virus world. We can no more steer our way round the viral world than they could steer their way to Mars.

We may already be at the limit of current technology. We must recognise where this is so, and develop what is needed.

For the macro level, we shall really only be able to research and scale the virus universe with a credible quantum computer. IBM promise upgrade of their front-runner System One to 1,000 qubits by 2023, still a nascent machine. But this will give us some decent exponential computing power. The full potential is closer to 1 million qubits, AI can be deployed progressively as we collect data.

At the biological level, we have pretty complete command of the situation. DNA sequencing has opened an incredible window. We can now track the virus across species and families, and through fossils across time. With progressive development of genbanks, we are extracting valuable information through metagenomics.

For the micro level, however, we need to go sub-molecular, past their “biology”, down to the level of the particle. This we know today is the common baseline of matter, where quantum effects apply. We may need to develop the nano-technology and quantum biology to investigate at this level. Then, we shall know how viruses are engineered, their memory storage and how they are hot-wired to kill and operate in groups. For all we know, they have been working superpositions and entanglements for years. We need to tag and observe them, or their squad leaders. We may need to tamper with them or switch them off if necessary.

It is only as we build up our knowledge that we will master the virus, and command all the options in dealing with them. The more hopeful view is that, perhaps in the long run, we are the nemesis of the virus, not vice versa.

(Back to TOC)

Future Defence Framework

Notwithstanding our limitations, as the world has become more complicated and inter-dependent, we have successfully rigged up co-operative infrastructures to keep going. Some have been obligatory conventions and treaties, such as for telecommunications and aviation. Some are by voluntary participation, such as for CERN and the Internet. There are many models.

It is time to have some international framework and infrastructure permanently in place as our viral defence and response system.

WHO would be the most feasible organisation around which to build it. In this pandemic, it has demonstrated its natural leadership for this role, and the major countries will be quick to recognise the need.

Such a framework can be started, in steps, as soon as there is a nucleus of major countries. It is beyond me to draw up a blueprint. I do however identify these components of the infrastructure as key:

.(a) There should be a Central hub, hosted by/at WHO. It should have front-line research capabilities, enabling us to have the next vaccine ready before the next virus. In time, it would become the central repository of all viral data, samples, and gen banks. It would be both the heart of our scientific counter-offensive and the hub our defence response system.

.(b) There must be a surveillance and early warning node in each designated country, region or territory of risk, linked to the hub and every other node, forming a total on-line defence network. Each must be equipped, resourced and trained to centrally certifiable standards.

.(c) All nodes must also be interlinked through the main system to one another, neighbour to neighbour. All nodes must in turn be hooked to the country's own public health systems. The latter in effect become extension and outposts feeding back to the nodes.

.(d) Central will develop, maintain and issue global and country level preparedness plans, to be operational in stages of alert, eg. Def Con1, 2 or 3. Central will hold adequate reserves of equipment and supplies and move them to suitable forward locations to deploy these to areas of attack.

.(e) Countries must maintain centrally prescribed reserves of local resources and infrastructure to operationalise counter-measures on alert of an outbreak. These should include stockpiles of hospital beds, ICU equipment, drugs, etc. on the one hand, and transport control and essential supplies on the other.

The overall object is to work an integrated global surveillance and immediate response network , with full sharing of information resources. Country nodes must provide instant feedback to the entire system on a suspicious outbreak, and even request external help for first level investigation. The principle must be: if there is some occurrence in one location, it must be logged in and uploaded at once, so everyone at all levels in the defence system and all relevant people in the country's health framework know about it at the same time, even those in the neighbouring countries. We will be getting somewhere when a country of origin is told from the outside (say a neighbour) that it is about to be invaded, not vice versa.

There are a host of other features to be put in place. The organisation will need legal identity, international authority and its own career staff, probably as an adjunct of the UN. At some stage it will need authority to act or intervene in a country, especially to carry out inspections. At some stage it

will probably take on regulatory functions. There must be provision for it to impose penalties and sanctions for non-compliance.

A fundamental feature must be that all data, samples and research findings must be transparent and shared It may be necessary for staff, nodes and data to be protected with UN immunity.

It is essential that there be provision for membership and participation by scientific, professional, humanitarian and philanthropic organisations. Research will need to work closely with the first two, and there will inexhaustible demand for support from the other two in the field in the LMICs..

Lastly, there is the matter of funding. Financiers are better at this. Basically countries must fund at least regular expenditure, perhaps scaled by population and GNP. In research and the build-up of other infrastructure, there is much room and need for other participation and financial instrumentalities. Countries that cannot afford nodes and preparedness will need to be subsidised.

It can be expected that the new organisation will take over a significant amount of work now shouldered by WHO. The latter's resources and funding so deployed can be transferred over to form the new working nucleus.

Classically, loss of the food chain is a road to extinction. The future structural changes must integrate the FAO and the under-organised ocean people into the global defence system of the future. Perhaps there are some resources there that can also be transferred to the new organisation.

