http://bit.ly/2U1rM2j

Ancient mantis-man petroglyph discovered in Iran

A unique rock carving found in the Teymareh rock art site (Khomein county) in Central Iran with six limbs has been described as part man, part mantis.

Rock carvings, or petroglyphs, of invertebrate animals are rare, so entomologists teamed up with archaeologists to try and identify the motif. They compared the carving with others around the world and with the local six-legged creatures which its prehistoric artists could have encountered.

The 'squatter mantis man' petroglyph next to a 10 cm scale bar. **Credit: Dr. Mohammad Naserifard**

Entomologists Mahmood Kolnegari, Islamic Azad University of Arak, Iran; Mandana Hazrati, Avaye Dornaye Khakestari Institute, Iran; and Matan Shelomi, National Taiwan University teamed up with freelance archaeologist and rock art expert Mohammad Naserifard and describe the petroglyph in a new paper published in the open access *Journal of Orthoptera Research*.

The 14-centimetre carving was first spotted during surveys between 2017 and 2018, but could not be identified due to its unusual shape. The six limbs suggest an insect, while the triangular head with big eyes and the grasping forearms are unmistakably those of a praying mantid, a predatory insect that hunts and captures prey like flies, bees and even small birds. An extension on its head even helps narrow the identification to a particular genus of mantids in this region: Empusa.

Even more mysterious are the middle limbs, which end in loops or circles. The closest parallel to this in archaeology is the 'Squatter Man,' a petroglyph figure found around the world depicting a person flanked by circles. While they could represent a person holding circular objects, an alternative hypothesis is that the circles represent auroras caused by atmospheric plasma discharges.

It is presently impossible to tell exactly how old the petroglyphs are, because sanctions on Iran prohibit the use of radioactive materials needed for radiocarbon dating. However, experts Jan Brouwer and Gus van Veen examined the Teymareh site and estimated the carvings were made 40,000-4,000 years ago.

A praying mantis, Empusa hedenborgii, which may have inspired the petroglyph, according to the research team. **Mr Mahmood Kolnegari**

One can only guess why prehistoric people felt the need to carve a mantis-man into rock, but the petroglyph suggests humans have linked mantids to the supernatural since ancient times. As stated by the authors, the carving bears witness, "that in prehistory, almost as today, praying mantids were animals of mysticism and appreciation."

Original source: *Kolnegari M, Naserifard M, Hazrati M, Shelomi M (2020) Squatting (squatter) mantis man: A prehistoric praying mantis petroglyph in Iran.* Journal of Orthoptera Research *29(1): 41-44. https://doi.org/10.3897/jor.29.39400*

http://bit.ly/2U2Uik5

Johns Hopkins Experts Are Trying a Clever Antibody Method From The 1890s on COVID-19

Viral antibodies, in the blood serum of patients who have recovered could be injected into other people

Peter Dockrill

Blood from recovered coronavirus patients could be used in a vital stop-gap treatment to help protect humanity from the COVID–19 pandemic currently spreading around the world, researchers propose.

In a new paper, infectious disease experts explain how viral antibodies, contained in the blood serum of patients who have already recovered from the new coronavirus, could then be injected into other people, offering them short-term protection.

This long-established medical remedy – called passive antibody therapy – dates back to the late 19th century, and was widely used during the 20th century to help stem outbreaks of measles, polio, mumps, and influenza.

Much as it aided us before, it could be a crucial and practical tool now in the fight against COVID–19, a team from Johns Hopkins University argues in the new study, adding that antibody therapies can also be made available with urgency. "Deployment of this option requires no research or development," says immunologist Arturo Casadevall. "It could be deployed within a couple of weeks since it relies on standard blood-banking practices."

For the treatment to work, recovered coronavirus patients would need to donate their blood after recovering from COVID–19 and while still convalescing from the disease. During this phase, the blood serum would contain high amounts of natural antibodies produced to combat the SARS-CoV–2 virus.

Once the body produces them in response to pathogens, such antibodies can remain circulating in the blood for months and even years after an infection.

But these antibodies aren't just useful for the recovered individual. If we extract and process them, antibodies can be injected into other people to provide a short-term benefit; this could be used for patients at serious risk, uninfected family members of an infected patient, or to bolster the immunity of medical workers at greater exposure to the pathogen.

"Passive antibody administration is the only means of providing immediate immunity to susceptible persons," the researchers explain in their paper. "Depending on the antibody amount and composition, the protection conferred by the transferred immunoglobulin can last from weeks to months."

Using modern blood banking techniques – which can screen for other kinds of infectious agents that might be contained in blood – the therapy is arguably low risk for healthy people, the researchers say, especially in comparison to the threats inherent in the COVID–19 outbreak, for which there are no vaccines or drugs currently available.

Against that backdrop, the team proposes that the use of convalescent sera should be considered as an emergency response to help protect against COVID–19, just as it was trialled against other coronavirus diseases of this century, including SARS1 and MERS.

Of course, COVID–19, being a pandemic, is on a much larger scale to those smaller outbreaks – but that sad reality will actually help the making of convalescent sera supplies, as there will be a much greater number of recovered coronavirus patients who could supply their blood.

At time of writing, over 77,000 people have already recovered from COVID–19, according to John Hopkins University's latest statistics on the outbreak (which are updated frequently); their blood could readily help make vital antibodies for others, whereas other sorts of antiviral treatments and a much-hoped-for vaccine are expected to take considerably longer to develop.

"In addition to public health containment and mitigation protocols, this may be our only near-term option for treating and preventing COVID–19, and it is something we can start putting into place in the next few weeks and months," Casadevall says.

To that end, John Hopkins University is funding efforts to begin setting up antibody therapy operations for COVID–19 in the Baltimore area in the coming weeks. Doctors in New York are also investigating the treatment, Casadevall says, while internationally,

Japan's largest pharmaceutical company is looking at developing an antibody-based drug to combat coronavirus. There are still a lot of unknowns, including how much convalescent serum is needed to be effective to protect people, but early, unconfirmed media reports from China suggest this therapy is already working there.

Nobody is expecting passive antibody therapy to become a silver bullet for the new coronavirus, but as something that could help us flatten the curve while other treatments are developed, it could make a huge difference, if we all act together – and act quickly. "Clearly, the use of convalescent serum would be a stopgap measure that could be used in the midst of the current epidemic," the authors write.

"However, even local deployment will entail considerable coordination between different entities... Hence, as we are in the midst of a worldwide pandemic, we recommend that institutions consider the emergency use of convalescent sera and begin preparations as soon as possible. Time is of the essence."

The findings are reported in *The Journal of Clinical Investigation*.

http://bit.ly/2J2vC4Q

Parkinson's disease linked to gene targeted by blue-green algae toxin

Scientists have discovered a possible link between Parkinson's disease and a gene impacted by a neurotoxin found in blue-green algae.

University of Queensland scientist Dr Jacob Gratten said the findings increased the understanding of the environmental risk factors of Parkinson's disease. "We looked for a link between Parkinson's and changes in the human genome that control how genes are turned on and off, because these changes can be influenced by the environment," Dr Gratten said.

"We found a gene, previously not known to be linked to Parkinson's, which displayed reduced activity in people with the disease. "This same gene is known to be targeted by a blue-green algae neurotoxin." Blue-green algae is found in inland waterways and poses a health risk to people, domestic animals and stock that come into contact with the toxic algal blooms.

The research team at MRI-UQ made the discovery in collaboration with Professor George Mellick at Griffith University and colleagues from New South Wales and New Zealand. Their findings are the culmination of more than a decade of scientific effort.

Neurotoxins released by blue-green algae reduce activity of the gene identified in the study. Researchers predict this will lead to higher oxidative stress levels in nerve cells associated with Parkinson's disease, which can lead to cell death.

Dr Gratten said that while the study does not provide a direct link with Parkinson's, blue-green algae had previously been associated with other neurodegenerative diseases such as motor neurone disease. "This gives us confidence that we're moving in the right direction towards understanding the environmental causes of Parkinson's disease," Dr Gratten said.

UQ geneticist Professor Peter Visscher, from the the Institute for Molecular Bioscience, who co-led the study, said Parkinson's disease affects 1 in 100 people over 60-years-old and that figure is projected to double by 2040 as the population ages.

"This disease destroys lives and devastates families, so we're determined to unlock the mystery behind Parkinson's," Professor Visscher said. "More work is needed to confirm our findings, and to explore other possible explanations for the link between this gene and Parkinson's disease, such as pesticides."

The research is a collaboration between researchers from the Brain and Mind Centre, University of Sydney, University of Otago, New Zealand Brain Research Institute and the University of Canterbury, New Zealand.

This study was published in Nature Communications *(DOI: 10.1038/s41467-020-15065-7)*.

http://bit.ly/2wcWn46

Newly discovered ‘magic methyl’ reaction could turbocharge the potency of some drugs

A new catalyst replaces a hydrogen atom with a methyl group, which can dramatically increase a drug’s potency.

By Robert F. Service

For years, drug discovery chemists have struggled to streamline a process that can boost a drug’s potency up to 2000-fold: “magic methylation.” The reaction sweeps out single hydrogen atoms and replaces them with methyl groups—reshaping the drug molecule to more easily interact with its biological targets. But carrying out this sleight of hand is so difficult that few researchers even try. Now, a team of chemists reports it has created a new catalyst that performs this delicate exchange with ease on a wide variety of druglike molecules, an advance that could lead to novel treatments for everything from cancer to infectious diseases.

“This paper is just stunning,” says Tim Cernak, an organic chemist at the University of Michigan, Ann Arbor, who was not involved in the research. The new catalyst manages the reaction in one easy step—a huge improvement on previous multistep methods that were expensive and time-consuming. “This is the wish [of] every drug hunter,” Cernak says. “It really is a dream reaction.”

To understand the dream, it helps to know one way chemists build drug molecules, explains M. Christina White, an organic chemist at the University of Illinois, Urbana-Champaign. Most drug molecules contain a skeleton of carbon atoms shaped as a rod or a ring, with multiple hydrogen atoms hanging off each carbon. Chemists act as molecular surgeons, cutting out specific carbon or hydrogen atoms and replacing them with oxygen or nitrogen atoms. If researchers want to add a magic methyl group (which consists of one carbon atom bonded to three hydrogen atoms), they often have to start over, building a new skeleton from scratch.

White wanted to find a way to add a methyl group at the end of the drug building process. To do that, she needed to surgically snip one carbon-hydrogen (C-H) bond at a time, without cleaving the other dozen or more C-H bonds in the molecule. Adding further difficulty, C-H bonds are among the strongest in organic molecules, which makes it harder to target just one bond without affecting others, White says.

Nature builds and reshapes molecules “in a totally different way,” White says. Chemical changes are made using large, complex enzymes that grasp hydrocarbon scaffolds so that just one C-H bond nuzzles up to the enzyme’s catalytic site—the point at which a reaction takes place. However, each enzyme typically works with only one specific molecule. “If I want to work on a different molecule, I need a new enzyme,” White says. “We want [a reagent that is] just as selective, but general.”

In an effort to find just such a catalyst, White and then–graduate student Mark Chen in 2007 devised a snowflake-shaped compound with an iron atom at its center that added oxygen atoms to desired spots in druglike molecules. The catalyst could work as selectively as an enzyme. But it simply didn’t work on a lot of molecular structures or when it was next to a nitrogen atom, which are common in drug molecules.

But White’s team kept at it. In 2015, she and her colleagues devised a set of conditions that allowed the iron catalyst and a variant to add oxygen atoms to druglike molecules. And in 2019, they created a similar manganese-based catalyst that performed the oxygen-for-hydrogen swap on druglike molecules containing nitrogen and other common add-ons.

But that was just the first step. Now, White’s team reports it has come up with chemical additives that help this latest catalyst complete the “magic methyl” process. After replacing a hydrogen with an oxygen, it steals a methyl group from a reagent known as

trimethylaluminum and inserts it in oxygen's place. White's team carried out this molecular surgery on 41 different hydrocarbons, including 16 common druglike scaffolds, the researchers report today in *Nature*.

The upshot, White says, is that this reagent will now make it simple and cheap for drug hunters to insert "magic methyl" groups into their molecules. "We hope a lot more drugs with the magic methyl effect will be discovered," White says.

This could help "across the board" in drug discovery, says David Rees, chief scientific officer of Astex Pharmaceuticals. Where adding a methyl group does increase a drug's potency, doctors may be able to give their patients less of a drug. That could improve safety and reduce side effects. Among the drugmakers he knows, Rees says, "Everyone will jump on this."

http://bit.ly/3dcRAA7

New study reveals early evolution of cortex

Pushing the birth of the cortex back in time by some 300 million years to over 500 million years ago

Research on the lamprey brain has enabled researchers at Karolinska Institutet in Sweden to push the birth of the cortex back in time by some 300 million years to over 500 million years ago, providing new insights into brain evolution. Their study is published in the scientific journal *Nature Ecology & Evolution*.

The human brain is one of the most complex structures that evolution has created. It has long been believed that most of the forebrain evolution took place largely in mammals, and that the brains of simpler, pre-mammalian animal groups such as fish and amphibians lack a functional cortex. The cortex, which is the outer layer of the brain, controls the more complex cerebral functions like vision and movement and higher skills such as language, memory and emotion.

"We've spent a long time studying brain evolution using the lamprey, which is one of the oldest groups of extant vertebrates," says Sten Grillner, last author of the study and professor of neurophysiology at the Department of Neuroscience, Karolinska Institutet. "Here, we've made detailed studies of the lamprey brain, combining neurophysiological analyses with histochemical techniques."

In the study, the researchers show that even the lamprey, which existed hundreds of millions of years before mammals, possesses a detailed blueprint for the development of the cortex, the basal ganglia and the dopamine system—all the vital ingredients of integrative cerebral function.

The researchers also found that the lamprey's cortex has a visual area on which different parts of its visual field are represented. Sensory and motor areas have also been discovered.

