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The Executive Summary is produced weekly and contains in-depth analysis.  
International SOS publishes a COVID-19 [Daily Case Summary](#).

## INTRODUCTION

In this week's edition of the International SOS COVID-19 Executive Summary we explore:

1. The addition of the "waning" category to the International SOS COVID-19 country status map
2. The B's and T's of immunity
3. Accuracy of antibody tests
4. Update on Texas
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7. A View from the Lab: Professor John Oxford
  - We will have to learn to live with this virus
  - Obesity and risk with COVID-19: virology vs physiology
  - Hospitals are safer places from COVID-19 virus than you might think (letter in the Lancet)
  - COVID-19 virus mutation (or not) is a hot topic
  - Is COVID-19 and the highly visual ICU respirators "our generations equivalent of the polio epidemics of the 1950's"

## INTERNATIONAL SOS ADDS "WANING" CATEGORY

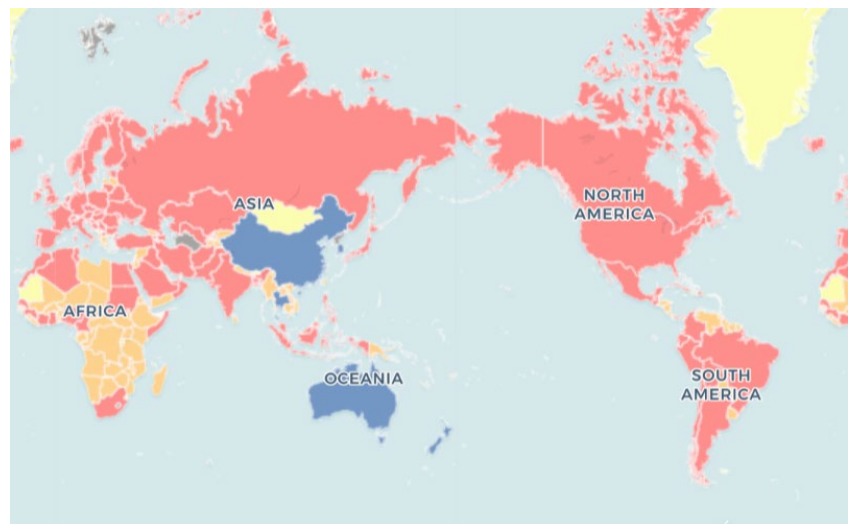
International SOS has added the category of "waning" (dark blue) to its COVID-19 country status map.

**Waning follows "outbreak" status, and these countries have:**

- <100 cases per day
- 2 weeks declining case numbers
- Sporadic cases or clusters as per WHO
- Some lifting of restrictions

**Countries currently "waning" are:**

- Australia
- China
- Luxembourg
- New Zealand
- Norway
- South Korea
- Thailand



## THE B's AND T's OF IMMUNITY

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On 24 April, the World Health Organisation issued a [briefing note](#) on why immunity passports are not a good idea: “There is currently no evidence”, it said, “that people who have recovered from COVID-19 and have antibodies are protected from a second infection.”

Here we spell out the steps the body's immune system takes when confronted with a virus.

### 1. Non-specific response:

- Macrophages, neutrophils, and dendritic cells slow the progress of the virus and may even prevent it from causing symptoms.

### 2. Adaptive response:

- “B” lymphocytes (“B” because they mature in the bone marrow) begin to produce antibodies (aka immunoglobulins), specifically tailored proteins that latch onto the virus. Some, called “neutralising” antibodies, inactivate the virus. All antibodies, “neutralising” and “non-neutralising” mark the virus for destruction by macrophages. This is also called “humoral” immunity.
- “T” lymphocytes (“T” because they mature in the thymus) recognise and kill body cells which have been invaded by the virus. This is also called “cellular” immunity.
- If the combined efforts of macrophages, “B” cells and “T” cells are sufficient, the virus will be cleared from the body, and, if the response is strong enough, may prevent progression to severe illness and/or re-infection by the same virus. This “strength” of this process is often measured by the presence and level of antibodies in the blood.
- Later, “memory” B and T cells will help the immune system remember the virus and to respond if it returns.

How long does that memory last? For measles, protection is lifelong; for influenza it can last many years or even a lifetime. We currently do not know how long our immune memory of SARS-CoV-2 lasts; it will take a year or two of observation to find out.