I venture to say that without something like the above in place, the world is not ready to take on the next virus pandemic. We need to attune ourselves to semi-mobilisation, as though we are expecting hostile aliens. We are.

Finally, I further venture to say, the cost of setting up the defence response system and operating it for one year will be less than the cost of say six months of a new pandemic. It is good investment economics, if not also good insurance.

Needless to say we must build international safeguards against any temptation to use future viral technology against one another, as happened after the atom was discovered. These safeguards must be fool-proof, while carrying crippling sanctions to deter the even the most maniacal political or military leaders. Above all, we need to believe that we are all rowing in the same boat.

As we learn to protect ourselves from them, viruses may yet find themselves busy in the fourth industrial revolution in more productive occupations (perhaps making honey or cotton wool). Not the least would be guarding us and our food sources from other enemies, perhaps even other viruses. It is still too early though to think of them as friendly.

In HIV, the medical battle seems to have been won outright. The HIV virus seems so far to have been unable to out-mutate the antiretroviral drugs. There has been no use of a vaccine, nor is there one, except one on trial. This should be the primary research target.

Perhaps, the last word is that we may have to fight viral pandemics at other frontiers. The most conspicuous is climate change, and the consequent break down of the ecology. These affect the virosphere. The more their world is upset, the more they will go zoonotic. It may not be in appropriate to suggest that the many of the global defence measures against virus could be used for other frontiers.

(Back to TOC)

Next Steps Forward

There are some correctional steps we can take now to improve immediate capability and trigger off the desired changes.

We are dependent on adequate implementation of internal counter-measures before a pandemic breaks out of its boundaries. Some international agreement for unfettered entry of external expertise and assistance would be a very desirable step for the world as a whole.

The next important limitation is that WHO has no authority in directing action in member countries, not even the country of origin, except as and when permitted. WHO can prescribe, but cannot enforce the provision of country early warning systems, first line response facilities and even essential initial diagnostic research. We must patch this weakness.

And, WHO is woefully underfunded even for its regular operations, and has no reserves to deal with a pandemic. It is incredible that annually it must go out with a begging bowl. We were only assured of funds to vaccinate the minimum herd community at the June 2021 Global Summit. WHO depends heavily on the foundations and a few far-sighted governments. We need to overhaul the funding base. Perhaps WHO can begin to charge for some of its services.

The practical step is for WHO to present amendments to the International Health Regulations (IHR) 2005 to the WHA addressing the above. Even partial agreement would be progress. The real purpose however is to introduce the following paper.

The parallel step is for WHO to present a Concept Paper for the new viral defence and response system for in-principle endorsement. To give it realism WHO must offer to lead its formation inter alia by transfer of its relevant components to

form the new nucleus. Discussion of both papers together will re-in force the need for the comprehensive changes we want. WHA meets twice a year, nowadays virtually.

THANK YOU.

End.

(Back to TOC)

APPENDIX

Bacteria

No study of viruses would be complete without including bacteria. Bacteria (also known as Eubacteria), together with an ancient branch, the Archaea, constitute the taxonomical prokaryotic kingdom of Monera (of Living Things).

Description

Although among the simplest of living organisms, bacteria are considerably more complex than viruses.

Bacteria are prokaryotes[1]. They are living things, fully capable of reproduction. They are unicellular, and have a cell wall of peptidoglycan, a unique polymer, together with a circumferential cytoplasmic membrane. Unlike more complex organisms (eukaryotes), they have one chromosome, instead of two, encoded in a single DNA loop. They have no protective membrane surrounding their genetic nucleoid, which floats free in the cytoplasm. They have no organelles or sub-cellular structures. All their working components function in the cytoplasm. Bacteria have ribosomes.

On their exterior surface they carry an assortment of tools, like the flagellum for motion, and the pilus, fimbria, capsule, and receptors, etc for attachments and other purposes. Some bacteria have an extra circle of genetic material called a plasmid.

Bacteria replicate by binary fusion. The whole cell divides, creating two daughter bacteria, or clones. They have full metabolism. However they do not have mitochondria. Instead, different species use different combinations of resources for carbon metabolism (for building organic molecules), energy metabolism(for energy for growth) and ATP (internal energy

requirements.). Thus, *Photoautotrophs* capture sunlight and use carbon dioxide. *Chemoautotrophs* break down inorganic molecules to supply growth energy and also use carbon dioxide. Both may alternatively get their carbon from organic sources. in fact *(chemoheterotrophs*) get both their energy and building materials for growth from metabolising sugars (aplenty in humans).

Bacteria's metabolic processes can be either aerobic (oxygen dependent) or anaerobic (no oxygen needed); some have both faculties..
Some can "facultatively" swing both ways. Their core working tool (in the cytoplasm) is the "electron transport chain"[1], as in the mitochondria, to create ATP.
μ
Notwithstanding their complexity, bacteria are small, measuring around 0.1 to 5.0 μm in diameter, while the human cell (eukaryote) range from 7.0 to 8.0 μm up. Bacteria are 50 times bigger than a virus, which range from 0.02 to 0.5 μm

Bacteria mutate, but not as much as viruses. But bacteria can divide rapidly, at about once in 20 minutes in optimum conditions.