"This shows that the birth of the cortex has to be pushed back about 300 million years," says Professor Grillner. "This, in turn, means that the basic plan of the human brain was defined already over 500 million years ago, that's to say before the lamprey branched off from the evolutionary line that led to mammals and humans."

The study shows that all the main components of the human brain are also to be found in the lamprey brain, albeit with much fewer nerve cells in each part.

"That vital parts of the lamprey brain are conserved and organised in the same way as in the human brain was unexpected," he continues. "These findings are crucial to our understanding of how the brain evolved and how it has been designed through evolution."

More information: *The evolutionary origin of visual and somatosensory representation in the vertebrate pallium, Nature Ecology & Evolution (2020). DOI: 10.1038/s41559-020-1137-2 , https://nature.com/articles/s41559-020-1137-2*

https://bit.ly/2U5MJcv

New Evidence Shows How COVID-19 Has Affected Global Air Pollution

It's very likely that the lives saved locally from the reduction in pollution exceed COVID-19 deaths in China

Jacinta Bowler

The COVID-19 pandemic is getting more overwhelming by the day, with increasing lockdowns, a death toll of more than 7,000 people across the world, and a direct hit to the global economy. But if there's a sliver of good news, it's about how the spread of the new coronavirus has been decreasing air pollution, and possibly even saving lives in the process. Back on March 8, Stanford University environmental resource economist Marshall Burke did some back-of-the-envelope calculations about the recent air pollution drop over parts of China and potential lives saved, posting it on a global food, environment and economic dynamics blog, G-FEED.

The situation has continued to unfold since then, so those numbers won't stay current for long; but according to Burke, even conservatively, it's very likely that the lives saved locally from the reduction in pollution exceed COVID-19 deaths in China.

"Given the huge amount of evidence that breathing dirty air contributes heavily to premature mortality, a natural - if admittedly strange - question is whether the lives saved from this reduction in pollution caused by economic disruption from COVID-19 exceeds the death toll from the virus itself," Burke writes. "Even under very conservative assumptions, I think the answer is a clear 'yes'."

The two months of pollution reduction, Burke calculates, has probably saved the lives of 4,000 children under 5 and 73,000 adults over 70 in China. That's significantly more than the current global death toll from the virus itself.

Although this might seem a little surprising, it's something we've known about for quite a long time. Earlier this month, research suggested that air pollution costs us three years, on average, off our global life expectancy.

"It is remarkable that both the number of deaths and the loss in life expectancy from air pollution rival the effect of tobacco smoking and are much higher than other causes of death," physicist Jos Lelieveld from the Cyprus Institute in Nicosia stated at the time.

"Air pollution exceeds malaria as a global cause of premature death by a factor of 19; it exceeds violence by a factor of 16, HIV/AIDS by a factor of 9, alcohol by a factor of 45, and drug abuse by a factor of 60."

So, it's well established that air pollution really does kill.

But Burke's analysis was just using data from China, and was completed before there was more information about how COVID-19 has affected the rest of the world.

With the second largest number of cases occurring in Italy, and the country putting in place strict quarantine measures, satellite data over northern Italy have now shown a large drop in air pollution - specifically nitrogen dioxide, a gas mainly emitted by cars, trucks, power plants and some industrial plants.

Using the Tropomi instrument on the Copernicus Sentinel-5P satellite, images taken from 1 January to 11 March 2020 showed nitrogen dioxide dropping dramatically.

You can see that happening in the video below:

"The decline in nitrogen dioxide emissions over the Po Valley in northern Italy is particularly evident," explains Claus Zehner, ESA's Copernicus Sentinel-5P mission manager.

"Although there could be slight variations in the data due to cloud cover and changing weather, we are very confident that the reduction in emissions that we can see, coincides with the lock-down in Italy causing less traffic and industrial activities."

For now, we don't have peer-reviewed studies measuring the true health impact reduced emissions will bring, but given what we

know about the dangers of widespread air pollution, it's likely that there will be a direct benefit in the shape of fewer pollution-related deaths.

Even such a tiny silver lining can hardly make up for the devastation of the COVID-19 pandemic. But these preliminary numbers demonstrate that this global health disaster is an opportunity to assess - which aspects of modern life are absolutely necessary, and what positive changes might be possible if we change our habits on a global scale.

https://wb.md/33z2xaN

Coronavirus Stays in Aerosols for Hours, on Surfaces for Days

The novel coronavirus, SARS-CoV-2, remains viable in aerosols for hours and on surfaces for days, according to a new study.

Ricki Lewis, PhD

The data indicate that the stability of the new virus is similar to that of SARS-CoV-1, which caused the SARS epidemic, researchers report in an article published on the medRxivpreprint server. (A version of the article has been published online by the *New England Journal of Medicine*.)

Transmission of SARS-CoV-2, which causes COVID-19, has quickly outstripped the pace of the 2003 SARS epidemic. "Superspread" of the earlier disease arose from infection during medical procedures, in which a single infected individual seeded many secondary cases. In contrast, the novel coronavirus appears to be spread more through human-to-human transmission in a variety of settings. However, it's not yet known the extent to which asymptomatic or presymptomatic individuals spread the new virus through daily routine.

To investigate how long SARS-CoV-2 remains infective in the environment, Neeltje van Doremalen, PhD, of the Laboratory of Virology, Division of Intramural Research, National Institute of Allergy and Infectious Diseases, in Hamilton, Montana, and colleagues conducted simulation experiments in which they compared the viability of SARS-CoV-2 with that of SARS-CoV-1 in aerosols and on surfaces.

Among patients infected with SARS-CoV-2, viral loads in the upper respiratory tract are high; as a consequence, respiratory secretion in the form of aerosols (<5 µm) or droplets (>5 µm) is likely, the authors note.

van Doremalen and colleagues used nebulizers to generate aerosols. Samples of SARS-CoV-1 and SARS-CoV-2 were collecting at 0, 30, 60, 120, and 180 minutes on a gelatin filter. The researchers then tested the infectivity of the viruses on Vero cells grown in culture.

They found that SARS-CoV-2 was largely stable through the full 180-minute test, with only a slight decline at 3 hours. This time course is similar to that of SARS-CoV-1; both viruses have a median half-life in aerosols of 2.7 hours (range, 1.65 hr for SARS-CoV-1, vs 7.24 hr for SARS-CoV-2).

The researchers then tested the viruses on a variety of surfaces for up to 7 days, using humidty values and temperatures designed to mimic "a variety of household and hospital situations." The volumes of viral exposures that the team used were consistent with amounts found in the human upper and lower respiratory tracts.

For example, they applied 50 µL of virus-containing solution to a piece of cardboard and then swabbed the surface, at different times, with an additional 1 µL of medium. Each surface assay was replicated three times.

The novel coronavirus was most stable on plastic and stainless steel, with some virus remaining viable up to 72 hours. However,

by that time the viral load had fallen by about three orders of magnitude, indicating exponential decay. This profile was remarkably similar to that of SARS-CoV-1, according to the authors.

However, the two viruses differed in staying power on copper and cardboard. No viable SARS-CoV-2 was detectable on copper after 4 hours or on cardboard after 24 hours. In contrast, SARS-CoV-1 was not viable beyond 8 hours for either copper or cardboard.

Table. Median Half-Life on Surfaces

Surface	SARS-CoV-2 (hr)	SARS-CoV-1 (hr)
Copper	3.4	3.76
Cardboard	8.45	1.74
Steel	13.1	9.77
Plastic	15.9	17.7

"Taken together, our results indicate that aerosol and fomite transmission of HCoV-19 [SARS-CoV-2] are plausible, as the virus can remain viable in aerosols for multiple hours and on surfaces up to days," the authors conclude.

Andrew Pekosz, PhD, codirector of the Center of Excellence in Influenza Research and Surveillance and director of the Center for Emerging Viruses and Infectious Diseases at the Johns Hopkins Center for Global Health, Baltimore, Maryland, applauds the real-world value of the experiments.

"The PCR [polymerase chain reaction] test used [in other studies] to detect SARS-CoV-2 just detects the virus genome. It doesn't tell you if the virus was still infectious, or 'viable.' That's why this study is interesting," Pekosz said. "It focuses on infectious virus, which is the virus that has the potential to transmit and infect another person. What we don't know yet is how much infectious (viable) virus is needed to initiate infection in another person."

He suggests that further investigations evaluate other types of environmental surfaces, including lacquered wood that is made into desks and ceramic tiles found in bathrooms and kitchens.

One limitation of the study is that the data for experiments on cardboard were more variable than the data for other surfaces tested.

Editor's note: Find the latest COVID-19 news and guidance in Medscape's Coronavirus Resource Center.

The investigators and Pekosz have disclosed no relevant financial relationships.

MedRxiv. Published online March 13, 2020. Abstract

https://bit.ly/33xRmzb

Common anti-parasite treatments used on cattle have devastating impacts on wildlife

Experts have stressed an urgent need to find alternatives to wormers and anti-ectoparasitic products used widely on cattle

Experts have stressed an urgent need to find alternatives to wormers and anti-ectoparasitic products used widely on cattle, following the findings of a study just published in Environmental Toxicology and Chemistry.

Researchers from the University of Sussex looked at a body of published evidence into the environmental impact of anthelmintics -- products used as wormers and anti-parasitic agents and widely applied across the world. They found that, across all drug classes, the products were having a devastating impact on dung beetles - species that are vital prey items for a range of bat and bird species.

The study conducted by Domhnall Finch and Professor Fiona Mathews also found that some of the products actively attracted adult dung beetles, before impairing the development of their larvae.

Fiona Mathews, Professor of Environmental Biology at the University of Sussex, said: "When compared with controls, we found that dung samples from cattle treated with these products had about a third fewer dung beetle larvae.

"What's particularly worrying is that the beetles actually seemed to be more attracted to treated dung but, because of the toxicity of the chemicals, their larvae have poor survival rates and face impaired

development. "Over time, this reduces the number of dung beetles which is troubling news for a range of bird and bat species - for which dung beetles are key prey items. "Many of these species are already listed as vulnerable so any decline in prey availability is a serious concern."

Dung beetles are commonly preyed upon by the serotine bat, noted as Vulnerable to Extinction on the new British Red List; the greater horseshoe bat, protected under European Law because of its perilous conservation status right across Europe; and the Nightjar and the Chough, both of which are protected by the Wildlife and Countryside Act 1981. The Nightjar has been given an amber UK conservation status.

The study, published in the journal Environmental Toxicology and Chemistry, highlighted the particularly negative impact on dung beetle larvae of pour-on treatments - the most common form of application. It also revealed that one of the most widely used products, the anti-parasitic agent Ivermectin, is extremely toxic. These treatments are available for purchase in most EU countries without the involvement of a veterinarian. But the authors stress that more research is needed into the other treatment types and newer drugs in order to determine the exact effects of each.

The results are particularly timely as they come just a few months after the government announced that it would not be funding extensions to higher-tier organic stewardship agreements in England. This means that farms who currently avoid the use of insecticides will be faced with a difficult choice moving forward.

Prof. Mathews explained: "Many farmers are now facing a gap in their income as they have to make new applications. Sticking to an insecticide-free approach may not be economically attractive compared with switching to conventional systems where the routine use of anti-parasitic agents is normal. Once applied, the residues can remain in the soil -- affecting a wide range of invertebrates -- for months."

"Some of these farms are also critical for British wildlife, particularly rare bats, and the introduction of chemicals could really impact their numbers - as demonstrated in our study."

Dung beetles themselves provide important ecosystem services for farmers. By ensuring that dung is cleared from pasture quickly, they help to control pest flies and also allow for rapid grass regrowth through nutrient cycling, soil aeration and dung removal. The presence of dung beetles has also been shown to reduce the prevalence of cattle nematode infections by 55 to 89% (Fincher 1975) and pest flies by 58% (Benyon et al. 2015). In the UK alone, these services are estimated to exceed £350M per year.

Domhnall Finch, doctoral student at the University of Sussex, said: "Dung beetles are an overlooked but hugely important part of our landscape. "Studies have proven that they can help to reduce the prevalence of worm infections in cattle, which is ironic when we consider that they're now under threat from chemical products which essentially do the same thing.

"While more research is needed to determine the effects of newer agents, our work has clearly shown that those chemicals which are present in pour-on treatments have a long-lasting negative impact.

"There is an urgent need to find alternatives."

https://s.nikkei.com/2QoF32C

China says Japan-developed drug Avigan works against coronavirus

Positive reception by Chinese government contrasts with reservations in Japan

Shin Watanabe, Michelle Chan, and Wataru Suzuki, Nikkei staff writers

Dalian, China/Hong Kong/Tokyo -- An influenza medicine developed by a Fujifilm Holdings group company is effective against the new coronavirus, the Chinese government said on Tuesday.

Beijing has already begun recommending the drug favipiravir, developed by Fujifilm Toyama Chemical and sold under the brand name Avigan. "It is very safe and clearly effective," said Zhang Xinmin, director of the science ministry's China National Center for Biotechnology Development, in a news conference.

Fujifilm Toyama developed the drug in 2014. It has been administered to coronavirus patients in Japan since February.

On Wednesday, shares in Fujifilm shot up 15.4% in Tokyo in the afternoon session. Morning trade in the stock was suspended after a glut of buy orders following Beijing's announcement.

Clinical trials were conducted on 200 patients at hospitals in Wuhan and Shenzhen. Results showed that patients who received the drug tested negative in a comparatively short time, while pneumonia symptoms were markedly reduced.

Patients taking favipiravir tested negative after a median of four days, compared to 11 days in the control group, according to Zhang. There were no clear side effects, he added.

Another clinical trial in Wuhan revealed that patients treated with favipiravir recovered from fever in 2.5 days on average, versus 4.2 days for other patients. Coughing symptoms also improved within 4.6 days -- about 1.4 days earlier than those who did not take the drug. Only 8.2% of the patients taking favipiravir needed respiratory aids, whereas 17.1% of the patients in the control group were put on devices.

The positive reception in China contrasts with reservations over Avigan in Japan, where the drug obtained regulatory approval in 2014 on condition that it would only be used if the government decided to fight new or re-emerging influenza viruses. Studies found that the drug may cause fetal deaths or deformities, and can be transferred in semen.

