SPER NEWSLETTER
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GET INSIGHTS ABOUT:

- MUCORMYCOSIS
- ONGOING EFFECTIVE TREATMENTS
- ONGOING CLINICAL TRIALS
- UPCOMING RISKS AND PREVENTION IN PHARMACEUTICALS

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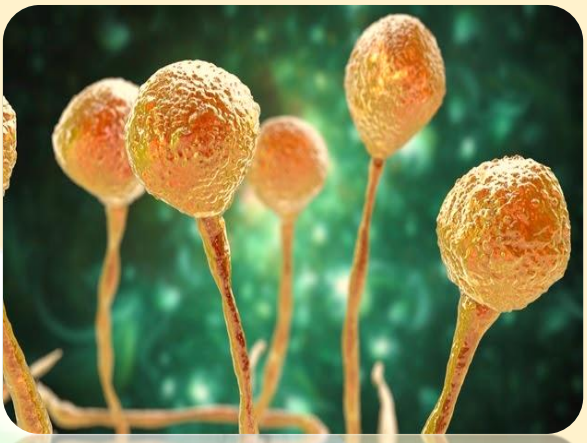
Mucormycosis



Mucormycosis (also known as zygomycosis) or black fungus is a dangerous but uncommon fungal infection caused by mucormycetes, a type of mould. These fungi can be found all over the environment, but they thrive in soil and decaying organic materials like leaves, compost piles, and rotten wood.

Mucormycosis is contracted when people come into touch with fungus spores in the environment. After inhaling spores, for example, the illness can manifest as in the lungs or sinuses. These types of mucormycosis are most common in people who have health issues or who use medications that reduce the body's capacity to fight germs and illness. After the fungus enters the skin by a cut, scrape, burn, or another sort of skin trauma, mucormycosis can develop.

What causes mucormycosis?

Mucormycosis is caused by a fungus called Mucoromycotina. Rhizopus and Mucor are the most prevalent mold genera found in human illnesses. Rhizomucor, Cunninghamella, Lichtheimia, Saksenaea, and Apophysomyces are other Mucoromycotina genera that cause infection less frequently.

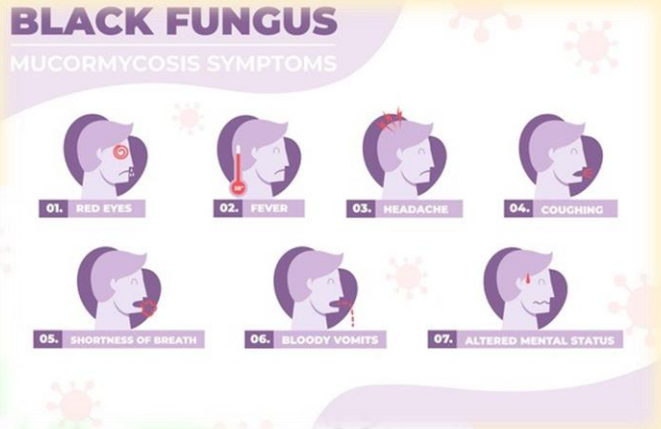
Mucormycosis infection occurs in two ways:

- Pulmonary or sinus form: When people inhale the fungal spores, the infection can develop in the sinuses and lungs. It can also affect the eyes, face, and rarely, the central nervous system.
- Cutaneous form: The fungus enters the skin through cuts, scrapes, burns, or other open wounds.

Signs and symptoms-

- Sinusitis — nasal blockage or congestion, nasal discharge (blackish/bloody);
- Local pain on the cheekbone, one-sided facial pain, numbness or swelling;

- Thrombosis, necrosis, skin lesion;
- Chest paBlackish discoloration over the bridge of nose/palate;
- Loosening of teeth, jaw involvement;
- Blurred or double vision with pain;
- in, pleural effusion, worsening of respiratory symptoms.