Bacteria in the Biosphere

Bacteria dominate the biosphere. Like viruses, they have invaded all the living kingdoms, plants, animals, the marine world and humans. They outnumber all eukaryotes (plants and animals, etc) combined. They live in soil and water, and subsist in the air. One teaspoon of common dirt can harbour 100 million or more bacteria. They are found in all environments, from the bottom of the ocean deeps and beneath the ice caps, to the extreme deserts.

Bacteria are part of the biomass. Some 86% of the biomass live on land, including 100% of plants, but only 22% of animals, However, 89% of all bacteria llve in the oceans.

I could not find the figure for viruses but this quotation gives a microscope view into the constituents of the oceans

> "In the ocean, microbes (organisms from 0.2 to 100 microns) are very abundant. It has been calculated that they account for about half of the biomass on Earth. In the ocean, Bacteria and Archaea account for billions of tonnes of carbon (estimates range from 3 to 14 billion) while, in contrast, all people on Earth combined only account for about 0.03 billion tonnes of carbon. In **a drop (one millilitre) of seawater**, one can find **10 million viruses**, **one million bacteria** and about 1,000 small protozoans and algae (called "protists")"
> http://www.coastalwiki.org/wiki/Microbial_research

The total number of bacteria in the world is estimated at $5x10^{30,}$ which is still smaller than the number of viruses, at $1x10^{31}$. Few of both are infectious agents to larger animals like fish, whales, or humans, because almost all of the marine viruses are "phages"—viruses that specifically attack marine bacteria.

Bacteria have totally colonised the human body, and number therein the same[1] as all human cells put together, namely $3x10^{13.}$ Again, we might remember that virus are 10 times more numerous than bacteria in the body. Where one finds a bacteria, the could be 10 virus around, the later 50 times less visible.

Discovery and Classification

With the invention of the single-lens microscope, Antoine van Leeuwenhoek first observed bacteria in 1676, two hundred years before the virus was discovered. Christian Gottfried Ehrenberg named it in 1828, and Louis Pasteur first cultured it in 1860. With the last, scientists made much progress to understand it, and to develop effective sanitation, public health and anti-biotics, which subsequently enabled mastery over the worst of the bacterial pathogens and pandemics. One growing problem was classifying the bacteria.

In 1884, Hans Christian Gram invented “Gram staining”. The Gram stain procedure distinguishes between Gram-positive and Gram-negative groups, by colouring the bacteria cell walls. Gram-positive bacteria stained violet, due to the presence of a thick layer of peptidoglycan in the cell walls, while Gram-negative bacteria stained red, due to having a thinner peptidoglycan wall surrounded by a second lipid membrane. As it turns out, most bacteria are Gram-negative. Some bacteria have cell walls that are neither Gram-positive or Gram-negative, but the staining feature is pervasive enough to have served, and still serves, as a basis for classification.

The shape of individual cells has also been used to classify prokaryotes. Bacteria can be either spherical (*coccus*), rod-shaped (*bacillus)*, or *helical* (spirillum). While they are often described as single-celled organisms, bacteria can form colonies that show a remarkable complexity.

The year 1923 was a landmark, for being the year in which the first edition of Bergey's Manual of Determinative Bacteriology was published by the Society of American Bacteriologists (now called the American Society for Microbiology). The manual was prepared by an Editorial Board chaired by David H. Bergey. The Board published a second and a third edition in 1925 and 1930. In 1936, the Bergey’s Manual Trust was formed to publish successive editions and provide for research. The Trustees went on to publish the fourth through ninth editions.

At the First International Congress of Microbiology in Paris in 1930, proposals were made for bacteriology to establish its own Code of Nomenclature. At the Second Congress in London in 1936, a draft Code was presented and placed under the aegis of the International Committee for Bacteriological Nomenclature, later the International Committee on Systematic Bacteriology (ICSB), and now, the International Committee on Systematics of Prokaryotes (ICSP]. Today, the ICSP updates and publishes the Code of

Nomenclature of Bacteria, and its Judicial Commission overviews the nomenclature (taxonomy) of bacteria.