South Korea's ministry of food and drug safety also decided not to import Avigan after infectious disease experts ruled that there was not enough clinical data to prove the drug's efficacy, the country's Yonhap news agency reported this week.

Despite Fujifilm's surging stock price, it is unclear how the company will benefit if Chinese companies begin to mass produce favipiravir. A Fujifilm spokesperson said the company is not involved in the Chinese clinical trials and is currently evaluating them.

Fujifilm signed a patent license agreement concerning Favipiravir with China's Zhejiang Hisun Pharmaceutical in 2016. But the spokesperson said the agreement was canceled last year, although the two parties are still in a "cooperative relationship."

The Chinese company said it received official approval to produce the drug in February and can ramp up output of a generic version.

Fujifilm's favipiravir patents are valid in Japan, but the substance patent in China expired last year, according to the spokesperson. This clears the way for Zhejiang Hisun to produce the generic version.

Fujifilm is providing Avigan to Japanese hospitals for clinical research and is also preparing to conduct its own clinical tests in Japan. Research in Japan began in March, with results not expected for several months.

Shares in Nichi-Iko Pharmaceutical were also up about 15% on Wednesday after the University of Tokyo announced that the company's Nafamostat drug blocks the coronavirus from entering human cells, effectively inhibiting infections.

Additional reporting by Jada Nagumo.

https://bit.ly/3bbGQA5

When fish gave us the finger: this ancient four-limbed fish reveals the origins of the human hand

When did fish evolve into tetrapods and crawl out of the water

John Long Richard Cloutier

One of the most significant events in the history of life was when fish evolved into tetrapods, crawling out of the water and eventually conquering land. The term tetrapod refers to four-limbed vertebrates, including humans.

Katrina Kenny, Author provided

To complete this transition, several anatomical changes were necessary. One of the most important was the evolution of hands and feet. Working with researchers from the University of Quebec, in 2010 we discovered the first complete specimen of *Elpistostege watsoni*. This tetrapod-like fish lived more than 380-million-years ago, and belonged to a group called elpistostegalians.

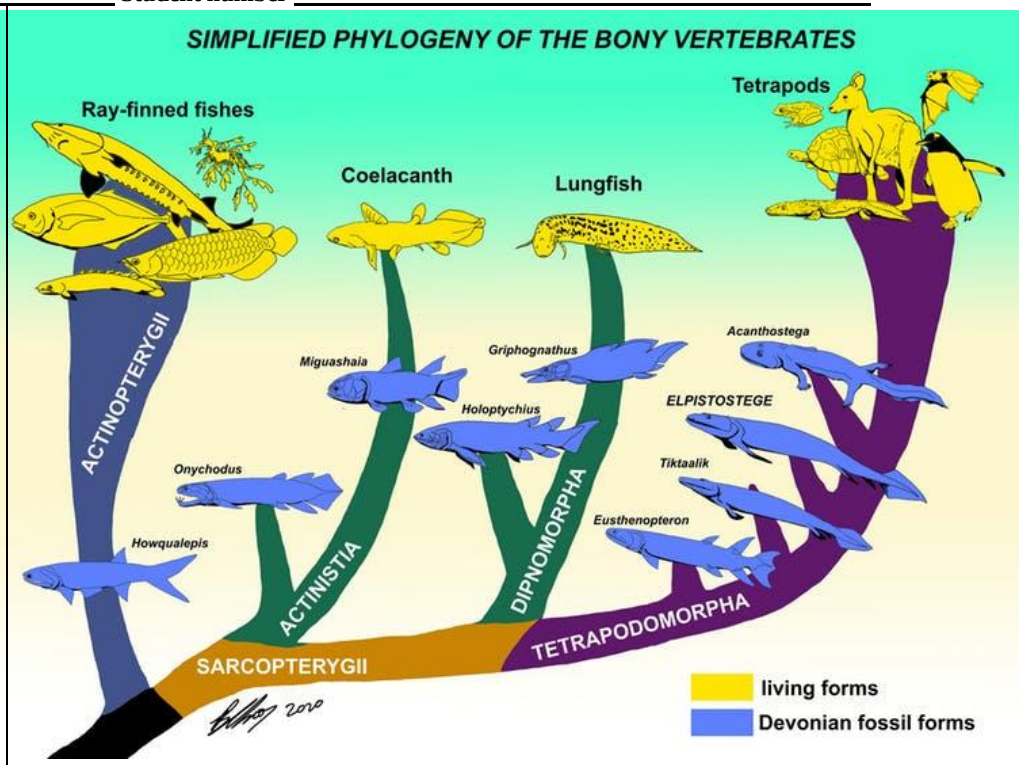
Our research based on this specimen, published today in Nature, suggests human hands likely evolved from the fins of this fish, which we'll refer to by its genus name, *Elpistostege*.

Elpistostegalians are an extinct group that displayed features of both lobe-finned fish and early tetrapods. They were likely involved in bridging the gap between prehistoric fish and animals capable of living on land. Thus, our latest finding offers valuable insight into the evolution of the vertebrate hand.

The best specimen we've ever found

To understand how fish fins became limbs (arms and legs with digits) through evolution, we studied the fossils of extinct lobe-finned fishes and early tetrapods. Lobe-fins include bony fishes (Osteichthyes) with robust fins, such as lungfishes and coelacanths.

Elpistostegalians lived between 393–359 million years ago, during the Middle and Upper Devonian times. Our finding of a complete 1.57m *Elpistostege* – uncovered from Miguasha National Park in Quebec, Canada – is the first instance of a complete skeleton of any elpistostegalian fish fossil.



Elpistostege, *from the Late Devonian period of Canada, is now considered the closest fish to tetrapods (four-limbed land animals), which includes humans.* Brian Choo

This animation shows what *Elpistostege* might have looked like when alive, and highlights the close similarities in its pectoral fin skeleton to the bones of our human arm and hand.

Prior to this, the most complete elpistostegalian specimen was a *Tiktaalik roseae* skeleton found in the Canadian Arctic in 2004, but it was missing the extreme-end part of its fin.

When fins became limbs

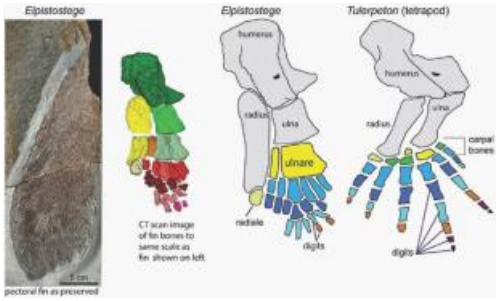
The origin of digits in land vertebrates is hotly debated.

The tiny bones in the tip of the pectoral fins of fishes such as *Elpistostege* are called "radial" bones. When radials form a series of rows, like digits, they are essentially the same as fingers in

tetrapods. The only difference is that, in these advanced fishes, the digits are still locked within the fin, and not yet free moving like human fingers.

Our recently uncovered *Elpistostege* specimen reveals the presence of a humerus (arm), radius and ulna (forearm), rows of carpal bones (wrist) and smaller bones organised in discrete rows.

We believe this is the first evidence of digit bones found in a fish fin with fin-rays (the bony rays that support the fin). This suggests the fingers of vertebrates, including of human hands, first evolved as rows of digit bones in the fins of *Elpistostegalian* fishes.



***The pectoral fin of* Elpistostege *shows the short rows of aligned digits in the fin - an intermediate stage between fishes and land animals such as the early tetrapod Tulerpeton.* Author provided**

What's the evolutionary advantage?

From an evolutionary perspective, rows of digit bones in prehistoric fish fins would have provided flexibility for the fin to more effectively bear weight.

***Our new specimen of* Elpistostege watsoni *measures 1.57 metres long from its snout to the tip of its tail.* Richard Cloutier, UQAR**

This could have been useful when *Elpistostege* was either plodding along in the shallows, or trying to move out of water onto land. Eventually, the increased use of such fins would have lead to the loss of fin-rays and the emergence of digits in rows, forming a larger surface area for the limb to grip the land surface.

Our specimen shows many features not known before, and will form the basis of a series of future papers describing in detail its skull, and other aspects of its body skeleton.

Elpistostege blurs the line between fish and vertebrates capable of living on land. It's not necessarily our ancestor, but it's now the closest example we have of a "transitional fossil", closing the gap between fish and tetrapods.

***The original finds of the* Elpistostege *skull roof (left) and front half of the skull. The new specimen confirms these all belong to the one species.* Richard Cloutier/UQAR**

The full picture

The first *Elpistostege* fossil, a skull fragment, was found in the late 1930s. It was thought to belong to an early amphibian. In the mid 1980s the front half of the skull was found, and was confirmed to be an advanced lobe-finned fish.

Our new, complete specimen was discovered in the fossil-rich cliffs of the Miguasha National Park, a UNESCO World Heritage site in Eastern Canada. Miguasha is considered one of the best sites to study fish fossils from the Devonian period (known as the "Age of Fish"), as it contains a very large number of lobe-finned fish fossils, in an exceptional state of preservation.

https://bit.ly/3940FIo

Oldest modern bird fossil looks like a duck from the back and a chicken from the front

New fossil has clear characteristics of modern land and waterfowl

By Gretchen Vogel

Go to a Cajun restaurant in New Orleans, and you might be offered a slice of turducken: a fancy dish of chicken stuffed inside of a duck stuffed into a turkey. Now, paleontologists have their own version: the oldest modern bird skull ever found, which predates the split between the duck lineage and that of both chickens and turkeys—and so has traits of all three.

"This is an incredibly informative specimen," says Amy Balanoff, a paleontologist at Johns Hopkins University, Baltimore, who wasn't involved in the work. Whereas the earliest birds, like the 150-million-year old *Archaeopteryx*, look very different from today's, the new fossil has clear characteristics of modern land and waterfowl, perhaps offering a glimpse of their common ancestor.

Duck? Chicken? This seagull-size Cretaceous shorebird had features of ducks, chickens, and turkeys. **Phillip Krzeminski**

Discovered near the Dutch town of Maastricht, in famous fossil beds that formed between 66.8 million and 66.7 million years ago, the turducken lived just before the mass extinction that killed off the dinosaurs. And because at least some of its descendants survived the cataclysm, "it gives us some clues about what characteristics were key in surviving that event," Balanoff says.

Luck and technology prompted the find, says Daniel Field, a paleontologist at the University of Cambridge, who led the work. John Jagt, a curator at the Maastricht Natural History Museum, had spotted "four very small blocks of rock with broken limb bones poking out" in the museum's collection, Field says. "It's hard to imagine a less exciting looking fossil."

Just the same, Field and his postdoctoral fellow Juan Benito put the rock into a computed tomography scanner, hoping the x-rays would reveal the structures inside. When they saw the scan, Field says, their shouts made the technician run back into the room. "She thought we had broken the machine."

The scan revealed a complete skull of what looked like a modern bird. The bones in the top and the back of the head closely resemble those of modern ducks, whereas the face and beak have unfused bones, as seen in today's chickens and turkeys. "You can play this game all day: 'Oh, it's a duck! No, it's a chicken!'" Field says.

Most of the bird's body is missing, but a piece of leg bone suggests it had long legs for its head size. Combined with the fact that the Maastricht deposits formed in a shallow sea, the fossil's proportions suggest it was a small shorebird, about the size of a modern seagull.

In a *Nature* paper this week, Field and his colleagues named the bird *Asteriornis maastrichtensis*, for Asteria, the Greek goddess of falling stars who turns herself into a quail. The falling stars nod to the asteroid impact and extinction that struck not long after the bird lived.

Some scientists had argued that modern birds evolved in the Southern Hemisphere because the oldest modern bird fossils found until now came from Antarctica. But the new* fossil is likely older than the Antarctic ones, arguing against that assumption.

The ability to look inside the intact rock was crucial to the discovery, Field says. The skull is less than 1 millimeter away from the femur, so "if we had started chipping away, we would have destroyed the skull." So was the team's willingness to gamble on an unassuming rock, he adds. "We have to be more hopeful in our collecting."

https://bit.ly/2vBBpvq

Scorpion venom shows promise for treating fetal alcohol spectrum disorder

Investigational drug reverses motor deficits in pre-clinical models, even administered one month after birth

Washington - A research team led by Children's National Hospital faculty was able to "rescue" a pre-clinical model of fetal alcohol spectrum disorder (FASD) in juvenile models, reversing motor skill deficits with the help of a novel drug derived from scorpion venom. The finding, in the *Nature Neuroscience*, could offer hope to an

estimated 119,000 children born with this condition worldwide each year.

FASD, caused by alcohol consumption during pregnancy, causes numerous learning disabilities, including cognitive and intellectual deficits. Motor skills problems can be an early indicator for these other issues, explains study leader Kazue Hashimoto-Torii, Ph.D., a principal investigator at the Center for Neuroscience Research at the Children's National Research Institute.

Many parents and caregivers first notice a problem when babies show delays in achieving motor developmental milestones. Although these effects are well documented, Hashimoto-Torii adds, it's been unclear what molecular mechanisms cause these deficits.

Hashimoto-Torii has been studying these effects ever since her postdoctoral training when, pregnant herself; she became interested in the consequences of environmental exposures on development. Over the past several years, she and colleagues have published a series of papers toward understanding FASD's molecular mechanisms.

In the most current paper, her team worked with a pre-clinical model of FASD in which gestating fetuses were exposed to alcohol at embryonic days 16 and 17, a period in which brain cells grow predominantly in the upper cortex, a brain region that plays a key role in motor abilities. This embryonic period corresponds to early mid-gestation in human fetuses.

When the researchers tested these pre-clinical models 30 days after birth--in two exams designed to assess both large-- and small-muscle motor skills--they showed significant deficits in both areas. Searching for the molecular differences that might underlie this diminished performance, the researchers found that prenatal alcohol exposure immediately activated a signaling pathway known as "heat shock," which causes cells to produce protective proteins. These heat shock proteins were produced randomly in some cells, rather than uniformly throughout the cell population.