People who are at risk-

Anyone of any age can develop the virus. The fungus will come into contact with the majority of humans at some point during their life. However, if a person's immune system is impaired as a result of medicine or a health condition such as:

- Uncontrolled diabetes and diabetic ketoacidosis (a complication of diabetes where the body produces harmful acids called ketones)
- Those who have received high doses of intravenous or oral steroids for a prolonged period
- And those who have received immunomodulators (drugs used in diseases like cancer to modify the immune system's response)
- Cancer
- Organ transplant
- Stem cell transplant
- Neutropenia (low number of white blood cells)
- Too much iron in the body (iron overload or hemochromatosis)
- Skin injury due to surgery, burns, or wounds
- Prematurity and low birth weight (for neonatal gastrointestinal mucormycosis)

Treatment options are available-

- Antifungal medicines and, in some cases, surgical excision of diseased tissue are used to treat mucormycosis.
- Early treatment with antifungal drugs improves the outcome of mucormycosis infection. Amphotericin B is frequently given

intravenously as the first line of defense. Oral posaconazole (Noxafil) or isavuconazole (Cresemba) may be used once patients have responded to amphotericin B or if they are unable to take it.

- Mucormycosis often requires surgery to remove infected tissue.
- There is currently no vaccine to prevent mucormycosis.

Current status-

Over 28,200 cases of mucormycosis, a fatal fungal infection, have been reported in India. Too far, there have been 28,252 cases of mucormycosis reported from 28 states. A total of 86 percent, or 24,370 cases, have a COVID-19 history, whereas 62.3 percent, or 17,601 cases, have a diabetes history. In addition to a severe COVID-19 outbreak, India is facing a new threat in the form of mucormycosis, a fungal illness with a high fatality rate known as "black fungus." The fungal infection, which mostly affects the sinuses, lungs, and brain, is most common in the western states of Maharashtra and Gujarat, and can be especially severe for persons with diabetes and weakened immune systems.

Covid-19: Shortage of black fungus drug Amphotericin-B

- The treatment of mucormycosis needs 5-7 vials per patient per day over 42 days or six weeks, about 250 vials per patient. For 11,700 patients, about 70,200 vials would be needed each day.
- The government has procured and distributed over 1.5 lakh vials since May 22 and says production of just over 1.63 lakh vials in May 2021 and is expected to go up to 2.55 lakh in June. It also plans to import 3.63 lakh vials in May and 3.15 lakh in June.
- There are two kinds of amphotericin being used.

✓ Liposomal amphotericin, the more expensive version is said to be slightly less toxic for kidneys.

✓ Lipid complex or lipid emulsion is the less expensive version

- Doctors involved in treating black fungus say the cheaper version is just as good and that the claims about kidney

toxicity are mostly industry driven to sell the more expensive version. The Indian Council of Medical Research (ICMR) said that other amphotericin formulations are also available and can be used with supplementary medicines to reduce toxic effects.

- It also informed the Delhi High Court that Liposomal Amphotericin B is not the only medication available for the treatment of mucormycosis, also called a black fungus. ICMR said it while submitting a policy on the distribution of the said drug for treating black fungus. The apex health research body further told the court that other amphotericin formulations are also available and can be used with "supplementary medicines to reduce toxic effects."

Clinical Trials and Approvals About Covid

- DCGI approves Phase II/III clinical trial of COVAXIN in the age group of 2 to 18 Years

The National Regulator of the country, the Drugs Controller General of India (DCGI), accorded permission to conduct the Phase II/III clinical trial of Covaxin (COVID vaccine) in the age group 2 to 18 years, to its manufacturer Bharat Biotech Ltd on 12.05.2021.

M/s Bharat Biotech International Ltd., Hyderabad (BBIL) had proposed to carry out a Phase- II/III clinical trial of Covaxin in the age group of 2 to 18 years. As a rapid regulatory response, the proposal was deliberated in the Subject Expert Committee (SEC) (COVID-19) on 11.05.2021. The Committee after detailed deliberation recommended for grant of permission to conduct the proposed Phase II/III clinical trial to certain conditions.