The year 1975 was another landmark, for that year's edition of Bergery's Manual incorporated the International Code of Nomenclature of Bacteria of the ICSP approved by the Plenary Session of the First Congress for Bacteriology in Jerusalem in 1973. It unified the two initiatives, provided a common framework, and set 1 Jan 1980 as the world implementation date, with an initial approved list of 2,300 bacteria names. The last revision of the Manual, published in 2001-2012 comprised five volumes, with nearly 1,000 contributors. Bergey's Manual of Systematics of Archaea and Bacteria, an online book, replaces the five-volume set in 2015. The last revision of the Code of Nomenclature was by the Fourteenth International Congress of Bacteriology and Applied Microbiology (BAM) in Montréal, in 2014.
Nothing could be more succinct than World Cat's flyer on this resource:

> "Bergey's Manual of Systematics of Archaea and Bacteria (BMSAB) is a reference work. . About a hundred new genera and 600+ new species have been described per year for each of the last 5 years. ,,,,Bergey's is the most complete and authoritative description of bacterial and archaeal diversity. Now available online for the first time, this edition provides descriptions of the taxonomy, systematics, ecology, physiology and other biological properties of all described prokaryotic taxa. This is a new, unique, single point of online reference for microbiology with over 1,750 articles - equivalent to over 8 volumes in print." (Edited) https://www.worldcat.org/title/bergeys-manual-of-systematics-of-archaea-and-bacteria/oclc/910521425

In 1987, Carl Woese, forerunner of the molecular phylogeny revolution, divided bacteria into 11 divisions based on 16S ribosomal RNA (SSU) sequences . Modern biotechnology relies on sequence analysis of DNA and RNA for much of the foundation for classification, but taxonomists are still much in discussion

It is curious that neither of the preceding bodies maintains a database or statistics. The US National Center for Biotechnology Information (NCBI) however maintains a register. Allowing for my lack of subject expertise,, I extracted that there were 20,955 bacteria (eubacteria) and 57,728 cellular organisms listed.

A somewhat dated NCBI resource had this statement:

> **"There** are about 30,000 formally named **species** that are in pure culture and for which the physiology has been investigated. **Species** now are being defined by PCR[1] amplifying ribosomal genes and sequencing.
> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3160642/ 2011

Searches for bacterial pathogens did not provide conclusive information. From again a 2005 source I have, "Indeed, approximately 1400 human pathogens have been described." We can take that as including bacteria.. Wikipedia has a detailed partial list of 59 species from 17 genus. Other sources cite 1% to 5% of (presumably only catalogued) bacteria to be pathogens.

In the Human Biome

Bacteria are **not** constitutional predators. They take up residence in living things for the environmental benefits, mainly rich nutrients. They do not hunt or kill cells compulsively. They replicate but not have to do so inside a cell.

Through a long evolutionary relationship, they have come to regard the human gut as their home, and have even developed defensive measures against other bacterial invaders, i.e. phages. They also confer benefits, and have been put to beneficial use.

Externally bacteria live on the skin (our largest organ), and they enter us through open wounds and our bodily orifices. They live the latter, namely in the nose, the throat, in the mouth, and in the vagina.

Bacteria float in and out as we breathe. Most bacteria in exhaled breath remain airborne for a long time.

Bacteria are also picked up from every surface and most fluids. Sources include the light switches, door knobs, handphones and remotes at home, and lift buttons, railings faucets and washbasins in public places. We can become infected by contaminated food or water. Human to human transfer is the most common route. People infect one another most rampantly during an epidemic.

Inside the body, bacteria generally reside directly in the host cytoplasm or in host-derived vacuoles. They concentrate in the respiratory tract, the gastrointestinal or digestive tract, and the urinogenital tract[1]. The greatest numbers are found in the gut, it being the richest repository of food. They grow there from a child's first year, and make up most of its micro-flora. Their descendants keep us company to the end of our lives. We call our in-house bacteria "commensals".

One source reported that there are an estimated 100 trillion bacteria, both good and bad, living inside the digestive system, mainly obligate anaerobes. An NCBI research report in 2013 suggested that "within the human gastrointestinal microbiota exists a complex ecosystem of approximately 300 to 500 bacterial species, comprising nearly 2 million genes." More recently, on 11 Feb 2020, researchers at the European Bioinformatics Institute and the Wellcome Sanger Institute identified " almost 2,000 bacterial species living in the human gut, yet to be cultured in the lab."

Bacterial Life Cycle

Inevitably, I asked the question: is there any danger of the human body being "over-populated" by bacteria, given they can double as rapidly as every 20 minutes? I was relieved to find that they have a rational life-cycle, which keeps the population in check, Here it is, left substantially as extracted from this excellent source (albeit a lab), with some editing

"**The Lag Phase**
The beginning of the growth curve represents a small number of cells, referred to as an inoculum, that are added to a fresh culture medium, a nutritional broth that supports growth. The initial phase of the growth curve is called the lag phase, during which cells are gearing up for the next phase of growth. The number of cells does not change during the lag phase; however, cells grow larger and are metabolically active, synthesizing proteins needed to grow within the medium.

If any cells were damaged or shocked during the transfer to the new medium, repair takes place during the lag phase. The duration of the lag phase is determined by many factors, including the species and genetic make-up of the cells, the composition of the medium, and the size of the original inoculum.

The Log Phase
In the logarithmic (log) growth phase, sometimes called exponential growth phase, the cells are actively dividing by binary fission and their number increases exponentially. For any given bacterial species, the generation time under specific growth conditions (nutrients, temperature, pH, and so forth) is genetically determined, and this generation time is called the intrinsic growth rate. During the log phase, the relationship between time and number of cells is not linear but exponential.