Using a pre-clinical model that allowed them to track the descendants of these rapidly dividing neurons, the team found differences in the expression of 93 genes. One gene in particular, known as Kcnn2, which encodes a calcium-activated potassium channel, was over-expressed in the cells that produced heat shock proteins. This gene already has been implicated as playing an important role in learning and memory. Cells in which Kcnn2 was over-expressed showed abnormal firing patterns.

When the researchers administered a drug that blocks this channel, known as Tamapin and derived from Indian red scorpion venom, the affected cells' firing patterns reverted to normal. More importantly, pre-clinical models that received this drug at 30 days of life showed marked improvements in both large- and small-muscle motor skills.

The fact that the pre-clinical models could still show improvements long after the initial damage suggests that treatment for children with FASD with a similar agent might also be effective, says Hashimoto-Torii. To that end, she and colleagues have launched a biotech company to further investigate this drug to see if it might hold promise in humans.

"Usually investigators looking for the molecular mechanisms behind disease stop there, but we want to move forward to have a real impact on public health," she says. "We really want to give patients the hope of having a better life through treating the neurodevelopmental problems caused by FASD."

Other Children's National researchers who contributed to this study include Shahid Mohammad, Stephen J. Page, Li Wang, Seiji Ishii, Peijun Li, Toru Sasaki, Aiesha Basha, Zenaide Quezado, Joshua Corbin, and Masaaki Torii.

Funding for this study was provided by the Scott-Gentle Foundation

https://bit.ly/2WyKWOF

'Sushi parasites' have increased 283-fold in past 40 years

The next time you eat sashimi, nigiri or other forms of raw fish, consider doing a quick check for worms.

A new study led by the University of Washington finds dramatic increases in the abundance of a worm that can be transmitted to humans who eat raw or undercooked seafood. Its 283-fold increase in abundance since the 1970s could have implications for the health of humans and marine mammals, which both can inadvertently eat the worm.

Thousands of papers have looked at the abundance of this parasitic worm, known as Anisakis or "herring worm," in particular places and at particular times. But this is the first study to combine the results of those papers to investigate how the global abundance of these worms has changed through time. The findings were published March 19 in the journal Global Change Biology.

"This study harnesses the power of many studies together to show a global picture of change over a nearly four-decade period," said corresponding author Chelsea Wood, an assistant professor in the UW School of Aquatic and Fishery Sciences. "It's interesting because it shows how risks to both humans and marine mammals are changing over time. That's important to know from a public health standpoint, and for understanding what's going on with marine mammal populations that aren't thriving."

Despite their name, herring worms can be found in a variety of marine fish and squid species. When people eat live herring worms, the parasite can invade the intestinal wall and cause symptoms that mimic those of food poisoning, such as nausea, vomiting and diarrhea. In most cases, the worm dies after a few days and the symptoms disappear. This disease, called anisakiasis or anisakidosis, is rarely diagnosed because most people assume they merely suffered a bad case of food poisoning, Wood explained.

After the worms hatch in the ocean, they first infect small crustaceans, such as bottom-dwelling shrimp or copepods. When small fish eat the infected crustaceans, the worms then transfer to their bodies, and this continues as larger fish eat smaller infected fish.

Humans and marine mammals become infected when they eat a fish that contains worms. The worms can't reproduce or live for more than a few days in a human's intestine, but they can persist and reproduce in marine mammals.

Seafood processors and sushi chefs are well-practiced at spotting the worms in fish and picking them out before they reach customers in grocery stores, seafood markets or sushi bars, Wood explained. The worms can be up to 2 centimeters in length, or about the size of a U.S. 5-cent nickel. "At every stage of seafood processing and sushi preparation, people are good at finding worms and removing them from fish," Wood said.

Some worms can make it past these screening steps. Still, Wood -- who studies a range of marine parasites -- said she enjoys eating sushi regularly. For sushi consumers who remain concerned about these worms, she recommends cutting each piece in half and looking for worms before eating it.

For the analysis, the study's authors searched the published literature archived online for all mentions of Anisakis worms, as well as another parasitic worm called Pseudoterranova, or "cod worm." They whittled down the studies based on set criteria, ultimately keeping only those studies that presented estimates of the abundance of each worm in fish at a given point in time. While Anisakis worms increased 283-fold over the study period of 1978 to 2015, Pseudoterranova worms did not change in abundance.

Although the health risks of these marine worms are fairly low for humans, scientists think they may be having a big impact on marine mammals such as dolphins, whales and seals. The worms actually reproduce in the intestines of these animals and are released into the ocean via the marine mammals' feces. While scientists don't yet know the physiological impacts of these parasites on marine mammals, the parasites can live in the mammals' bodies for years, which could have detrimental effects, Wood said.

"One of the important implications of this study is that now we know there is this massive, rising health risk to marine mammals," Wood said. "It's not often considered that parasites might be the reason that some marine mammal populations are failing to bounce back. I hope this study encourages people to look at intestinal parasites as a potential cap on the population growth of endangered and threatened marine mammals."

The authors aren't sure what caused the large increase of Anisakis worms over the past several decades, but climate change, more nutrients from fertilizers and runoff, and an increase in marine mammal populations over the same period could all be potential reasons, they said.

Marine mammals have been protected under the Marine Mammal Protection Act since 1972, which has allowed many populations of seals, sea lions, whales and dolphins to grow. Because the worms reproduce inside marine mammals -- and their rise occurred over the same time period as the mammals' increase -- this is the most plausible hypothesis, Wood said.

"It's possible that the recovery of some marine mammal populations has allowed recovery of their Anisakis parasites." Wood said. "So, the increase in parasitic worms actually could be a good thing, a sign that the ecosystem is doing well. But, ironically, if one marine mammal population increases in response to protection and its Anisakis parasites profit from that increase, it could put other, more vulnearble marine mammal populations at risk of increased infection, and that could make it even more difficult for these endangered populations to recover."

Other co-authors are Evan Fiorenza, who completed the work as a UW graduate student; Catrin Wendt, a graduate student in the UW School of Aquatic and Fishery Sciences; Katie Dobkowski of Bates College; Teri King of Washington Sea Grant; Marguerite Pappaioanou and Peter Rabinowitz of the UW School of Public Health's Department of Environmental and Occupational Health Sciences; and Jameal Samhouri of NOAA's Northwest Fisheries Science Center.

This study was funded by Washington Sea Grant, the National Science Foundation, the Alfred P. Sloan Foundation and the University of Washington.

https://wb.md/39di8ho

Digestive Symptoms Tied to Worse COVID-19 Outcomes

Patients GI symptoms admitted to the hospital and diagnosed with COVID-19 more likely to have severe disease than patients without GI symptoms

Ricki Lewis, PhD

Patients with gastrointestinal (GI) symptoms who were admitted to the hospital and were diagnosed with COVID-19 were more likely to have severe disease than patients who did not have GI symptoms, according to findings published March 18 in the *American Journal of Gastroenterology*.

However, the unexpectedly large proportion is due in part to the inclusion of anorexia, said Brennan M. R. Spiegel, MD, MSHS, co–editor-in-chief of the *American Journal of Gastroenterology*.

"If you leave out anorexia, which is very nonspecific, the percentage of COVID-19 patients with GI symptoms is about 30%," *Spiegel told Medscape Medical News.*

Lei Pan, MD, PhD, of Binzhou Medical University Hospital in Binzhou, China, and colleagues in the Wuhan Medical Treatment Expert Group conducted a descriptive, cross-sectional, multicenter study on 204 patients who had polymerase chain reaction–confirmed COVID-19 at three hospitals in Hubei province from

January 18, 2020, to February 28, 2020. The team considered clinical characteristics, laboratory data, and treatment.

Ninety-nine patients (48.5%) presented to the hospital with digestive symptoms as their chief complaint. Most of these patients did not have underlying digestive diseases. Their symptoms included anorexia (83.8%), diarrhea (29.3%), vomiting (0.8%), and abdominal pain (0.4%).

Like Spiegel, David A. Johnson, MD, professor of medicine and chief of gastroenterology at the Eastern Virginia School of Medicine in Norfolk, says that the patients with anorexia should be excluded. A more realistic — if high — estimate is the 29% who presented with diarrhea, Johnson says.

"Other GI problems — abdominal pain, nausea, and vomiting — may raise the percentage slightly from the 29%," Johnson said.

For the overall study population, Pan and colleagues found that the average time from symptom onset to hospital admission was 8.1 days. However, it was 9.0 days for patients with GI symptoms, including those with anorexia, compared with 7.3 days for those who did not have digestive symptoms. Seven patients had digestive symptoms but no respiratory symptoms at admission.

Digestive symptoms appeared to be tied to worse outcomes. Whereas 60% of patients without digestive symptoms recovered and were discharged, only 34.3% of the patients with digestive symptoms recovered.

Spiegel explained how the digestive symptoms arise. "The virus enters human cells through the ACE2 receptor in the lungs but also in other body parts, including the GI tract. We think the virus gets into saliva and we swallow it, and then it passes through the acid layer in some patients and uses the ACE2 receptors to enter epithelial cells that line the intestine."

The virus replicates rapidly in the cells of the GI lining, enters the intestinal tract, and is shed, Spiegel said. "There is clear evidence from endoscopy that it can damage the stomach and the intestines. The fact that these patients do worse may be that more of the body is involved." An explanation for the longer time between symptom onset and COVID-19 diagnosis might be that patients with only GI symptoms or mild respiratory complaints did not think that they could have the coronavirus.

"When the patients were admitted to the hospital, no one yet knew they had COVID-19. Almost half, when asked why they were there, mentioned a digestive problem. They may have also had a respiratory symptom, like a cough or shortness of breath, but that's not what they said was their main complaint," Spiegel told *Medscape Medical News*.

The authors conclude, "Clinicians should recognize that digestive symptoms, such as diarrhea, may be a presenting feature of COVID-19, and that the index of suspicion may need to be raised earlier in at-risk patients presenting with digestive symptoms rather than waiting for respiratory symptoms to emerge."

Spiegel points out that the Centers for Disease Control and Prevention has yet to include GI symptoms in their guidance, although recommendations are changing rapidly.

Spiegel urges caution in evaluating patients with only GI symptoms. "A large part of the population has diarrhea, abdominal pain, nausea, and vomiting regularly, so it's clearly impossible and irresponsible to start testing everyone with diarrhea for COVID-19. But if somebody has new fever and diarrhea and suspects they may have had contact with a patient or carrier, I'd want to test them."

Limitations of the study include a relatively small sample, the retrospective design, and not testing for SARS-CoV-2 RNA in stool.

UPDATED March 19, 2020: This story has been updated to clarify the study findings. //

Am J Gastroenterol. *Published online March 18, 2020.* *Full text*

https://bit.ly/2WzxTNa

New Oral Vaccine Urgently Needed to Prevent Mutant Polio Outbreak

A new oral polio vaccine is needed to address an outbreak of paralytic polio.

by: Juwon Song

An oral vaccine able to replace today's oral polio vaccines that target type 2 poliovirus is urgently needed to address an outbreak of vaccine-derived polio, suggests a new study published March 19 in *Science*.

There were three natural or "wild" types of poliovirus until type 2 was eradicated in 2015. Although wild type 2 infections haven't been observed for more than 20 years, in 2000 researchers identified mutant viruses derived from the type 2 polio vaccine (OPV2) as the source of some rare cases of paralytic polio.

Despite the withdrawal of OPV2 in 2016, this statistical modelling study demonstrates that the after-effects of its administration continue to contribute to the highest number of vaccine-derived type 2 poliovirus outbreaks and transmission rates to date.

Children across the world who have never been immunized against type 2 poliovirus remain poorly equipped to fight the mutated virus, given that the only available vaccine that prevents transmission has been discontinued and the new oral vaccine is not yet ready.

"This study has illustrated that the world is currently facing an increasing spread of type 2 circulating vaccine-derived poliovirus outbreaks across parts of Africa, Southeast Asia and the Middle East, posing a major challenge to the eradication effort," said lead author Grace Macklin, a Ph.D. student at London School of Hygiene and Tropical Medicine and consultant for the World Health Organization.

Polio, along with Ebola and COVID-19, has been classified Public Health Emergencies of International Concern by the WHO.

"While it is difficult to draw comparisons with coronavirus at this time, this prevalence of infectious disease shows a need for strong health systems across the world to rapidly detect outbreaks and respond to them effectively," said Macklin.

Consider the path of type 2 poliovirus. During the six to eight-week interval after inoculation by OPV2, when the body continues to excrete the virus to build up immunity, the weakened virus from the vaccine can on occasion undergo mutations into a harmful, paralytic form. The vaccine-derived virus could mutate even further once transmitted to an under-immunized community.

Increased incidence of vaccine-induced poliovirus led to withdrawal of OPV2 in April 2016. The Global Polio Eradication Initiative instituted a global switch from trivalent oral polio vaccine, which protects against all three polio strains, to bivalent oral polio vaccine, which protects against type 1 and type 3. This is commonly referred to as "the Switch."

After the Switch, circulation of type 2 polioviruses was expected to disappear. Instead, cases of vaccine-derived poliovirus continue to be reported across several continents, posing a threat to unvaccinated children born after the Switch, who lack any immunity against type 2 poliovirus. Vaccination with OPV2 is currently the only available method to induce immunity and prevent transmission among these children, but further use of OPV2 risks seeding more of the mutated poliovirus. "These circulating vaccine-derived polioviruses can spread just like wild-type poliovirus: all countries run the risk of being infected until the viruses have been fully eliminated everywhere," said Macklin.

In their new study, Macklin and her colleagues showed the probability of new vaccine-derived poliovirus outbreaks and person-to-person transmission is increasing over time.

They ran statistical models on data from acute polio paralysis cases obtained through the Global Polio Laboratory Network (GPLN).