### **Antibody tests for epidemiologic studies are used in two main ways:**

#### 1. To determine if a person may be immune to a virus.

With well-known viruses, the level of antibodies in a person's blood gives some idea of their immunity to that virus. The higher the level of antibodies in a person's blood, the more likely they are to be immune to the virus. However, [as stated by the WHO](#), it is not yet known whether the detection of antibodies in a person's blood indicates that they have immunity to SARS-CoV-2. It is suspected that the presence of antibodies to SARS-CoV-2 indicates a level of immunity, however it is not known how long this immunity will last.

#### 2. To determine what proportion of a group has been infected with a particular virus.

In this instance, blood tests are taken from a group of people and tested for antibodies. The presence of antibodies indicates previous infection (with limitations – see below). Depending on the selection of the sample group, the results may show:

- The proportion of the population who have been infected by the virus (called a serosurvey), or
- The proportion of people who are known to have been infected who have developed antibodies, or
- How long after symptoms developed were antibodies produced, etc....

## ACCURACY OF ANTIBODY TESTS

There are two issues that are complicating the use of antibody testing, especially for the much-discussed “Immune Passports”.

### 1. Poor quality-control of tests kits

There are over 80 kits to measure antibodies to SARS-CoV-2 on the market. To allow early use of antibody testing, the US FDA relaxed its usually tight control of products allowed to go to market. This led to uncertainty on the accuracy of some of the kits as cross-reactivity with other coronaviruses, even those causing the common cold, was suspected to be giving false positives. That could make someone think [“Maybe I’m protected”](#). I can relax” – when actually they are still vulnerable.

### 2. Poor positive predictive value

Some definitions to start:

- Sensitivity: the probability that a test will indicate “disease among those with the disease
- Specificity: the fraction of those without disease who will have a negative test result
- Positive predictive value: the probability that subjects with a positive screening test truly have the disease

[From an interview in Medscape](#)

“If a test has a 3% false-positive rate - which is 97% specificity - and we apply that to a population that has less than 5% prevalence - so the majority of people haven’t had it - that test, in terms of what we call positive predictive value, could be wrong 50% of the time.

For a test to really work well in a disease that is only affecting 2%-3% of the population, we need a test that is at least 99.7% specific. So, the take-home point is that I would hold tight on getting antibody tests until we have a lot of validation.”

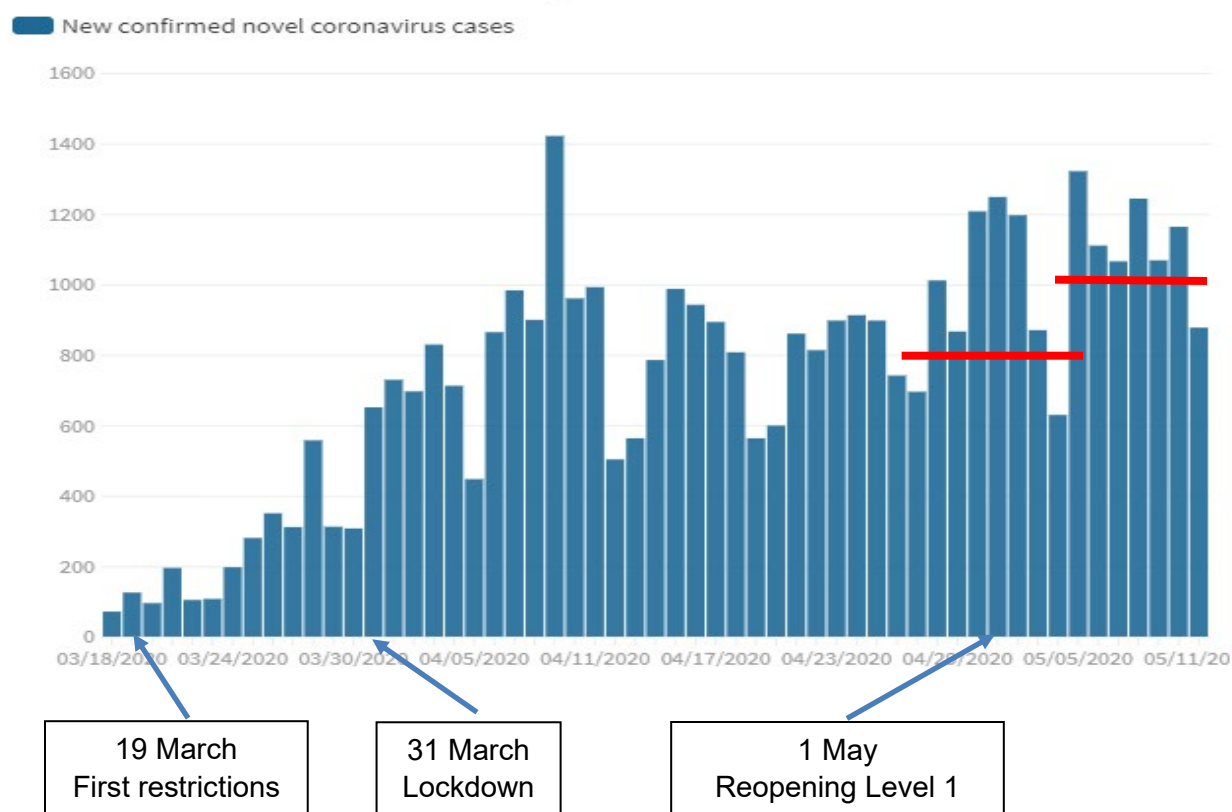
Table from: [Penn State Eberly College of Science](#)