- Neutralization of UK-variant VUI-202012/01 with COVAXIN vaccinated human serum

Covaxin is an indigenous inactivated whole-virion SARS-CoV-2 vaccine BBV152. It has been reported to have high neutralization potency in a phase I clinical trial against the homologous hCoV-19/India/2020770 strain,

as well as two other heterologous unclassified cluster strains, hCoV-19/India/2020Q111 and hCoV-19/India/2020Q100. Notably, all three strains possess the N501Y mutation characteristic of the UK strain spike RBD.

Phase II trials showed impressive results with the plaque reduction neutralization test (PRNT50), with immune serum from Covaxin recipients showing the ability to reduce the level of viral infection of cells in culture at low titers following immunization. Seroconversion and neutralizing antibody production occurred in 99.6% of subjects.

- Safety and immunogenicity study of mRNA-based vaccine (HGCO19) against COVID-19 in healthy adult participants.

Randomized, Phase I/II, Placebo-controlled, Dose-Ranging, study to evaluate the Safety, Tolerability, and Immunogenicity of the candidate HGCO19 (COVID-19 vaccine) in healthy adult subjects. The trial is being conducted by Genova Biopharmaceuticals Limited:-

1. Occurrence and severity of local reactogenicity AEs for 7 days following each dose of vaccination.
2. Occurrence, severity, and relationship of systemic reactogenicity AEs for 7 days following each dose of vaccination.
3. Occurrence, severity, and relationship of unsolicited AEs up to 28 days following each dose of vaccination.
4. Occurrence of SAE at any time during study participation.
5. Changes in safety assessments including laboratory parameters and vital signs from baseline.

New Drug Approval by FDA

- FDA Approves New Edema Treatment for Patients with Heart Failure, Renal Disease

Officials with the FDA have approved torsemide (Soaanz; Sarfez Pharmaceuticals) tablets as a once-daily treatment for patients with

persistent edema who are experiencing from heart failure and whose edema is not regulated with a loop diuretic therapy.

Torsemide is used alone or in combination with other medications to treat high blood pressure. Torsemide is used to treat edema (fluid retention; excess fluid held in body tissues) caused by various medical problems, including heart, kidney, or liver disease. Torsemide is in a class of medications called diuretics ('water pills'). It works by causing the kidneys to get relieved of unneeded water and salt from the body into the urine

➢ FDA Approves New OTC Nasal Spray for Allergy Relief

The FDA has approved azelastine hydrochloride 0.15% (Astepro Allergy; Bayer) as an OTC product for the temporary relief of nasal congestion, runny nose, sneezing, and itchy nose associated with upper respiratory allergies such as hay fever. According to Bayer, the approval is the FDA's first for a steroid-free, antihistamine nasal spray for allergies available OTC in the United States.

This medication is used to relieve nasal symptoms such as runny/itching/stuffy nose, sneezing, and post-nasal drip caused by allergies or other conditions. Azelastine belongs to a class of drugs known as antihistamines. It works by blocking certain natural substances called histamines that are responsible for nasal symptoms. Azelastine is currently only available with a prescription in the United States. According to Bayer, azelastine hydrochloride 0.15% is expected to become available in retail locations in early 2022.

➢ A Closer Look at Recent FDA Approvals for Multiple Myeloma

❖ The FDA approved idecabtagenevicleucel (Abecma) on March 27, 2021. It is the first cell-based gene therapy to treat adult patients with relapsed or refractory multiple myeloma after at least 4 prior different types of treatment. Orphan drug and breakthrough therapy

designations have also been granted to idecabtagenevicleucel by the FDA.

Idecabtagenevicleucel is a B-cell maturation antigen (BCMA)-directed genetically modified autologous chimeric antigen receptor (CAR) T-cell therapy. Each dose is customized using a patient's own T-cells, which are collected and genetically modified, and infused back into the patient.