According to their analysis, the vaccine-derived virus emerged between May 2016 and November 2019. Between these dates, GPLN had detected 859 strains of the vaccine-derived virus across 26 countries — of which 65.5% were most likely seeded after the Switch, the researchers found. They identified 62 post-Switch vaccine-derived poliovirus events and 41 outbreaks in various African and Asian countries.

Shortly after the first mutant polio outbreaks after the Switch, monovalent OPV2 vaccine, protecting against only type 2 poliovirus, was rolled out again in quantities of more than 300 million doses. This outbreak response caused 27 of the total 41 outbreaks between 2016 and 2019.

Based on these findings, Macklin and fellow researchers argue that other types of poliovirus derived from vaccines hold potential to mutate into virulent forms. Thus, complete removal of OPV vaccines — targeting types 1, 2 and 3 — is essential to halt the spread of paralytic polio.

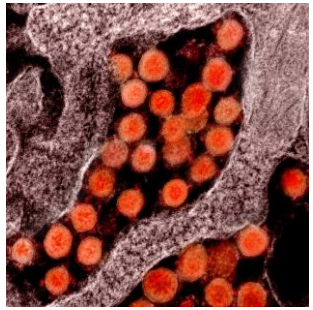
New tools are urgently needed, said Macklin. A new OPV2 vaccine is currently in phase II clinical trials and under review by the WHO Emergency Use Listing — the same process that could eventually review existing data on safety and efficacy of a potential coronavirus vaccine. The updated polio vaccine will be more genetically stable, with a substantially lower risk of seeding vaccine-derived poliovirus. But in case the vaccine takes too long or lacks efficacy, back-up strategies are critical, noted Macklin.

"It is important to remember that, as with all other vaccines, the impact of novel OPV2 will depend on the implementation of high-quality vaccination campaigns," said Macklin. "Increased political commitment is essential to stop the spread of vaccine-derived poliovirus: the situation is a Public Health Emergency of International Concern and has to be treated as such."

https://bit.ly/39csKx7

SARS-CoV-2 Coronavirus Has Natural Origin: Study

An analysis of the genomes of SARS-CoV-2, a novel coronavirus which causes COVID-19 disease, and related coronaviruses found no evidence that the virus was made in a laboratory or otherwise engineered.



Since the first reports of novel pneumonia COVID-19 in Wuhan, Hubei province, China, there has been considerable discussion on the origin of the causative virus, SARS-CoV-2. Also known as 2019-nCoV, SARS-CoV-2 is the seventh coronavirus known to infect humans.

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. **Image credit: NIAID.**

SARS-CoV-1, MERS-CoV and SARS-CoV-2 can cause severe disease, whereas HKU1, NL63, OC43 and 229E are associated with mild symptoms. Shortly after the epidemic began, Chinese scientists sequenced the genome of SARS-CoV-2 and made the data available to researchers worldwide.

Dr. Kristian Andersen from the Department of Immunology and Microbiology at the Scripps Research Institute and colleagues used this sequencing data to explore the origins and evolution of SARS-CoV-2 by focusing in on several tell-tale features of the virus.

“By comparing the available genome sequence data for known coronavirus strains, we can firmly determine that SARS-CoV-2 originated through natural processes,” Dr. Andersen said.

The researchers analyzed the genetic template for spike proteins, armatures on the outside of the virus that it uses to grab and penetrate the outer walls of human and animal cells.

More specifically, they focused on two important features of the spike protein: the receptor-binding domain (RBD), a kind of

grappling hook that grips onto host cells, and the cleavage site, a molecular can opener that allows the virus to crack open and enter host cells. They found that the RBD portion of the SARS-CoV-2 spike proteins had evolved to effectively target a molecular feature on the outside of human cells called ACE2, a receptor involved in regulating blood pressure.

The SARS-CoV-2 spike protein was so effective at binding the human cells, in fact, that the scientists concluded it was the result of natural selection and not the product of genetic engineering.

This evidence for natural evolution was supported by data on SARS-CoV-2's molecular structure. If someone were seeking to engineer a new coronavirus as a pathogen, they would have constructed it from the backbone of a virus known to cause illness.

But the scientists found that the SARS-CoV-2 backbone differed substantially from those of already known coronaviruses and mostly resembled related viruses found in bats and pangolins.

"These two features of the virus, the mutations in the RBD portion of the spike protein and its distinct backbone, rules out laboratory manipulation as a potential origin for SARS-CoV-2," Dr. Andersen said.

Based on their genomic sequencing analysis, the team concluded that the most likely origins for SARS-CoV-2 followed one of two possible scenarios. In one scenario, the virus evolved to its current pathogenic state through natural selection in a non-human host and then jumped to humans.

This is how previous coronavirus outbreaks have emerged, with humans contracting the virus after direct exposure to civets (SARS) and camels (MERS). The researchers proposed bats as the most likely reservoir for SARS-CoV-2 as it is very similar to a bat coronavirus. There are no documented cases of direct bat-human transmission, however, suggesting that an intermediate host was likely involved between bats and humans.

In this scenario, both of the distinctive features of SARS-CoV-2's spike protein — the RBD portion that binds to cells and the cleavage site that opens the virus up — would have evolved to their current state prior to entering humans.

In this case, the current epidemic would probably have emerged rapidly as soon as humans were infected, as the virus would have already evolved the features that make it pathogenic and able to spread between people.

In the other proposed scenario, a non-pathogenic version of the virus jumped from an animal host into humans and then evolved to its current pathogenic state within the human population.

For instance, some coronaviruses from pangolins, armadillo-like mammals found in Asia and Africa, have an RBD structure very similar to that of SARS-CoV-2. A coronavirus from a pangolin could possibly have been transmitted to a human, either directly or through an intermediary host such as civets or ferrets. Then the other distinct spike protein characteristic of SARS-CoV-2, the cleavage site, could have evolved within a human host, possibly via limited undetected circulation in the human population prior to the beginning of the epidemic.

The study authors found that the SARS-CoV-2 cleavage site, appears similar to the cleavage sites of strains of bird flu that has been shown to transmit easily between people.

SARS-CoV-2 could have evolved such a virulent cleavage site in human cells and soon kicked off the current epidemic, as the coronavirus would possibly have become far more capable of spreading between people.

"It is difficult if not impossible to know at this point which of the scenarios is most likely," said co-author Dr. Andrew Rambaut, a researcher in the Institute of Evolutionary Biology at the University of Edinburgh.

“If the SARS-CoV-2 entered humans in its current pathogenic form from an animal source, it raises the probability of future outbreaks, as the illness-causing strain of the virus could still be circulating in the animal population and might once again jump into humans.”

“The chances are lower of a non-pathogenic coronavirus entering the human population and then evolving properties similar to SARS-CoV-2.”

The study was published in the journal *Nature Medicine*.

K.G. Andersen et al. *The proximal origin of SARS-CoV-2*. Nat Med, *published March 17, 2020; doi: 10.1038/s41591-020-0820-9*

https://wb.md/2J6uhKz

Celebrity Suicide: 'Clear and Compelling' Contagion Effect

Media reports of celebrity suicides are associated with a "clear and compelling" increase in suicide rates in the general population, new research shows.

Megan Brooks

Results from a systematic review and meta-analysis show reports of celebrity suicide were linked to an increase in suicide of up to 18% over the following 1 to 2 months. In addition, reporting the method of suicide was associated with an increase of 18% to 44% in the risk of suicide by the same method.

"This is the most comprehensive summary of research findings on associations between reporting on suicide in news and information media," first author Thomas Niederkrotenthaler, MD, PhD, of the Department of Social and Preventive Medicine, Center for Public Health, Medical University of Vienna, Austria, told *Medscape Medical News.*

"It suggests that particularly reporting about deaths of celebrities by suicide has a clear and compelling impact on subsequent suicide rates. The association is even stronger for celebrities that have a strong social status in the population," he added.

The study was published online March 18 in *BMJ*.

Sensational Reporting Still Common

The researchers identified and analyzed 31 relevant studies. They included 20 studies at moderate risk of bias in the main analyses. The studies compared at least one time point before, and up to 2 months after, media reports of death by suicide on television, in print or online news, or in nonfiction books or films.

On average, suicide rates increased by 13% (95% CI, 8% - 18%) over a median of 28 days following media reports of a celebrity death by suicide.

When the media reported the method of celebrity suicide, there was an associated 30% (95% CI, 18% - 44%) increase in deaths by the same method. General reporting of suicide did not appear to be associated with suicide. Media stories on celebrity suicides might increase suicidal thoughts and contribute to planning suicide using a specific method, the data suggest.

Niederkrotenthaler said media reporting on suicide has improved substantially in several countries where media guidelines for suicide reporting have been developed and implemented in collaboration with media professionals.

"But this does not consistently apply to all reporting instances, and in some world regions sensationalist reporting is still very frequent. The findings highlight that media guidelines for the reporting of suicide need to be widely distributed and implemented," he noted.

"Reporting Can Cost Lives"

In an accompanying editorial, David Gunnell, MBChB, PhD, and Lucy Biddle, PhD, University of Bristol, UK, notes these findings will help give media outlets a "clearer sense of the potential effect of their reporting."

The authors note that a 13% increase in suicide rate in the general population following media reports of a celebrity suicide is "substantial." In the UK, for example, where 6507 people died by

suicide in 2018, a 13% increase would amount to around 70 additional deaths.

As reported by *Medscape Medical News*, in the weeks following the death of actor and comedian Robin Williams in 2014, which was widely reported as a suicide by hanging, there was a surge in suicides by this method.

"Suicide is a major and distressing cause of potentially preventable mortality, accounting for over 800,000 deaths worldwide every year," Gunnell told *Medscape Medical News*, and this new analysis is "a really important contribution to the prevention literature."

"The key message is that journalists, news editors, and social media platforms must carefully consider the costs to population health, and impacts on families and friends, of sensationalist, detailed reporting of these tragic deaths. Reporting of suicide methods is a particular concern. Reporting may cost lives," said Gunnell.

Although this review showed no apparent increase in the rate of death by suicide following media reports of noncelebrity suicides, "this is not grounds for complacency," Gunnell and Biddle write.

They point to a recent US study published in *Lancet Psychiatry*, which showed that news reports of suicides can trigger suicide clusters in young people, with a higher risk associated with front page reporting, description of the suicide method, and detailed accounts of the suicide.

The study had no specific funding. Niederkrotenthaler and Gunnell have reported no relevant financial relationships.

BMJ. Published online March 18, 2020. Full text, Editorial

https://bit.ly/2UbreXV

Ibuprofen and COVID-19 symptoms – here's what you need to know

There's been some confusion recently on whether we should or shouldn't take ibuprofen to treat symptoms of COVID-19

Parastou Donyai*

There's been some confusion recently on whether we should or shouldn't take ibuprofen to treat symptoms of COVID-19 – especially after the World Health Organization (WHO) changed its stance. After initially recommending people avoid taking ibuprofen to treat symptoms of the new coronavirus disease, as of March 19 the WHO now does not recommend avoiding ibuprofen to treat COVID-19 symptoms.

The confusion began after France's Minister of Solidarity and Health Oliver Véran announced on Twitter that taking anti-inflammatory drugs (such as ibuprofen or cortisone) could be a factor in worsening a COVID-19 infection. He recommended that paracetamol should be taken instead to treat the associated fever.

At the moment, the NHS only recommends taking paracetamol for COVID-19 symptoms, even though it admits there is no strong evidence showing ibuprofen worsens symptoms. The BMJ also states that ibuprofen should be avoided when managing COVID-19 symptoms.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID). NSAIDs, including ibuprofen, normally have three main uses: they help with inflammation, pain, and fever. People might also take them for inflammatory conditions such as arthritis and for pain. However, paracetamol can also help treat pain and fever.

Fever is a higher than normal body temperature, and is one of the signs of COVID-19, along with a persistent cough and shortness of breath. The body develops a fever as a defence mechanism, where the immune system produces a chain of molecules that tell the brain to make and keep more heat inside to fight the infection.

While getting fever during an infection is part of the body's defence mechanism, a serious rise in body temperature can be fatal and should be treated. Having fever is also uncomfortable because it often comes with shivering, headaches, nausea and stomach upsets. Taking an anti-inflammatory like ibuprofen or paracetamol will

bring down a high temperature by lowering some of the fever molecules. However, doctors who compared the two in 2013 suggested taking paracetamol over ibuprofen for normal chest infections because they found a small number of people's illness got worse with ibuprofen.

Cause for concern?

Some of the reasons that there's a concern taking ibuprofen will make COVID-19 symptoms worse comes from previous studies that have shown people with other serious chest infections (such as pneumonia) experienced worse symptoms and prolonged illness after taking an NSAID, including ibuprofen.

But it's difficult to say if taking ibuprofen in these instances directly causes worse symptoms and prolonged illness, or if it's because taking ibuprofen or other anti-inflammatories help manage pain, which may hide how serious the illness is and could stop people from asking for help earlier – delaying treatment. Or, it might be to do with ibuprofen's anti-inflammatory effects. One theory is that anti-inflammatory medicines can interfere with some of the body's immune response, although this is not proven for ibuprofen.

However, two French studies warn doctors and pharmacists not to give NSAIDs when they see signs of chest infections, and that NSAIDs shouldn't be given when children are infected with viruses. There's no agreement on why ibuprofen could make chest infections worse, but both studies reported worse outcomes in patients who had taken a NSAID to treat their condition.

A recent letter to The Lancet suggested that ibuprofen's harm in COVID-19 is to do with its effect on an enzyme in the body called angiotensin-converting enzyme 2 (ACE2) – though this has yet to be proven. This caused additional worries for patients taking angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) for existing heart conditions. Several leading organisations have rightly warned patients not to stop taking their regular medicines in light of unconfirmed theories.

Because novel coronavirus is a new type of virus, there is currently no evidence proving that taking ibuprofen will be harmful or make COVID-19 symptoms worse. Research in this area is developing fast, but with so much misinformation about COVID-19 and ibuprofen use, the cautious approach is to avoid ibuprofen with COVID-19 if at all possible – especially for those with pre-existing health conditions. Anyone who thinks they might have COVID-19 can consider using paracetamol instead of ibuprofen for managing their fever, unless they're told otherwise by their doctor or pharmacist.