Cells in the log phase show constant growth rate and uniform metabolic activity. For this reason, cells in the log phase are preferentially used for industrial applications and research work.

Stationary Phase
As the number of cells increases through the log phase, several factors contribute to a slowing of the growth rate. Waste products accumulate and nutrients are gradually used up. In addition, gradual depletion of oxygen begins to limit aerobic cell growth. This combination of unfavorable conditions slows and finally stalls population growth.

The total number of live cells reaches a plateau referred to as the stationary phase. In this phase, the number of new cells created by cell division is now equivalent to the number of cells dying; thus, the total population of living cells is relatively stagnant. The culture density in a stationary culture is constant.

During the stationary phase, cells switch to a survival mode of metabolism. As growth slows, so too does the synthesis of peptidoglycans, proteins, and nucleic-acids; thus, stationary cultures are less susceptible to antibiotics that disrupt these processes. In bacteria capable of producing endospores, many cells undergo sporulation during the stationary phase.

In certain pathogenic bacteria, the stationary phase is also associated with the expression of virulence factors, products that contribute to a microbe’s ability to survive, reproduce, and cause disease in a host organism. For example, quorum sensing can initiate the production of enzymes that can break down human tissue and cellular debris, clearing the way for bacteria to spread to new tissue where nutrients are more plentiful.

The Death Phase
As a culture medium accumulates toxic waste and nutrients are exhausted, cells die in greater and greater numbers.

Soon, the number of dying cells exceeds the number of dividing cells, leading to an exponential decrease in the number of cells This is the aptly named death phase, sometimes called the decline phase. Many cells lyse and release nutrients into the medium, allowing surviving cells to maintain viability and form endospores. A few cells, the so-called persisters, are characterized by a slow metabolic rate. Persister cells are medically important because".
https://courses.lumenlearning.com/microbiology/chapter/how-microbes-grow/

Luis Villazon, in BBC ScienceFocus[1], in an unusually correct display of typical media reverse thinking, deducts as follows

> "But if we assume that the global bacteria population is stable, then it follows that one bacterium must die for each new one that is produced. Bacteria divide somewhere between once every 12 minutes and once every 24 hours. So the average lifespan of a bacterium is around 12 hours or so."
> https://www.sciencefocus.com/nature/how-long-does-a-bacterium-live/

He also helpfully points out that bacteria can form spores that can survive for 250 million years.

Pathogens.

In nature there is always the aberrant one, the one who did not mutate properly, is genetically deficient, is damaged or is simply a chap looking for something better in life. The pathogenics would come from these. It is said that not more than 1% to 5% of (known) bacteria could be pathogenic. This is still a large number, up 1,500 on 30,000.(On the other hand, this percentage tends to confirm that bacteria are a stable lot.)

The principal difference between a pathogen and a commensal is that the latter does not encode aggressive tools for invasion. In fact, the commensal may join the immune system for action against pathogens. It is reported that the immune system, like the brain, can distinguish incoming commensals from pathogens.

The commensal has no interest in attacking the host. However, in conditions of adversity , ie depletion of nutrients or an inimical environmental change (wrong drugs) etc, some may go pathogenic.

The respiratory, digestive and urogenital mucosa[1] represent a surface area of approximately 300–400 square meters (i.e. 200 times larger than that of the skin). These surfaces constitute the frontlines of invasion by pathogens.

Bacteria have evolved a large arsenal of molecular strategies allowing them to target and adhere to host cells

In addition to surface attachments (pili), they have a range of surface adhesins with adhesive properties, which recognize various classes of host molecules. Some of these adhesins, after allowing the binding of bacteria to host cell surfaces, also can also trigger “internalisation” of the bacteria inside host cells.

Finally, adhesion to host surfaces is a key element in the formation of biofilms, i.e. matrix-enclosed microbial assemblies that adhere to biological or non-biological surfaces. Biofilm formation is a protective cloak that allows bacteria to grow in a hostile environment.

Other things being equal, the bacterial pathogens look for an intracellular lifestyle, i.e in a cell. There they become inaccessible to various immunity countermeasures and can access a wide range of nutrients. One of their means (tricks) is to be “phagocyted”[1] by one of the intestines’ macrophages[1] (M Cells).Many pathogens target cell–cell junctions to penetrate barriers, thereby enhancing bacterial movement in the host.

Infection

Infection begins when a harmful strain of bacteria enters the body and begins to multiply.

Bacterial diseases occur when the bacteria get into the body and begin to reproduce and crowd out healthy bacteria, or to grow in tissues that are normally sterile.

Bacteria also cause disease by secreting or excreting toxins (as in botulism), by producing toxins internally, (as in typhoid) or by inducing sensitivity to their antigenic properties (as in tuberculosis).

Bacterial infections can range from minor external irritations to serious, even mortal, diseases. Today, they are curable, with antibiotics.