- ❖ Isatuximab (Sarclisa) is a monoclonal antibody that received FDA approval March 31, 2021, in combination with carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma who have received 1-3 prior different types of therapies. This marks isatuximab's second FDA approval for multiple myeloma treatment.

The FDA approval was based on positive results from the phase 3 IKEMA trial, which showed that isatuximab reduced the risk of disease progression or mortality by 45%.

Ongoing Effective Treatments

Coviself

- CoviSelf, India`s first Covid-19 test kit for self-use, has been commercially rolled out by Biotechnology company Mylab Discovery Solutions.
- After getting approval from Indian Council for Medical Research (ICMR), the coronavirus self-test kit was launched by Mylab Discovery Solutions.

Purpose-

- India's first Covid-19 test kit for self-use can get results within 20 minutes.
- The package contains an Intelligently designed tube filled with a solution which inactivates the virus and designed in the manner to control & contain biohazard, said e-commerce website Flipkart.
- Besides, in drug stores and chemist shops, India`s first Covid-19 test kit for self-use will be made available on the e-commerce website.

- "Biohazard bag for easy & safe disposable Unique QR Code for accurate report generation. Safe Swab is designed intelligently for biocontainment," said Flipkart under product descriptions. [Zee News]

CoviFind

- Merril Diagnostics from Gujarat has announced that its self-use Rapid Antigen Test kit for COVID-19, CoviFind, has received approval from the Indian Council of Medical Research (ICMR).
  Purpose-
- "This indigenously researched and developed test kit can detect the SARS-CoV-2 virus reliably in infectious individuals and can therefore be used for testing symptomatic individuals and immediate contacts of confirmed coronavirus cases as specified by the recent ICMR guidelines," the company said in a statement.

- "The CoviFind test for at-home self-testing is highly effective in individuals with mid to high viral load, especially in detecting infection in the case of individuals more likely to transmit the disease to others," the statement added.
- The test kit will be made available as a single-pack, with additional purchase options including a pack of 3, 5, and 25 tests.
- "This will limit the spread of infections, contributing to the nation's ongoing efforts to quell the second wave of the pandemic. We are committed to producing our indigenously developed self-use test in high volumes to support India's testing needs," he added. [The Hindu]

What is 2-deoxy-D-glucose (2-DG) and is it effective against Covid?

- The Drug Controller General of India (DCGI) has given emergency use approval to 2-deoxy-D-glucose (2-DG), an anti-Covid drug

developed by INMAS, a DRDO lab, in collaboration with Dr. Reddy's Laboratories (DRL), Hyderabad.

Purpose-

- The drug is used as an adjunct therapy. Adjunctive therapy is administered along with primary treatment.
- The clinical trials showed that the drug helps in faster recovery of those who have been hospitalized and also reduces the need for supplemental oxygen.

"During clinical trials, it has yielded an effective result in curing patients infected with COVID-19. The medicine has gone through clinical trials on around 110 patients in the second phase. In the third phase, it was tried on 220 patients. It has shown better efficacy in phase two itself as compared to the standard care," ANI quoted DrSudhirChandna of the Institute of Nuclear Medicine and Allied Sciences (INMAS) as saying.

DrChandna further added that data suggests that the drug is effective in cutting oxygen dependence.

"This data has indicated that oxygen dependence reduced in a better way when we use this medicine along with standard care," DrChandna added.

How To Prevent Cyber-Attacks in the Pharmaceutical and Health care sector

In recent years it has been noted that the pharmaceutical sector has emerged as a prime target for cyber-attacks as it is an industry. Since the pharmaceutical industry was built on innovation with extensive investments in R&D, intellectual property (IP) on medicines and new compounds, clinical patient data, and trade secrets. That information can be worth millions of dollars. When the information gets stolen, it can have a devastating impact on the company. Attackers deploy a wide range of tactics to target drug manufacturers, clinical researchers, and the overall

supply chain. Understanding the way threat actors operate in the pharmaceutical industry is an essential step to strengthen the industry from the perspective of cybersecurity.