	Truth		
	Disease (number)	Non Disease (number)	Total (number)
Positive (number)	<b>A</b> (True Positive)	<b>B</b> (False Positive)	$T_{\text{Test Positive}}$
Negative (number)	<b>C</b> (False Negative)	<b>D</b> (True Negative)	$T_{\text{Test Negative}}$
	$T_{\text{Disease}}$	$T_{\text{Non Disease}}$	Total

## UPDATE ON TEXAS

Last week we reported on the staged “re-opening” of Texas on 1 May. The graph below from the Houston Chronicle shows an apparent increase of daily confirmed cases from 800 to 1,000 per day over the last week. We will continue to report on Texas as a possible microcosm of the USA.

**Texas: new confirmed cases:** [Houston Chronicle](#)



### A little more from the USA:

#### Fauci's worrying testimony to Senate Committee

- Anthony Fauci testified to a Senate committee on 12 May that the "consequences could be really serious" for states and cities that reopen without meeting federal guidelines.
- "I feel, if [premature opening] occurs, there is a real risk that you will trigger an outbreak that you may not be able to control. Which, in fact, paradoxically will set you back, not only leading to suffering and death that could be avoided, but could even set you back on the road to trying to get economic recovery. It would almost turn the clock back rather than going forward. That is my major concern."

#### Just half of Americans would use phone-based contact tracing

- In a best-case scenario, just half of Americans would participate in voluntary virus contact tracing tracked with cellphones, Axios White House editor [Margaret Talev](#) writes from the latest installment of the Axios-Ipsos Coronavirus Index.

## MORE SECOND WAVES

### Wuhan orders fresh coronavirus tests for all residents as new cluster fans fears of second wave

- Roughly 11 million people to be tested for COVID-19 in 10-day campaign.
- Decision follows discovery of six cases at a residential compound, known as Sanmin, on the weekend
- A [Chinese professor of epidemiology](#) said large-scale testing was needed to prevent a new wave of infections. “The new cases in Wuhan show there is a real risk of a second wave in the community caused by the asymptomatic carriers or those with mild symptoms. COVID-19 started with a few after all,” he said. “Tests on such a broad scale can help find these hidden carriers and eliminate that risk.”

### Clusters in Korean nightclubs

- More than [100 new cases](#) linked to the nightclubs in Seoul's Itaewon nightlife neighbourhood, have brought fears of a second wave of infections in a country held up as a coronavirus-mitigation success story.
- Authorities have combed through mobile phone data, credit card statements and CCTV footage to identify people who visited the nightclubs.
- However, some could be put off coming forward for testing, as many of the clubs have been identified as gay bars.

### Increased transmission of coronavirus in Germany

- The coronavirus [reproduction number](#) has been slightly above 1 since Saturday, said Professor Lars Schaade at Germany's public health body, the Robert Koch Institute (RKI). This is significantly due to clusters linked to slaughterhouses.
- Clusters in slaughterhouses have also occurred in [Melbourne](#) and many locations in the [USA](#), where almost 5,000 meat workers have been infected.

*Interpretation:* when a country has an  $R_0$  of just less than 1, clusters such as these can push the  $R_0$  above 1 again. If the clusters are controlled, then the  $R_0$  should return to less than one. If not, they could trigger a wave through the community. Having a lower  $R_0$ , 0.5 or even 0.3, gives a country more “room” to cope with an outbreak such as these in slaughterhouses, without risking a community wave.