To my question to Wikipedia, what bacterial diseases are (still) incurable, I got no answer. It seems, science has got the measure of these bacteria. Nevertheless there is growing apprehension over their resistance to anti-biotics.

Disease

Bacteria had a horrendous early record. Of the 19 biggest past pandemics, with deaths of 1 million or more, see **Table 2,** eight were caused by bacteria. However, of the 27 epidemics since 1960 with deaths of 1,000 or more, only six were bacterial - with five due to cholera, four of these in Africa, and the highest deaths 10.075 in Haiti in 2018-9. Man has been successful against the bacteria – but not the virus.. The main historic culprit, the bubonic plague (*Yersinia Pestis*) has substantially been wiped out ,

But, we continue to live in a world in which bacterial diseases are still endemic, and millions are infected annually. Two historic bacteria still reach pandemic proportions. The problem is a combination of disease and poverty. They are

being countered by global programmes launched by the World Health Organization (WHO).

.(a) Tuberculosis (TB)

The bacterium responsible for causing TB is *Mycobacterium tuberculosis*. It attacks the lungs.

In 2019, an estimated 10 million people fell ill with tuberculosis(TB) worldwide. About one-quarter of the world's population has a TB infection, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit it. A total of 1.4 million people died in 2019, (including 208 000 people with HIV).

Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). IN 2014, WHO launched a world-wide End TB programme. Eradicating the TB scourge by 2030 is among the health targets of the United Nations Sustainable Development Goals

. (b) Cholera

The bacterium responsible for cholera is *Vibrio cholerae.* It is an acute diarrhoeal disease that can kill within hours if left untreated. It is caused by ingestion of food or water contaminated with the bacterium. . Provision of safe water and sanitation is critical to prevent and control the transmission of cholera.

Cholera is an indicator of lack of social development. It can be endemic in communities living on or below the poverty line. Each year there are 1.3 to 4.0 million cases of cholera, and 21,000 to 143,000 deaths worldwide.

In 2017, WHO launched a global strategy on cholera, namely Ending Cholera: a Global Roadmap to 2030, with a target to reduce cholera deaths by 90%.

.(c) Others

The following is list of some of the other bacterial diseases: pneumonia, diphtheria, meningitis, gonorrhoea, syphilis, botulism, tetanus, food poisoning and even tooth-ache. They sound familiar, both family-wise and personal. They are what I would call house-hold illnesses, compared to the new generation viral diseases, each with an alien name, which sweeps across our lives like a tornado.

One major problem in combating bacteria is their ability to develop resistance to ant-biotics. But it seems, science is sustaining the fight. Phage therapy has been a promising weapon, see also under “Bacteriophage.”

Finally, I see no new strains of bacteria jumping the animal and plant frontiers and rising to devour us, like HIV, SARS-Covid-2 and Ebola,

Beneficial Uses

Bacteria are essential to making many foods we enjoy, such as bread and cheese, and wine and whisky. Other foods include yogurt, tau-jee, tempeh, and vinegar.

They are used in the production of antibiotics, probiotics, drugs, vaccines, starter cultures, insecticides, enzymes, fuels and solvents

Bacteria can be used to create biofertilizers or to reduce metal pollutants. Microbes can also be used to produce certain non-microbial products, such as insulin.

There is compelling evidence that mitochondria and chloroplasts were once primitive bacterial cells. This evidence is described in the endosymbiotic theory.

Evolutionary Roles

Bacteria were among the first, if not the first, micro-organic life forms to evolve. They pioneered extracting energy from rocks through anaerobic respiration. Their earliest trace evidence goes back to from 4.28 bya[1] to 3.77 bya[1].

The Last Universal Common Ancaster (LUCA) has been estimated to have been as early as 4.5 bya to 3.5 bya, when these ancients split into the Archaea and Bacteria. The latter then went on to generate the vast majority of living things on this planet, including all eukaryotes, which includes the human species. Bacteria is the grand-daddy of us all, including the dinosaurs and the primates.

About 2.4 bya, when the world was still without an atmosphere, a particular bacteria, the *cyanobacteria,* discovered *photosynthe*sis, how to make more energy using sunlight. The bye-product was release of oxygen into the atmosphere. As more and more took up the practice, it lifted their growth path onto another plane and angle altogether. Over the next **billion** years or so, the **bacteria effected the Great Oxygenation**, transforming the planet for all oxygen-dependent eukaryotic genres to come. About 1.1 bya, algae appeared and about 0.475 vascular plants, progressively going photosynthetic and adding their contribution of oxygen. Today, oxygen has stabilised at 21% of the atmosphere, Bacteria still play a prominent part in the supply – from the ocean where most of them live. The following quotation gives some details:

> " Scientists estimate that 50-80% of the oxygen production on Earth comes from the ocean. The majority of this production is from oceanic plankton — drifting plants, algae, and some bacteria that can photosynthesize. One particular species, *Prochlorococcus,* is the smallest photosynthetic organism on Earth. **But this little bacteria produces up to 20% of the oxygen in our entire biosphere.** That's a higher percentage than all of the tropical rainforests on land combined."
> https://oceanservice.noaa.gov/facts/ocean-oxygen.html

Bacteria have come to play one other critical role in our planet's eco-system. Nitrogen is essential to life on earth because fixed inorganic nitrogen compounds are required for the biosynthesis of amino acids, proteins, nucleic acids, etc.