Cyber-attacks cause the following effects on any pharmaceutical organization-

1. Cyber-attacks disrupt the operation.
2. Cyberattacks disrupt the supply chain.
3. Cyberattacks result in massive losses in business and hefty regulatory fines.
4. Some investors may become skeptical of a company's ability to handle its investments.

One key problem is that the use of manufacturing systems works on outdated technologies that function as isolated systems. Such systems are inherently prone to cybersecurity attacks. For pharmaceutical companies, any compromises to manufacturing systems can result in a loss of integrity, security, and availability of the physical process. The same risks apply to medical devices that are having connectivity with the internet or smartphones. Vulnerabilities in the design or implementation of a medical device such as an insulin pump or anything interconnected to such devices could result in loss of device integrity and potential harm to patients if they are exploited in a cyber-attack.

Here are a few basic measures that organizations can implement to overcome cybersecurity challenges.

Integrating security awareness:

Drug manufacturers should train employees to understand cyber threats and the best practices they can follow to protect confidential information and critical systems. A security awareness program helps to encourage and enable employees to play an active role in identifying threats hence aids in a company's overall security strategy.

Classifying the data: The bioscientific community should classify sensitive data that serve as a backbone of a company. They should consult cybersecurity teams that can assist in securing the data from threat.

Implementing reliable security access controls:

Companies should implement adequate security measures, such as email security gateways, firewalls, and virtual private networks, to examine network packets and determine the appropriate course of action.

Creating backup:

Drug manufacturers should ensure that the critical data should be backed up regularly and they should separate it from the other departments. In case of a ransomware attack, the company can recover encrypted information from a tested backup.

How to Prevent Third Wave of Covid -19 in India

The infectiousness of coronavirus was much more giving rise to an exponential increase in the number of cases and even an oxygen shortage crisis.

The vaccination drive remains as a hope against the COVID-19 pandemic. However, experts have stated that a third wave of the pandemic in India is already on the way. According to the experts, four factors can majorly affect the basic reproductive ratio of the expected third wave of coronavirus:

1. The time and duration of the infection.
2. Mass gatherings may lead to a huge spread of the virus infection on a larger scale.
3. The probability of transmission of the Covid 19 infection.
4. The strength of the population which is susceptible to the virus infection.

Why Children Below 18 Years At Higher Risk Under COVID-19 Third Wave?

According to the CDC, mucormycosis or black fungus is a fungal infection, which is quite rare. It majorly impacts the sinuses or the lungs after one inhales fungal spores from the air. However, the black fungus can also occur on the skin after a burn, cut, or any other type of skin injury. The symptoms of mucormycosis or black fungus appear two to three days after an individual has recovered from COVID-19.

According to the experts, if proper medical attention is not given to the child, the level of infection may increase. As a matter of fact, in case a child is malnourished or is suffering from some other disease, they may even get a skin disease, liver or kidney disease.

If we are to tackle it, it is important to take proper precautions beforehand. One can take the following steps to prevent the third wave of covid-19.

1) Get Vaccinated as possible

Currently, three vaccines are being given out in India, Covaxin by Bharat Biotech, Covishield by Serum Institute of India, and the Sputnik V from Russia being distributed by Dr Reddy's Labs in India. The vaccine has proven to reduce the intensity of the infection as well as reduce transmissibility.

2) Continue Wearing the mask

Whether you are vaccinated and especially if you are not, it is necessary to wear a mask in public. There are many different masks available but the most effective ones are N95s/K95s. you can also wear a homemade cloth mask if it has up to six layers or more. Surgical masks are also a good option. However, they are typically made to be thrown away after a few times of wear. Double masking has also been

recommended if your mask does not have enough layers or it is not an N95.

3) Stay Indoors and Avoid gathering

After the first wave died down for a while, people were out and about without paying attention to social distancing rules. However, to prevent a third wave from becoming more devastating, we must remember not to repeat this mistake. It is essential to not have public gatherings even when you are vaccinated.