In the meantime, the UK's Committee of Human Medicines and the National Institute for Health and Care Excellence (NICE) have been asked to review all the evidence to understand ibuprofen's impact on COVID-19 symptoms. Naturally, people already prescribed an anti-inflammatory drug for a health condition should ask their doctor's opinion and not just stop their medication.

It's worth noting, however, that ibuprofen and NSAIDs can trigger stomach ulcers and indigestion and might not be suitable for some people with heart disease, kidney and liver problems, and asthma, as well as people over 65, and those who drink more alcohol. These drugs should not be used in people with very high blood pressure, and women trying to get pregnant or already pregnant.

Paracetamol, which can also treat pain and fever, may be preferred. Though it takes up to an hour to work, it's safe to use for women who are pregnant or breastfeeding, and can be taken with or without food. Some people need to take extra care with paracetamol and should speak with their doctor or pharmacist first, for example if they have liver or kidney problems.

The usual dose of paracetamol for adults is one or two 500 milligram tablets up to four times in 24 hours, with at least four

hours in between doses. Most people use a syrup to give paracetamol to children. How much to give depends on your child's age, but again paracetamol should only be given up to four times in 24 hours, with at least four hours between doses.

Pharmacies have been running short of paracetamol and some shops have been rationing sales. For those exhibiting symptoms, a box of 32 tablets should last for at least four days. At this time of crisis, it's important people make sure they're not stockpiling medicines unnecessarily and depriving others who are equally in need of paracetamol and other vital drugs.

*Professor and Director of Pharmacy Practice, University of Reading

Disclosure statement

Parastou Donyai does not work for, consult, own shares in or receive funding from any company or organisation that would benefit from this article, and has disclosed no relevant affiliations beyond their academic appointment.

https://bit.ly/2QF4pJR

Why Warmer Weather Probably Won't Stop COVID-19

Yes, most infectious diseases are seasonal. But waiting for COVID-19 to wane on its own is a bad idea

By Katherine J. Wu

COVID-19 is not the flu. But amidst the ongoing pandemic, many people hold out hope that the two diseases have something crucial in common: a seasonality that will loosen the global grip of SARS-CoV-2 as the weather warms.

Many infectious diseases wax and wane with the changing months. Some, like flu, spike when the weather turns cold, while others, like cholera, thrive during warm, rainy summers. Whether such a pattern applies to SARS-CoV-2 is unclear. With spring just barely sprung, scientists haven't had the time to suss out SARS-CoV-2's annual schedule—if it sticks to one at all.

Besides, relying on seasonality to curb a pandemic can be a dangerous line of thought, says C. Brandon Ogbunu, a computational epidemiologist at Brown University. "Seasonality has the potential to decrease the rate of infection," he says. But this factor alone won't get the world anywhere close to resolving the outbreak. "If I was a betting person … all [my money] would be on the impact of human behavior and infrastructure" to slow transmission, he adds. "That's where we need to put our emphasis."

Why Are Diseases Seasonal, Anyway?

The first time a severe infectious disease tears through a new population, it's sure to wreak havoc. Without previous exposure, no members of the community are immune, leaving the virus with numerous potential hosts to sustain it for months to come, regardless of the weather forecast.

Columbia University epidemiologist Micaela Martinez compares early outbreaks to a fire igniting in a forest full of kindling. The occasional rainstorm might do a bit to slow the conflagration. But with so many vulnerable trees, a touch of precipitation would be nowhere near enough to snuff out the flames. "For the first wave, the seasonality is not as relevant," she says. "We can't expect [the virus] to just go away."

Peak flu activity in the United States by month for the 1982-1983 through 2017-2018 flu seasons. During this 36-year period, flu activity most often peaked in the winter months. (CDC)

Once the current pandemic subsides, however, future infections would propagate amongst a population with a smaller proportion of immune individuals. These likely tamer outbreaks could reveal a seasonal cycle, which Martinez believes is a quality ubiquitous among infectious diseases. In 2018, she set out to catalog these trends and was surprised to find that all of the nearly 70 infections she studied showed some sort of seasonal rise and fall.

Generally speaking, Martinez says, each season comes with a distinct infectious twist: Winter winds bring bouts of pneumonia,

flu and other respiratory diseases before the blooms of spring usher in bursts of chickenpox and herpes. The arrival of summer sees spikes in Lyme disease, polio and syphilis before autumn resets the cycle with blips of yellow fever. Other diseases are generalists, favoring any extended period of dryness or rain, especially in and around the tropics where seasonal boundaries blur.

Disentangling the drivers of these patterns is a complex pursuit. Some factors are obvious: Infections caused by bacteria, parasites or viruses that must be ferried from host to host by an insect vector like a mosquito will inevitably ebb and flow with the natural breeding seasons of their buggy chauffeurs. In other cases, the environment can have a direct effect on the pathogen, Ogbunu says. Some viruses—including influenza and SARS-CoV-2—are packaged in a fragile, fatty outer layer called an envelope that's both necessary for infection and sensitive to harsh conditions, including heat and the ultraviolet rays found in sunlight. High humidity can weigh down the infectious, airborne droplets needed to ferry the virus from person to person, preventing the microbes from traveling as far.

To further complicate matters, our bodies feel the effects of weather and climate. Studies in mice have shown that low humidity can compromise the germ-trapping mucus in their airways and impair the production of critical immune molecules, leaving the rodents more vulnerable to flu viruses, explains Laura Yockey, a virologist at Massachusetts General Hospital.

And biology doesn't manifest in a vacuum. Disease-transmitting behavior also shifts with the seasons, triggering outbreaks that can even override a pathogen's typical itinerary. Children returning to school at the beginning of fall, for example, can prompt an uptick in certain infections like chickenpox. Similarly, people gathering indoors during rainy summer months can spread flu during its "off" season.

These patterns are so pronounced that they "almost form a calendar" of pathogens that humans can track and follow, says Elena Naumova, an epidemiologist at Tufts University. "I honestly believe by nature, life on our planet is seasonal," she says. "Therefore, infections are seasonal, too."

What We Can Do Right Now

As a respiratory virus with a delicate envelope, SARS-CoV-2 has several traits that might someday reveal a seasonal pattern. Years from now, if or when the pathogen returns to the human population, COVID-19 cases may peak when the weather is consistently cold and dry, before dipping down in summer months. For now, though, Naumova says that passively waiting for the virus to disappear is "nonsense." A population's suceptibility to a given infection trumps all else. And with so many vulnerable individuals around, any warmth-related wanes in disease will do little to rein in its spread.

Seasonality's influence—or lack thereof—on this coronavirus shouldn't inspire feelings of helplessness. Quite the opposite, Naumova says. "We cannot control the weather," she says, but we can control "how we prepare for that specific weather." The same goes for infectious disease. As such, humans should take charge of the disease driver they know best: their behaviors. As the pandemic continues to evolve, Ogbunu stresses the importance of continuing to drive down risks for transmission. Practicing good hygiene, avoiding crowds and being mindful of our surroundings remain crucial—to protect not only ourselves, but also those around us whose wellbeing depends on the actions of their fellow community members.

"One of the main drivers of epidemics are contact rates," Martinez says. "It can make a huge impact on disease transmission. Just like it can drive epidemics, it can stop them."

https://bit.ly/33Iv2CX

Newfound Comet ATLAS is getting really bright, really fast

For years, amateur astronomers have been waiting for a bright, naked-eye comet to pass by Earth — and finally, such an object may have arrived.

By Joe Rao - Meteorologist 2 days ago

The possible celestial showpiece is known as Comet ATLAS, or C/2019 Y4. When it was discovered on Dec. 28, 2019, it was quite faint, but since then, it has been brightening so rapidly that astronomers have high hopes for the spectacle it could put on. But given the tricky nature of comets, skywatchers are also being cautious not to get their hopes up, knowing that the comet may fizzle out.

It's been awhile since a comet gave skywatchers a good show, particularly in the Northern Hemisphere. In March 2013, Comet PanSTARRS was visible right after sunset, albeit low in the western sky. But although it briefly attained first magnitude with a short, bright tail, its low altitude and a bright, twilight sky detracted from what otherwise would have been a much more prominent object. Comet Lovejoy in 2011 and Comet McNaught in 2007 both evolved into stunning objects, but unfortunately, when at their best, were visible only from the Southern Hemisphere.

It has now been nearly a quarter of a century since we have been treated to a spectacularly bright comet: Comet Hale-Bopp passed by during the spring of 1997 and Comet Hyakutake did so exactly one year earlier. Both were truly "great" comets, very bright and fantastically structured; in very dark conditions, Hyakutake's tail appeared to stretch more than halfway across the sky.

So now, after a "comet drought," Comet ATLAS may finally enliven the evening skies of early spring. Or then again, maybe not.

Guarded optimism

The comet's moniker is an acronym for Asteroid Terrestrial-impact Last Alert System (ATLAS), a robotic astronomical survey system based in Hawaii and optimized for detecting smaller near-Earth objects a few weeks to a few days before their closest approach. But on occasion, the survey will also find a comet.

When astronomers first spotted Comet ATLAS in December, it was in Ursa Major and was an exceedingly faint object, close to 20th magnitude. That's about 398,000 times dimmer than stars that are on the threshold of naked-eye visibility. At the time, it was 273 million miles (439 million kilometers) from the sun.

But comets typically brighten as they approach the sun, and at its closest, on May 31, Comet ATLAS will be just 23.5 million miles (37.8 million km) from the sun. Such a prodigious change in solar distance would typically cause a comet to increase in luminosity by almost 11 magnitudes, enough to make ATLAS easily visible in a small telescope or a pair of good binoculars, although quite frankly nothing really to write home about.

Except, since its discovery, the comet has been brightening at an almost unprecedented speed. As of March 17, ATLAS was already magnitude +8.5, over 600 times brighter than forecast. As a result, great expectations are buzzing for this icy lump of cosmic detritus, with hopes it could become a stupendously bright object by the end of May.

A famous lineage

Another factor buoying hopes for ATLAS as a potential dazzler is that its orbit is nearly identical to that of the so-called Great Comet of 1844. Like the 1844 comet, ATLAS follows a trajectory that would require 6,000 years per orbit and take it to beyond the outer reaches of the solar system, roughly 57 billion miles (92 billion km) from the sun. Probably in the far-distant past, a much larger comet occupied this same orbit, but fragmented into several pieces — including the 1844 comet and ATLAS — upon rounding the sun.

But any comparison is dangerous. The 1844 comet was not discovered until shortly after perihelion, so we have no knowledge of its brightness behavior beforehand. But that information is currently all we know about ATLAS, and we won't be able to see the object after it reaches the sun. And let's not forget some of the comets of the past that seemingly had "glory" written all over them, only to utterly fail to live up to expectations: Comet ISON in 2013, Comet Austin in 1990 and Comet Kohoutek in 1974.

So what's ahead?

John Bortle, who has observed hundreds of comets and is a well-known expert in the field, got his first look at Comet ATLAS through 15 x 70 binoculars on Sunday night (March 15). And he's stumped, he wrote. "For the first time in many years I am left at a bit of a loss as to what honestly worthy advice I can offer would-be observers. I really don't know quite what to make of this object."

The head (or coma) of Comet ATLAS is big, albeit "very faint and ghostly," Bortle said, which doesn't make sense. "If it's a truly significant visitor, it should be considerably sharper in appearance. Instead we see, at best, a quite modestly condensed object with only a pinpoint stellar feature near its heart."

The unpredictability of comets is an old story. Astronomers use special formulas to try to anticipate how bright a comet will get. Unfortunately, comets' individual behavior and characteristics can be as varied as people: No two are alike.

Now, here is the conundrum regarding Comet ATLAS: Until a couple of weeks ago, it was brightening at an astounding rate. That brightening has slowed somewhat, but it is still an impossible rate of brightening to maintain. Were ATLAS to continue to brighten at this rate all the way to its closest approach to the sun at the end of May, it would end up rivaling the planet Venus in brightness!

"We should expect the rate of increase to slow again," Carl Hergenrother, an assiduous comet observer based in Arizona, said. "This is where it gets tricky for predicting just how bright it will get." Right now, no one can predict how long it will continue to quickly brighten and how dramatically that brightening will slow.

The only thing left to do is to track Comet ATLAS in the days and weeks ahead. Fortunately, its path in March and April will be very favorable for Northern Hemisphere observers, as it will be circumpolar and always remain above the horizon. As darkness falls, it will be positioned more than halfway up in the north-northwest sky. Right now, the comet is in western Ursa Major, and it will shift into the boundaries of Camelopardalis the Giraffe — a rather dim, shapeless star pattern — by March 29. There it will stay, right on through the month of April.

As to how bright Comet ATLAS will get, that's anybody's guess. It might become faintly visible to the naked eye under dark sky conditions by mid- or late April. By mid-May, when it disappears into the bright evening twilight, perhaps it will have brightened to second magnitude — about as bright as Polaris, the North Star.

Whether ATLAS continues to overperform and shines even brighter, develops a significant tail or suddenly stops brightening altogether and remains very faint and ghostly are all unknown right now. We'll just have to wait and see.

"It's going to be fun the next few weeks watching Comet ATLAS develop (and provide a nice distraction from the current state of the world), Hergenrother wrote. "Here's to good health and clear skies!"

https://bit.ly/2xlPzRy

Supercomputer finds 77 drugs that could halt coronavirus spread

The ultra-powerful IBM supercomputer Summit has identified 77 compounds that could help prevent the spread of the novel coronavirus.

By Mike Wehner @MikeWehner

These compounds could be used to develop treatments and vaccines that would halt the spread of the virus and prevent further infections. With dozens of possible options, each of these drugs will have to be tested to see how effective they are in a real-world scenario.

Scientists have enlisted the help of a supercomputer to fight back against the rapid spread of the novel coronavirus. Researchers from the Oak Ridge National Laboratory just published the results of a project in which they tasked the massive IBM supercomputer known as Summit with finding the most effective existing drugs that could combat COVID-19.