## ARTICLE / JOURNAL ROUNDUP

### Buffets are super-spreaders

- [Japanese TV station](#) simulates viral spread and finds one diner can infect nine others.
- When the experiment was repeated, under conditions designed to limit infection spread, no paint was found on participants' hands.
- In this alternative set of conditions, foods were separated, tongs were changed frequently and all guests were encouraged to wash their hands.



### Singapore is giving 20,000 [blood oxygen monitors to migrant workers](#)

- Five weeks into its partial coronavirus lockdown, Singapore continues to record hundreds of new COVID-19 infections per day, with low-wage migrant workers living in cramped dormitories now accounting for about 90% of the city state's 23,822 infections.
- Many of these workers exhibit few, if any, of the symptoms usually associated with the respiratory disease, which is why thousands of pulse oximeters are now being distributed, to help detect the early warning signs of a coronavirus-related deterioration in health, even before a diagnosis has been made.

## The eye a symptom and source of contagion?

- There is [evidence](#) that COVID-19 can first present conjunctivitis / pink eye.
- A new study into Italy's first coronavirus patient has found she had traces of the virus in her eyes for several weeks, even after it had become undetectable in nasal swabs. The research, published in [Annals of Internal Medicine](#), is the latest piece of literature to establish a connection between COVID-19 and ocular fluids, suggesting the eye is not only a potential entry point for the virus, but also a source of contagion.



## FDA clears home saliva test



- The US Food and Drug Administration (FDA) has granted emergency authorization for the first at-home saliva collection kit to test for the coronavirus.
- Rutgers University received FDA permission last month to collect saliva samples from patients at test sites but can now sell the collection kits for individuals to use at home. They must be ordered by a physician and must be processed in a laboratory.
- The expanded FDA approval will permit testing of people who cannot get to a collection center, or who are homebound because they are sick, quarantined, or at increased risk of infection.

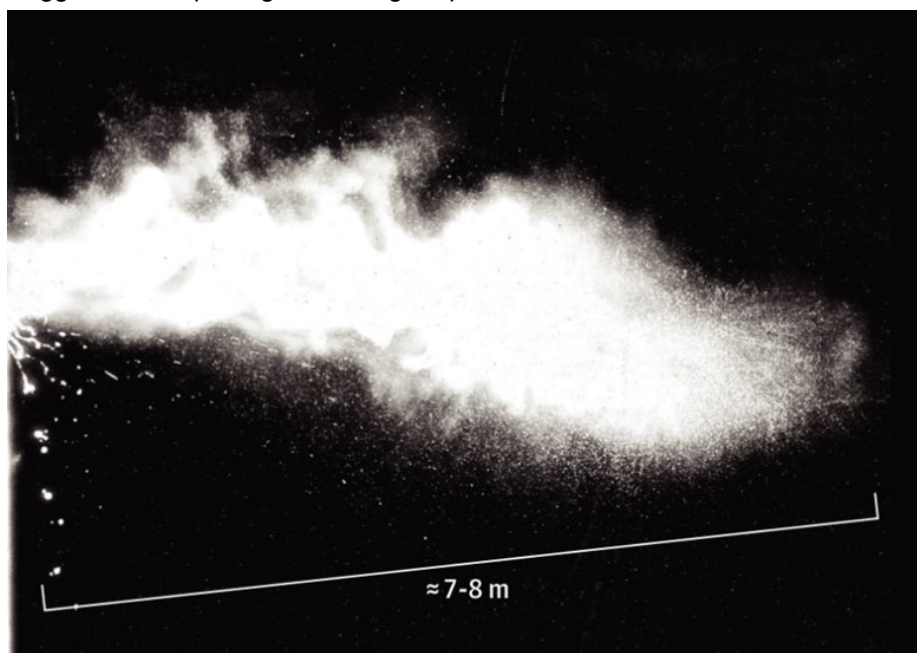
Photo: [Spectrum Solutions](#)

## Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19

- A study published in the [Lancet](#) has shown a triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19 to be superior to treatment with lopinavir–ritonavir alone. The endpoint tested was negative nasopharyngeal swab: this was seven days in the triple therapy group and 12 days in the double therapy group.

## Why 1.5m might not be far enough

The concept of differentiating droplet spread from aerosols was developed in the 1930s. Recent [laboratory work](#) has suggested that pathogen-bearing droplets of all sizes can travel 23 to 27 feet (7-8 m).