Nitrogen in the air must be converted into inorganic nitrogen by Nitrogen Fixation. About 90 percent of the world's requirements is produced by bacteria, with help from other micro-organisms.. Through this transformation nitrogen is made available to plants which in turn ultimately sustain all animal life. At the other end of the cycle, bacteria decompose waste living matter by the process of ammonification, releasing ammonia and ammonium. Finally, bacteria can transform the ammonia back into nitrates.

Nitrogen fixation is carried out naturally in soil by free-living bacteria. Cyanobacteria also do nitrogen fixation in addition to photosynthesis. They are especially important in open-ocean ecosystems.

Nearly all animals are dependent on bacteria for survival as only bacteria and some archaea possess the genes and enzymes to synthesize vitamin B12 and provide it through the food chain. Vitamin B_{12} is involved in the metabolism of every cell of the human body. It is a co-factor in DNA synthesis, and in both fatty acid and amino acid metabolism. . It is important in the normal functioning of the nervous system via its role in the synthesis of myelin.

Bacteria have another key role, in keeping the oceans clean and maintaining the global carbon balance. They function as the scavengers of the ocean: They assimilate the organic carbon that comes from waste material in the food chain (from phytoplankton to fish). They are the only organisms in the sea capable of transforming this kind of waste. The amount of carbon that remains as cell material determines the role that ocean biology plays in locking up atmospheric carbon dioxide in the ocean. Thus, these "recycling" bacteria

play an important role in regulating how much of the planet's carbon dioxide is stored in the oceans.

The oceans are home to possibly the most abundant microbe on the planet, a bacterium called *Pelagibacter.* It usually accounts for about 25 percent of all the microbes in the ocean, but during a bloom it likely will account for up to 50 percent. It feeds on dead organic matter that is dissolved in the water, a process that is part of the microbial loop. It helps keep the ocean clean and clear and contributes to the carbon balance.

Bacteriophages

Viruses need compulsorily to capture living cells in order to replicate. In the earliest days, there would not have been much else to capture besides bacteria, and even those very few and far between. It is not surprising therefore that “bac-hunting” it became their classic sport over the eons.

A virus, on replication inside a bacteria, becomes a bacteriophage, also known as a phage. Thereafter, it only hunts and replicates other bacteria. As this has been going on since things began, and not been interrupted by the five extinctions and 11 glaciations of pre-history, it is not surprising that bacteriophages are today thought to be the most numerous entity on this planet, including bacteria[1].

Bacteriophages are found wherever bacteria exist. Up to 70 percent of marine bacteria may be infected by phages.

In normal respects, a phage is a virus, and attacks and replicates in the same way, depending whether it is a non-enveloped or enveloped virus, etc. They may adopt the lytic or lysogenic cycle of replication. This means they kill the bacteria in the end. Phages have become specialised and only target and attack certain bacteria. In fact, phages only attack bacteria, and are harmless to humans.

Phages have been used since the late 20th century as an alternative to antibiotics They are seen as a possible therapy against multi-drug resistant bacteria . In USA, the FDA has approved a food additive containing a phage that kills a foodborne pathogen and one that causes meningitis. As bacteria can rapidly become resistant to a single bacteriophage, a "phage cocktail" is a current option being worked on.

I thought viruses might be using bacteria through phages as an evolutionary "back-door" to achieving "living thing" status. I am told categorically that phage replication does not qualify as reproduction. Phages are still non-living things.

The rate of viral infection in the oceans stands at 1 × 1023 infections per second, and these infections remove 20–40% of all bacterial cells each day. Considering the importance of bacteria, this may seem a drastic happening. But I read somewhere else that in just seven hours one bacterium, in top gear, can generate 2,097,152 bacteria. After one more hour the number of bacteria will have risen to a colossal 16,777,216. I think the bacteria win out. No doubt some painstaking oceanographer will one day check the math.

Bacterial Genes

Bacteria have more variation in their metabolic properties, cellular structures, and lifestyles than can be accounted for by mutation alone. The evidence suggests that horizontal gene transfer has bolstered the diversification and speciation of many bacteria.

Unlike eukaryotes, which evolve mainly through the modification of existing genetic information, bacteria have acquired a large percentage of their genetic diversity by the horizontal transfer. This creates a dynamic genomic environment in which DNA can be introduced into and removed from the chromosome.

Bacterial species also differ widely. As a result, sequences that are newly acquired through lateral transfer can be identified via their characteristics which remain with the donor.
Comparisons of completely sequenced genomes confirm that bacterial chromosomes are amalgams of ancestral and laterally acquired sequences.