The paper, which was published in the journal ChemRxiv, focuses on the method the virus uses to bind to cells. Like other viruses, the novel coronavirus uses a spike protein to inject cells. Using Summit with an algorithm to investigate which drugs could bind to the protein and prevent the virus from doing its duty, the researchers now have a list of 77 drugs that show promise.

Starting with over 8,000 compounds, Summit's incredible power shortened the time of the experiment dramatically, ruling out the vast majority of possible medications before settling on 77 drugs which it ranked based on how effective they would likely be at halting the virus in the human body.

"Summit was needed to rapidly get the simulation results we needed. It took us a day or two whereas it would have taken months on a normal computer," Jeremy Smith, co-author of the research, said in a statement.

"Our results don't mean that we have found a cure or treatment for the coronavirus. We are very hopeful, though, that our computational findings will both inform future studies and provide a framework that experimentalists will use to further investigate these compounds. Only then will we know whether any of them exhibit the characteristics needed to mitigate this virus."

These promising compounds could now play a role in developing new treatments or even a highly-effective vaccine that would keep the virus from taking root inside a person's body. Right now, our best defense against the virus is social distancing, but a vaccine or treatment to ease symptoms and shorten recovery time would go a long way toward getting us on track for a return to normalcy.

Going forward, the researchers plan to run the experiment again with a new, more accurate model of the protein spike that the virus uses. It's possible that the new model will change which drugs are most effective against the virus, and hopefully shorten the road to a treatment option. It will still be many months before we have a vaccine available, but scientists are hard at work on those solutions.

https://bit.ly/2wlnMRu

The FDA just approved a new rapid coronavirus test that can diagnose the virus in 45 minutes

The test can detect the novel coronavirus within 45 minutes, and can be processed by providers without training

Mia de Graaf

The US FDA on Saturday approved a new rapid coronavirus test by California-based Cepheid.

The test can detect the novel coronavirus within 45 minutes, and can be processed by providers without training on one of the company's 5,000 machines across the country.

On March 13, the FDA also gave emergency clearance for a test by Roche, which can diagnose COVID-19 in about three hours.

Previously, patients have had to wait days for a diagnosis.

The US Food and Drug Administration has approved a coronavirus test that can deliver a diagnosis in 45 minutes.

The test, made by California-based Cepheid, got emergency clearance on Saturday, eight days after the agency gave fast-track approval for a test by Roche, which can diagnose the novel

coronavirus within three hours. Medical-equipment giant Thermo Fisher also has a test on the market.

The approval is part of a concerted effort to make up for lost time after delays, a flawed test, and then a global shortage of the essential chemicals needed to make a new test meant the US was testing its citizens at a far slower rate than other countries. States are now also implementing drive-through tests, which have proven successful in other countries, including South Korea.

The Cepheid test will be dispatched next week — first to hospitals, but the FDA's emergency clearance means it can be used in all care settings.

Crucially, providers will not need training to administer the test, which is processed on one of Cepheid's GeneXpert testing system, of which there are 23,000 worldwide and 5,000 in the US.

"An accurate test delivered close to the patient can be transformative — and help alleviate the pressure that the emergence of the 2019-nCoV outbreak has put on healthcare facilities that need to properly allocate their respiratory isolation resources," David Persing, chief medical and technology officer at Cepheid, said in a statement.

https://bit.ly/2U96FLE

WHO launches global megatrial of the four most promising coronavirus treatments

A drug combo already used against HIV. A malaria treatment first tested during World War II. A new antiviral whose promise against Ebola fizzled last year.

By Kai Kupferschmidt, Jon Cohen

Could any of these drugs hold the key to saving COVID-19 patients from serious harm or death? On Friday, the World Health Organization (WHO) announced a large global trial, called SOLIDARITY, to find out if any can treat infections with the new coronavirus for the dangerous respiratory disease. It’s an unprecedented effort—an all-out, coordinated push to collect robust scientific data rapidly during a pandemic. The study, which could include many thousands of patients in dozens of countries, has been designed to be as simple as possible so that even hospitals overwhelmed by an onslaught of COVID-19 patients can participate.

With around 15% of COVID-19 patients suffering from severe disease and hospitals being overwhelmed, treatments are desperately needed. So rather than coming up with compounds from scratch that may take years to develop and test, researchers and public health agencies are looking to repurpose drugs already approved for other diseases and known to be largely safe. They’re also looking at unapproved drugs that have performed well in animal studies with the other two deadly coronaviruses, which cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).

Drugs that slow or kill the novel coronavirus, called SARS-CoV-2, could save the lives of severely ill patients but might also be given prophylactically, to protect health care workers and others at high risk of infection. Treatments may also reduce the time patients spend in intensive care units, freeing critical hospital beds.

Scientists have suggested dozens of existing compounds for testing but WHO is focusing on what it says are the four most promising therapies: an experimental antiviral compound called remdesivir; the malaria medications chloroquine and hydroxychloroquine; a combination of two HIV drugs, lopinavir and ritonavir; and that same combination plus interferon-beta, an immune system messenger that can help cripple viruses. Some data on their use in COVID-19 patients has already emerged—the HIV combo failed in a small study in China-but WHO believes a large trial with a greater variety of patients is warranted.

Enrolling subjects in SOLIDARITY will be easy. When a person with a confirmed case of COVID-19 is deemed eligible, the physician can enter the patient's data into a WHO website, including any underlying condition that could change the course of the disease, such as diabetes or HIV infection. The participant has to sign an informed consent form that is scanned and sent to WHO electronically. After the physician states which drugs are available at his or her hospital, the website will randomize the patient to one of the drugs available or to the local standard care for COVID-19.

"After that, no more measurements or documentation are required," says Ana Maria Henao-Restrepo, a medical officer at WHO's Department of Immunization Vaccines and Biologicals. Physicians will record the day the patient left the hospital or died, the duration of the hospital stay, and whether the patient required oxygen or ventilation, she says. "That's all."

The design is not double-blind, the gold standard in medical research, so there could be placebo effects from patients knowing they received a candidate drug. But WHO says it had to balance scientific rigor against speed. The idea for SOLIDARITY came up less than two weeks ago, says Henao-Restrepo, and the agency hopes to have supporting documentation and data management centers set up next week. "We are doing this in record time," she says.

Arthur Caplan, a bioethicist at New York University Langone Medical Center, says he likes the study's design. "No one wants to tax the frontline caregiver who's overwhelmed and taking risks anyway," says Caplan. Hospitals that aren't overburdened might be able to record more data on disease progression, for instance by following the level of virus in the body, Caplan suggests. But for public health, the simple outcomes WHO seeks to measure are the only relevant ones for now, says virologist Christian Drosten of the Berlin University Clinic Charité: "We don't really know enough about this disease to be sure what it means when the viral load decreases in the throat, for instance."

On Sunday, the French National Research Institute for Medical Research (INSERM) announced it will coordinate an add-on trial in Europe, named Discovery, that will follow WHO's example and will include 3200 patients from at least 7 countries, including 800 from France. That trial will test the same drugs, with the exception of chloroquine. Other countries or groups of hosptals could organize add-on studies as well, says Heneo Restrepo. They are free to do additional measurements or observations, for instance on virology, blood gases, chemistry, and lung imaging. "While well-organized additional research studies of the natural history of the disease or of the effects of the trial treatments could well be valuable, they are not core requirements," she says.

The list of drugs to test first was put together for WHO by a panel of scientists who have been assessing the evidence for candidate therapies since January, says Restrepo. The group selected drugs that had the highest likelihood of working; had the most safety data from previous use; and are likely to be available in supplies sufficient to treat substantial numbers of patients if the trial shows they work.

Here are the treatments that SOLIDARITY will test:

Remdesivir

The new coronavirus is giving this compound a second chance to shine. Originally developed by Gilead to combat Ebola and related viruses, remdesivir shuts down viral replication by inhibiting a key viral enzyme, the RNA-dependent RNA polymerase.

Researchers tested remdesivir last year during the Ebola outbreak in the Democratic Republic of the Congo, along with three other treatments. It did not show any effect. (Two others did.) But the enzyme it targets is similar in other viruses, and in 2017 researchers at the University of North Carolina in Chapel Hill showed in test

tube and animal studies that the drug can inhibit the coronaviruses that cause SARS and MERS.

The first COVID-19 patient diagnosed in the United States—a young man in Snohomish County, Washington—was given remdesivir when his condition worsened; he improved the next day, according to a case report in the *New England Journal of Medicine (NEJM)*. A Californian patient who received remdesivir—and who doctors thought might not survive—recovered as well.

Such evidence from individual cases doesn't prove a drug is safe and effective. Still, from the drugs in the SOLIDARITY trial, "remdesivir has the best potential to be used in clinics" says Jiang Shibo, of Fudan University in Shanghai, China, who has long worked on coronavirus therapeutics. Jiang particularly likes that high doses of the drug can likely be given without causing toxicities.

However, it may be much more potent if given early in an infection, like most other drugs, says Stanley Perlman, a coronavirus researcher at the University of Iowa. "What you really want to do is give a drug like that to people who walk in with mild symptoms," he says. "And you can't do that because it's an [intravenous] drug, it's expensive and 85 out of 100 people don't need it."

Chloroquine and hydroxychloroquine

At a press conference on Friday, President Donald Trump called chloroquine and hydroxychloroquine a "game changer." "I feel good about it," Trump said. His remarks have led to a rush in demand for the decades-old antimalarials. ("It reminds me a little bit of the toilet paper phenomenon and everybody's running to the store," says Caplan.)

The WHO scientific panel designing SOLIDARITY had originally decided to leave the duo out of the trial but had a change of heart at a meeting in Geneva on 13 March, because the drugs "received significant attention" in many countries, according to the report of a WHO working group that looked into the drugs' potential. The widespread interested prompted "the need to examine emerging evidence to inform a decision on its potential role."

The available data are thin. The drugs work by decreasing the acidity in endosomes, compartments inside cells that they use to ingest outside material and that some viruses can coopt to enter a cell. But the main entryway for SARS-Cov-2 is a different one, using its so-called spike protein to attach to a receptor on the surface of human cells. Studies in cell culture have suggested chloroquines have some activity against SARS-CoV-2, but the doses needed are usually high—and could cause serious toxicities.

Encouraging cell study results with chloroquines against two other viral diseases, dengue and chikungunya, didn't pan out in people in randomized clinical trials. And non-human primates infected with chikungunya did worse when given chloroquine. "Researchers have tried this drug on virus after virus, and it never works out in humans. The dose needed is just too high," says Susanne Herold, an expert on pulmonary infections at the University of Giessen, Germany.

Results from COVID-19 patients are murky. Chinese researchers who report treating more than 100 patients with chloroquine touted its benefits in a letter in *BioScience*, but the data underlying the claim have not been published. All in all, more than 20 COVID-19 studies in China used chloroquine or hydroxychloroquine, WHO notes, but their results have been hard to come by. "WHO is engaging with Chinese colleagues at the mission in Geneva and have received assurances of improved collaboration; however, no data has been shared regarding the chloroquine studies."

Researchers in France have published a study in which they treated 20 COVID-19 patients with hydroxychloroquine. They concluded that the drug significantly reduced viral load in nasal swabs. But it

was not a randomized controlled trial and it didn't report clinical outcomes such as deaths. In guidance published on Friday, the US Society of Critical Care Medicine said that "there is insufficient evidence to issue a recommendation on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19."

Hydroxychloroquine in particular might do more harm than good. The drug has a variety of side effects and can in rare cases harm the heart. Since people with heart conditions are at higher risk of severe COVID-19, that is a concern, says David Smith, an infectious disease physician at the University of California, San Diego. "This is a warning signal, but we still need to do the trial," he says. What's more, a rush to use the drug for COVID-19 might make it harder for the people who need it to treat their rheumatoid arthritis or malaria.

Ritonavir/lopinavir

This combination drug, sold under the brand name Kaletra, was approved in the US in 2000 to treat HIV infections. Abbott Laboratories developed lopinavir specifically to inhibit the protease of HIV, an important enzyme that cleaves a long protein chain into peptides during the assembly of new viruses. Because lopinavir is quickly broken down in the human body by our own proteases, it is given with low levels of ritonavir, another protease inhibitor, that lets lopinavir persist longer.

The combination can inhibit the protease of other viruses as well, specifically coronaviruses. It has shown efficacy in marmosets infected with the MERS virus, and has also been tested in SARS and MERS patients, though results from those trials are ambiguous.

The first trial with COVD-19 was not encouraging, however. Doctors in Wuhan, China, gave 199 patients two pills of lopinavir/ritonavir twice a day plus standard care, or standard care alone. There was no significant difference between the groups, they reported in *NEJM* on 15 March. But the authors caution that patients were very ill—more than a fifth of them died—and so the treatment may have been given too late to help. While the drug is generally safe it may interact with drugs usually given to severely ill patients, and doctors have warned it could cause significant liver damage.

Ritonavir/lopinavir + interferon beta

SOLIDARITY will also have an arm that combines the two antivirals with interferon-beta, a molecule involved in regulating inflammation in the body that also has shown an effect in marmosets infected with MERS. A combination of the three drugs is now being tested in in MERS patients in Saudi-Arabia in the first randomized controlled trial for that disease.

But the use of interferon-beta on patients with severe COVID-19 might be risky, says Herold. "If it is given late in the disease it could easily lead to worse tissue damage instead of helping patients," she cautions.

Thousands of patients

The design of the SOLIDARITY trial can change at any time. A global data safety monitoring board will look at interim results at regular intervals and decide whether any member of the quartet has a clear effect, or whether one can be dropped because it clearly does not. Several other drugs, including the influenza drug favipiravir, produced by Japan's Toyama Chemical, may be added to the trial.

To get robust results from the study, several thousands of patients will likely have to be recruited, says Henao-Restrepo. Argentina, Iran, South Africa, and several other non-European countries have already signed up. WHO is also hoping to do a prevention trial to test drugs that might protect health care workers from infection, using the same basic protocol, says Henao-Restrepo.