Multiphase Turbulent Gas Cloud From a Human Sneeze:  
[JAMA](#)



## **New seroprevalence data from Geneva**

New [seroprevalence data from Geneva](#) estimates about 10 infections for every COVID-19 confirmed case. Overall, this is consistent with current rough estimates for the extent of under-reporting in Europe.

## **A VIEW FROM THE LABORATORY: PROFESSOR JOHN OXFORD**

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This week there is emphasis on emerging from lockdowns, virus mutations and a special comparison with polio.

### **"We will have to learn to live with this virus"**

Lars Schaade, Vice President of the famous Robert Koch Institute (RKI) in Berlin announced that the infection of COVID-19 in Germany had been "substantially pushed back". The world-famous institute has been giving daily briefings and high science 'free of political coloring'. Yesterday Germany had 166,000 confirmed cases and the  $R_0$  was 0.6 or thereabouts. He speculated that the virus could not be eradicated from Germany, at least until there was a vaccine or treatment. If the pace of new infections in municipality exceeded 50 per 100,000 inhabitants within seven days then lockdown would be restarted with schools and shops closed. "We will have to try to build this virus into our lives, changing our behaviour to reduce its transmission!"

Personally, I am hearing from scientific colleagues how the German nation has been dealing with the virus not by guessing or hoping and smoke and mirrors but by facing up to the true facts and taking immediate action. On a tourist note, the Institute is well worth visiting (even to a non-virologist), with a special Robert Koch museum showing the bacteria he discovered and his microscopes and equipment along with plenty of data on infectious disease then and now. The now rather famous virologist there, Christian Dorsten, has called the situation "the prevention paradox". In essence, Germany's early success in combatting the virus makes it more difficult now to convince citizens to adhere to even a partial shutdown. Already the  $R_0$  has moved from 0.6 to around 1.1 today (Monday).

### **Obesity and risk with COVID-19: virology vs physiology**

Two studies are published today including one of critically ill patients in UK intensive care and a study of NHS electronic health records. The latter found that the risk of dying was twice if the patient was obese. In the UK 64% of the population is overweight and/or obese, 35% with a BMI of 25.29 and 30% with a BMI of 30 or higher. This work confirmed reports from the US, China, and Italy. The UK data does not consider type 2 diabetes and heart disease when the risk would be higher. The most likely scientific reason is that an overweight body demands more oxygen. Another possible link has been suggested that high levels of ACE2 enzymes are found in adipose tissue; but given the receptor preference of COVID-19 it is difficult to envisage any direct virologic link.

As regards other higher-risk groups such as BAME (Black, Asian and minority ethnic) in the UK, the consensus explanation is towards overcrowded and poor housing rather than genetics. Also, the BAME sector are more likely to have higher-exposure jobs such as taxi and delivery drivers.

### **Hospitals are safer places from COVID-19 virus than you might think (letter in the Lancet)**

Given the relatively high rates of infection in the community in the UK, and the number of deaths, there is concern from the general public that hospitals themselves might be places where you could become infected. This attitude is not without foundation. In the SARS outbreak, family homes and hospitals were pinpointed as epicenters of

infections. In the present outbreak, despite the attention to social distancing in parks etc. the virus is still more likely to be spread in the same venues or at least indoors, rather than in the open air.

This recent letter to the Lancet by a consultant from my own hospital St Bart's, in collaboration with UCL and Queen Mary College, shows that infection amongst health care workers is more likely to reflect general community transmission than exposure within hospitals.

Professor Moon concludes "our research indicates that in the past 2-3 weeks in our wards and intensive care units, rates of staff infection have fallen so much that it is unlikely that staff are being infected by patients". The low level of infection amongst healthcare workers (HCWs) should reassure patients and visitors that as the pandemic recedes, infection from HCWs without symptoms is unlikely to present a major risk. The rate of asymptomatic infection amongst hospital staff fell from 7% to 1% after the UK-wide lockdown was introduced, in line with the general London population.

The authors collected samples from 400 staff at St Bart's Hospital displaying no coronavirus symptoms. Blood tests and nasal swabs were taken at weekly intervals. The authors suggest that routine screening of all without symptoms may not be necessary whilst infection rates in the general population are falling. If they begin to rise again, regular testing of HCW's irrespective of symptoms should be considered to protect these key workers and their patients.

There were today 10 May, 178 deaths in the UK of COVID-19 with 26 of them in London. The deaths in London have been overtaken by those in the North West (44), Midlands (28) and North East and Yorkshire (32).