A consortium report on the human genome in Feb 2021 found that 223 of the 30,000 human genes appear to have been acquired directly from bacteria.

An older report said that about 30% of healthy human genome consists of bacterial DNA (much more in cancer cells) and approximately eight percent of human genetic material comes from viruses and not from our ancestors.

It is likely that eukaryotic cells, of which humans are made, evolved from bacteria about two billion years ago. One theory is that eukaryotic cells evolved via a symbiotic relationship between two independent prokaryotic bacteria.

* * END**

(Back to TOC)

ABOUT THE AUTHOR

Gerald Francis Pillay was born in Melaka (then Malacca), Malaysia on 2 Dec 1934, son of Francis Joseph Pillay @ Odiang, a Chitty Melaka, and Janet Thomas, a Eurasian. The family migrated to Singapore in 1949. He is married to Mabel Narayanasamy, and they have two sons, Leslie married to Deirdre Goh, and Carl married to Sharon Loh. The latter have one son, Christian.

Educated at St Francis' Institution, Malacca and St Joseph's Institution, Singapore, he studied at the University of Malaya (then in Singapore), where he was a University Scholar. He won the Economics Book Prize (1956) and graduated with the B.A. Honours Upper II in Geography (1957).

Mr. Pillay served in the Singapore Administrative Service from 1957. He served in Home Affairs, PMO, Public Service Commission, Défence, Foreign Affairs and Telecommunications, before posting in 1971 to Education as Deputy Secretary (Technical Education).

In 1974 he transferred to the newly formed Industrial Training Board as Secretary. He retired in 1989 as the Deputy Director (Deputy CEO) of the board, which had enlarged to become the Vocational and Industrial Training Board – predecessor of the present Institute of Technical Education (ITE). Altogether he had 33 years in the public service.

In 1989, he formed GFP Consultancy. For another 17 years, until his second retirement in 2006, he practised as a consultant in Technical Education, serving international agencies such as the World Bank, UNDP, UNESCO and ILO, and employers and employers' organisations. In 1992-3, at their request for an External Commissioner, the Singapore Government nominated Mr. Pillay to serve on Botswana's Presidential National Commission on Education.

Mr. Pillay was Aide-de-Camp (Extra) to Tun Yusof bin Ishak, Yang di Pertuan Negara (Head of State), Singapore, 1961-64 He was twice Club President and four times a Cabinet Officer, of Lions Clubs International District 308 A1 and predecessors, 1973 to 2008. He was Secretary, Catholic Aids Response Effort (CARE) from 2007-10.

He has been Adviser to the Peranakan Indian (Chitty Melaka) Association Singapore since 2016

.

(Back to TOC)

* * *

OTHER BOOKS BY THE AUTHOR

(1) **The Chitty Melaka Story,** 6 Sep 2018, ISBN 978-981-11-7851-1 (paperback), issued under the auspices of the Peranakan Indian (Chitty Melaka) Association, Singapore. (Distribution by the Association).

(2) **The Chitty Melaka Story, Second Edition,** 31 Dec 2018, ISBN 978-981-11-7845-0 (e-book). The book provides an historical overview of the Chitty Melaka community (also spelt Chetty Malacca or Chetti Melaka). It does so through descriptive snapshots covering their beginnings in Sultanate times in Malacca through their different sojourns under four colonial powers, over five hundred years. The book also touches on their dispersion, their changing composition, and their future identity. Published at https://www.smashwords.com/books/view/902177

(3) **Japanese Conquest of Malaya and Singapore 194-42**, 16 Dec 19, ISBN: 978-981-14-0556-3 (e-book). Besides detailed descriptions of the British-Japanese engagements in the Far East, the book focuses on the Malaya-Singapore campaign, who was responsible for the Fall of Singapore, and whether the British redeemed their honour in the end. Published at https://www.smashwords.com/books/view/995977.

(4) **Quantum Mechanics, A Non-Technical Review** (19 Nov 2021), ISBN: 978-981-14-9875-6 (e-book) “QM turns out to be a breath-taking story of our breakthrough into an unbelievable future. Not science fiction, but what our world is likely to be in 50 years, if they get the Quantum Computer going.”(From “About This Book”). It covers
First Quantum Revolution – the primary discoveries, enabling the Information Age
Second Quantum Revolution –gestating the Quantum Computer’s computational core (up to the present)
Third Quantum Generation – roadmaps and breakthroughs to the hybrid and intermediate generations of Quantum Computers (by 2040), and
Fourth Quantum Generation – When the Quantum Computers and their associated inventions run the place, map the stars and take us beyond Absolute Zero. (beyond 2070).

Self-published and may be downloaded free at
https://geraldpillay.wordpress.com/2021/11/19/quantum-mechanics/

(5) **Virus* Biological Predator (An Investigative Review of Covid-19),** ISBN 978-981-18-3046-4,. This book. It is due to be self-published on 15 Dec 21 at https://geraldpillay.wordpress.com.

***

(Back to TOC)

** END **