The trial's European counterpart, Discovery, will recruit patients from France, Spain, the United Kingdom, Germany, and the Benelux countries, according to an INSERM press release today.

The trial will be led Florence Ader, an infectious diseases researcher at the University Hospital Center in Lyon.

Doing rigorous clinical research during an outbreak is always a challenge, says Henao-Restrepo, but it's the best way to make headway against the virus: "It will be important to get answers quickly, to try to find out what works and what doesn't work. We think that randomized evidence is the best way to do that."

https://bit.ly/398sNKt

New promise for universal blood transfusions

Scientists create blood cells that could be friendly to all.

By Paul Biegler

Scientists have created a "stealth" red blood cell that camouflages its immune status, meaning it could potentially be transfused into anybody in an emergency, regardless of their blood type.

The finding, published in *Science Advances*, promises to shake up my own former field of emergency medicine, where treating people who have lost litres of blood from shootings, stabbings and road trauma is all in a day's work. Here's why.

The resuscitation team has to quickly get an IV in the patient's vein and infuse salt water to get their blood pressure back up, otherwise you're looking at cardiac arrest and death.

But even if blood pressure is normalised there's still an issue – salt water can't carry oxygen around the body, so your patient might die anyway. The answer is to transfuse oxygen-carrying red blood cells, supplied by a very kind person who has donated blood.

But that comes with its own complications.

Red blood cells are host to a range of different antigens, signposts on their surface that tell antibodies and other immune cells whether they are yours or somebody else's. Some of those antigens are household names – A and B antigens are found on the red cells of people with blood types A and B (there's also blood type AB, which has both).

Give a person with type A blood a transfusion of type B, or vice versa, and you get something called a transfusion reaction that makes the red cells burst and the person gets very sick or dies.

Which is where blood type "O" comes in. It hasn't got A or B antigens and so you can give it to someone of any blood type without a reaction.

That's helpful, but it comes with a bit of fine print.

Some blood cells also have rhesus or "D" antigens on their surface. If you have those, your blood type gets an additional "positive" moniker: A+, B+, AB+ or O+. If you don't have the Rh antigen you are "negative": A-, B-, AB- or O-.

Put Rh positive blood into someone who is Rh negative and you also risk a transfusion reaction.

Which is why O negative blood is so special. It is the "universal donor" that can be transfused into anyone – emergency doctors like to have plenty of it on hand because it takes time to crossmatch a person's exact blood type, and in a trauma you need blood STAT.

But "O neg" blood is annoyingly rare – only about nine per cent of people have it. And when people stop donating blood, during a coronavirus epidemic for example, stockpiles can plummet.

Enter a team of researchers led by Ben Wang at Zhejiang University School of Medicine in Hangzhou, China.

They took Rh positive human red blood cells and coated them with a hydrogel sheath, anchored to the surface of the cell. Their goal was twofold: they wanted to hide the red cell's Rh status from the immune system and do it in a way that didn't render the cell useless in terms of carrying oxygen.

They ran the stealth cells through a battery of tests that suggests they achieved goal fulfilment.

First, they tested whether the engineered cells were made more fragile and likely to break. They weren't. Then they checked whether the cells were still able to clot. They were.

But they also wanted to make sure the cells were not more viscous than normal red cells. That would make them prone to clot excessively, causing problems like deep venous thrombosis (DVT). The stealth red cells' viscosity profile was healthy.

Perhaps most importantly, Wang's group ran the robo red cell through its oxygen-carrying paces and found that it took up and delivered oxygen with almost precisely the same dynamics as a real cell.

For ultimate proof of purpose, they drained mice of ten per cent of their blood volume, then resuscitated them with stealth red cells. It worked. The mice survived and so did the red cells, which hung around in the critters for around 40 days, comparable to normal red cells. They also infused the cells into rabbits that were primed to react to the D antigens on the robo cell surface. There was no immune reaction, suggesting D stealth was fully enabled.

The researchers say that masking the D antigen combined with other methods that hide a red cell's A and B antigens could make it possible to manufacture O negative blood from other types.

"This study provides new hope for the generation of universal blood cells based on cell surface framework engineering," they write. Which will also give hope to trauma doctors and, most importantly, their patients.

https://nyti.ms/2wnc6xA

As Coronavirus Looms, Mask Shortage Gives Rise to Promising Approach

Surgical masks are supposed to be used just once. But doctors in Nebraska are attempting a novel experiment as gear shortages arise.

By Gina Kolata

Facing a dire shortage of protective face masks for health care workers, administrators at the University of Nebraska Medical Center decided they had no choice.

Masks are certified for one-time use only. But on Thursday, the center began an experimental procedure to decontaminate its masks with ultraviolet light and reuse them. Administrators plan to use each mask for a week or longer.

To the knowledge of the program's administrators, the medical center is the first to disinfect and reuse masks.

"We have talked with a lot of others around the country who are going after a similar approach," said John Lowe, the medical center's assistant vice chancellor for health security training and education, who designed the program.

When administrators made the decision, they knew the procedure violated regulations promulgated by the Centers for Disease Control and Prevention, which said that if masks were decontaminated they could no longer be certified for use.

But late Thursday night, the agency issued new guidance, saying that "as a last resort, it may be necessary" for hospitals to use masks that were not approved by the National Institute for Occupational Safety and Health.

That change would seem to mean it is now acceptable for hospitals to decontaminate and reuse masks during the coronavirus pandemic, said Shawn Gibbs, a professor of environmental health at Indiana University.

If that were not the case, he added, then many hospitals would find themselves in a tightening bind as gear shortages spread: "What is preferred — not using respirator protection equipment, or using a decontaminated respirator whose certification is voided?"

No one thinks reuse of face masks is ideal, and the practice may raise legal liability issues. But there seemed to be little choice.

Doctors and administrators at the University of Nebraska Medical Center calculated that if they continued to use masks only once, they would run out of masks in just weeks.

"We are making the best of bad choices," said Dr. Mark Rupp, the medical center's chief of infectious diseases.

He feels confident that the masks will still protect health care workers. "The data is very clear that you can kill and inactivate viruses with UV germicidal irradiation," he said. "It is also very clear that you will not damage the respirators."

The alternative, Dr. Lowe said, would be to ask health care workers to carefully store their masks and reuse them without cleaning them. Handling a mask repeatedly also increases the chances that it will be contaminated.

"Health care workers are very apprehensive about that," he said.

Decontamination and reuse of masks is not a new idea. Researchers have tested a variety of methods — ultraviolet light, bleach, ethylene gas, moist heat — and have concluded in published papers that decontamination can work.

But the studies were small, and scientific interest in decontamination has been sporadic and fleeting.

"People get interested around the time of a SARS epidemic or an H1N1 flu epidemic, and then they forget," said Dr. Lynn Goldman, dean of George Washington University's Milken Institute School of Public Health.

"When you have an epidemic, it's very cool," she added. "When you don't have an epidemic, it's not cool."

"If you are talking about cures, you can get very large grants" to study decontamination, Dr. Goldman added. "But if you are doing studies on prevention and protection, it's very hard. It's not clear whose job in the federal government it is to fund it."

UV light was the Nebraska hospital's choice because it is effective and convenient. Hospitals already use UV light to decontaminate rooms after patients with dangerous infections, like C. difficile, are moved.

The medical center also used UV light to disinfect rooms when it was treating Ebola patients a few years ago. Patients were sent there because the center has a sophisticated biocontainment area.

"We bring in large UV lamps, hit 'start' and leave the room," Dr. Lowe said. "We let it shine for three to five minutes. It disinfects anywhere it can shine."

As for N95 masks, the kind used by health care workers, "there are really good data that it can decontaminate and that it doesn't degrade the masks a significant amount," Dr. Lowe said.

But, he added, "we inspect the masks before every use." And the protocol Dr. Lowe designed uses three times the concentration of UV light needed to kill coronaviruses.

Masks conform somewhat to the health care worker's face, and a tight seal is necessary. So each health care worker's mask is returned to its user after decontamination.

Health care workers write their names on their masks before they first use them. After they remove the masks for decontamination, they are placed in brown bags labeled with their names.

The bags are transported to a special room covered in a beige paint that reflects UV light. After the masks are treated, each one goes into a white bag with the health care worker's name on it.

The procedure is experimental, and there are uncertainties.

For instance: How many times can a mask be reused? For now, staff members will use each mask for a week before disposing of it. But the medical center may decide to keep using the masks for 10 days, or even two weeks, Dr. Rupp said.

"Hopefully, that will at least buy us enough time to offer protection through this epidemic," he added.

He knows there may be risks, but he believes the medical center has made the right choice.

"I sleep very well," he said. "If we get sued, I still think we are doing the right thing."

https://bit.ly/2WIiw4O

If you've lost your sense of smell or taste, you could be a 'hidden carrier' of the coronavirus

A sudden loss of smell — known as anosmia or hyposmia — could be a symptom of the coronavirus

Adam Bienkov

- ***A sudden loss of smell — known as anosmia or hyposmia — could be a symptom of the coronavirus, even if patients experience no other symptoms, according to leading rhinologists in the UK.***
- ***Evidence from South Korea, China, and Italy suggests that many patients with COVID-19 may have experienced a loss of smell without any other symptoms.***
- ***The British Association of Otorhinolaryngology calls on the authorities to advise anyone with a loss of smell or taste to self-isolate.***
- ***Young people could be more likely to carry the disease without presenting the more commonly recognised symptoms of fever and coughing, they believe.***

Anyone experiencing a sudden loss of smell could be a "hidden carrier" of the coronavirus, even if they have no other symptoms, according to evidence compiled by leading rhinologists in the UK.

In South Korea, China, and Italy, about a third of patients who have tested positive for COVID-19 have also reported a loss of smell — known as anosmia or hyposmia — leading ear, nose, and throat experts in the UK have reported.

"In South Korea, where testing has been more widespread, 30% of patients testing positive have had anosmia as their major presenting symptom in otherwise mild cases," the president of the British Rhinological Society Professor, Clare Hopkins, and the president of the British Association of Otorhinolaryngology, professor Nirmal Kumar, said in a joint statement.

The professors said that many patients around the world who have tested positive for COVID-19 are presenting only the symptoms of loss of smell and taste — without the more commonly recognised symptoms of high fever and coughing.

"There have been a rapidly growing number of reports of a significant increase in the number of patients presenting with anosmia in the absence of other symptoms," the statement says. "Iran has reported a sudden increase in cases of isolated anosmia, and many colleagues from the US, France, and Northern Italy have the same experience."

The lack of other recognised symptoms in these cases may mean they are unlikely to be tested and isolated, meaning they could be contributing to the rapid spread of the disease worldwide.

"These patients may be some of the hitherto hidden carriers that have facilitated the rapid spread of COVID-19," they added.

Young people may not present common coronavirus symptoms

Professor Kumar told Sky News that younger patients in particular may demonstrate only a loss of smell or taste, without demonstrating the more commonly recognised coronavirus symptoms of high fever and persistent coughs.

"In young patients, they do not have any significant symptoms such as the cough and fever, but they may have just the loss of sense of smell and taste, which suggests that these viruses are lodging in the nose," he said.

The professors called for anyone presenting the symptoms of loss of taste or smell to self-isolate for seven days to prevent the further spread of the disease.

https://bit.ly/39cT5eu

Loss of sense of smell as marker of COVID-19 infection

Loss of sense of smell as marker of COVID-19 infection

Post-viral anosmia is one of the leading causes of loss of sense of smell in adults, accounting for up to 40% cases of anosmia. Viruses that give rise to the common cold are well known to cause post-infectious loss, and over 200 different viruses are known to cause

upper respiratory tract infections. Previously described coronaviruses are thought to account for 10-15% cases. It is therefore perhaps no surprise that the novel COVID-19 virus would also cause anosmia in infected patients.

There is already good evidence from South Korea, China and Italy that significant numbers of patients with proven COVID-19 infection have developed anosmia/hyposmia. In Germany it is reported that more than 2 in 3 confirmed cases have anosmia. In South Korea, where testing has been more widespread, 30% of patients testing positive have had anosmia as their major presenting symptom in otherwise mild cases.

In addition, there have been a rapidly growing number of reports of a significant increase in the number of patients presenting with anosmia in the absence of other symptoms – this has been widely shared on medical discussion boards by surgeons from all regions managing a high incidence of cases. Iran has reported a sudden increase in cases of isolated anosmia, and many colleagues from the US, France and Northern Italy have the same experience. I have personally seen four patients this week, all under 40, and otherwise asymptomatic except for the recent onset of anosmia – I usually see roughly no more than one a month. I think these patients may be some of the hitherto hidden carriers that have facilitated the rapid spread of COVID-19. Unfortunately, these patients do not meet current criteria for testing or self-isolation.

While there is a chance the apparent increase in incidence could merely reflect the attention COVID-19 has attracted in the media, and that such cases may be caused by typical rhinovirus and coronavirus strains, it could potentially be used as a screening tool to help identify otherwise asymptomatic patients, who could then be better instructed on self-isolation.

Given the potential for COVID-19 to present with anosmia, and the reports that corticosteroid use may increase the severity of infection, we would advise against use of oral steroids in the treatment of new onset anosmia during the pandemic, particularly if it is unrelated to head trauma or nasal pathology (such as nasal polyps).

There is potential that if any adult with anosmia but no other symptoms was asked to self-isolate for seven days, in addition to the current symptom criteria used to trigger quarantine, we might be able to reduce the number of otherwise asymptomatic individuals who continue to act as vectors, not realising the need to self-isolate. It will also be an important trigger for healthcare personnel to employ full PPE and help to counter the higher rates of infection found amongst ENT surgeons compared to other healthcare workers.

Yours sincerely,

Prof Claire Hopkins, BMBCh, MA FRCS(ORLHNS) DM(Oxon)
President of the British Rhinological Society Professor of Rhinology, King's College London Consultant ENT Surgeon, Guy's and St Thomas' Hospitals
Prof Nirmal Kumar, *President of ENT UK*