### **COVID-19 virus mutation (or not) is a hot topic**

There have been a number of papers published on the topic of mutation in COVID-19. Two of them reached the attention of journalists. I stayed with my previous assessment that compared to some the RNA viruses, like influenza and HIV, for example, this new respiratory virus comes from a family of coronaviruses where the genetic rule is more stability and recombination and not mutation.

To my knowledge the first human coronavirus studied, OC43 has not mutated significantly despite spreading around the world for each of the last 60 years! But writers are keen on the topic and it is strongly linked to science fiction films and books. Scientifically mutations of influenza lead to the virus circumventing vaccine. But the topic is complex and scientists, like everyone else, can be over enthusiastic about their own data. I feel this has happened with an unpublished article purporting to have detected mutations in COVID-19 associated with virulence. Gene experts are pouring cold water on the article and now I point here to a fully published and hence peer reviewed paper from the MRC group at the University of Glasgow.

The title gives the positioning of their data "No evidence for distinct types in the evolution of SARS-Cov-2". The paper is by O. Maclean *et al* in the journal "[Virus Evolution](#)". The authors set the scene by comparing the article by Tang *et al* (the unpublished paper) who claimed that two major virus types had evolved, one being "more aggressive". Maclean *et al* how assert that these major conclusions "cannot be substantiated" and feel that the data has been "over interpreted". Tang *et al* claimed that two major types (L and S) are present and that the L type evolved from the S type. Thus, the S type could be called "ancestral". Maclean *et al* however notes that one non-synonymous substitution cannot be used to define a "type". In fact, since 9 April there have been 2,334 such substitutions



catalogued! Importantly, there is no evidence that any of these point mutations are involved in virus function and transmission. Maclean *et al* note that the claim is not substantial and, moreover, is irresponsible. One would need experimental data.

### **Is COVID-19 and ICU ventilator shortage our generation's equivalent of the polio epidemics of the 1950's?**

A clinician at St Thomas's Hospital, who helped care for the Prime Minister, noted some similarities of the present pandemic with the epidemics of polio in the 1950's. Indeed, from a virologic perspective there are some connections.

Firstly, the vulnerable groups in the community in the 1940's and 1950's in western "high-hygiene" countries were young children and adults. The rest of the world experienced what was known as the "Cairo model" of polio where lack of safe water allowed very wide spread of the virus.

When the annual epidemic started in the USA, there was speculation about the virus being spread by flies, however when laboratories could culture the virus on monkey kidney cells in the laboratory, it soon became apparent that it was spread from person to person mainly by the faecal-oral route. There was also limited person to person spread in families from throat fluids. The virus was detected in rivers and in the sea during the summer months.

The main scientific push was to make two vaccines, the Salk (formalin inactivated whole virus) and Sabin (live attenuated virus) named after their inventors. As late as the 90's, Dr Salk would be recognized in restaurants and on planes and would raise applause, as I personally experienced in Washington when I was invited by him to dinner. The Americans, at the time, raised money for vaccines generously via the 'March of Dimes' charity. Everyone would give a 'dime' on their birthday. President Roosevelt had been a victim of childhood polio and needed crutches to walk as an adult but very few photos were allowed to be taken of him incapacitated.

And the relationships to COVID-19? The photos of that era from the USA were of very large hospital wards full of children and youngsters in "iron lungs". These huge machines completely enveloped the supine patient and took over muscular function of the respiratory tract as the nerve cells had been destroyed by the virus.

A clinician of that time recently asked me "what is the noise of influenza?" He meant in the wards but, of course, children do not normally die or develop pneumonia from epidemics of flu (with 2009 as an exception) or pandemic influenza. He said that there were two sounds in the polio wards, the hissing of the electric pumps on the 'iron lungs' and the crying of frightened children. Nearly half of the children confined to iron lungs died.

To return to COVID-19, but now to elderly patients in the ICU's of the world, fatalities can reach 50% as well. In the UK iron lungs were rather expensive for the still developing NHS. Lord Rootes whose motor car empire in Oxford included the famous Morris Minor car, promised "an artificial lung" for every hospital in the British Commonwealth. These small, light-weight, wooden units were powered by converted electric starter motors from his cars.

Finally, as another warning to come to us from the 20<sup>th</sup> century, the job of the nurses and doctors in the polio ward was frightening and hospital staff undoubtedly contracted the virus in the hospital itself. Many years later a medical student at the time told me his greatest fear was to be allotted a session on the polio ward. But then, as now, off he went to do his duty!

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