Some more Preventive Action Against 3rd Wave of Covid19

1) Use the Behavioral Vaccine

Covid-19 pandemic rushed scientists into developing vaccines at the fastest speed. Efficacy of lab-developed vaccines differs for each candidate and against different mutant variants of SARS-CoV-2. However, behavioural vaccines offer best defence against all variants of SARS-CoV-2.

Behavioural vaccines include appropriate wearing of face masks, practicing Covid-appropriate hygiene, and maintaining adequate physical-social distance.

2) Opening is staggered

Staggered opening of marketplaces and offices can stop overcrowding of places. Both public authorities and private managements should opt for staggering timings and sites, including continued adoption of work-from-home mode to prevent the congregation of the workforce in one place.

This is more important for offices requiring more indoor staff than those depending on-field workers. Studies have shown that spread of Covid-19 is greater indoors as wind and sun rays help faster disintegration of SARS-CoV-2 outdoors.

Targeted containment

Test, track and treat' has been the mantra of health agencies across the world, including the World Health Organisation. But what has been observed is that this principle has remained mostly on paper and enforced less rigorously on the ground for various reasons.

3) Increasing the rate of vaccinations

Pandemics or epidemics are known to fizzle out when a population attains herd immunity, meaning the virus has no further scope of growth. Vaccines offer herd immunity artificially. In absolute numbers, India's vaccination speed looks impressive compared to other countries, but not in terms of percentage. India has roughly provided vaccination coverage to its 16 percent of eligible (above 18) population. ..

4) Sequencing of genomes

Genetic sequencing helps detect new variants of SARS-2. Early detection of the genome of variants serves as a warning. Identification of a new variant is understood to be crucial in mitigating the chance of a fresh wave of the Covid-19 pandemic. The shortage of genome data on SARS-CoV-2 may bring about a fresh wave of the Covid-19 pandemic as neither scientists nor authorities would know that the virus was on a colonization mission.

SPER HIGHLIGHTS

References

1. https://qz.com/india/2009142/what-is-mucormycosis-and-why-is-it-affecting-covid-19-patients/
2. https://indianexpress.com/article/explained/mucormycosis-in-covid-patients-fungal-infections-7308721/
3. https://www.cdc.gov/fungal/diseases/mucormycosis/definition.html
4. https://www.emedicinehealth.com/mucormycosis/article_em.htm
5. https://www.aa.com.tr/en/asia-pacific/over-28-200-black-fungus-cases-recorded-in-india/2266396
6. *https://vaccine.icmr.org.in/images/pdf/PIB_Covaxin_age_2_18.pdf*
7. https://www.news-medical.net/news/20210201/Indias-Covaxin-vaccine-likely-effective-against-UK-SARS-CoV-2-variant-Study.aspx
8. *https://vaccine.icmr.org.in/images/pdf/2021.01.26.426986v2.full.pdf*
9. *http://ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=54697*
10. https://www.pharmacytimes.com/view/fda-approves-new-edema-treatment-for-patients-with-heart-failure-renal-disease
11. https://www.fda.gov/news-events/press-announcements/fda-approves-nasal-antihistamine-nonprescription-use
12. https://www.pharmacytimes.com/view/fda-approves-new-otc-nasal-spray-for-allergy-relief
13. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-isatuximab-irfc-multiple-myeloma
14. https://www.pharmacytimes.com/view/a-closer-look-at-recent-fda-approvals-for-multiple-myeloma

15. [https://timesofindia.indiatimes.com/india/covid-19-shortage-of-black-fungus-drug-looming/articleshow/83079300.cms]
16. https://www.businesstoday.in/current/economy-politics/amphotericin-b-not-the-only-cure-available-for-black-fungus-icmr-informs-delhi-hc/story/440843.html
17. [https://economictimes.indiatimes.com//industry/healthcare/biotech/pharmaceuticals/what-is-2-deoxy-d-glucose-2-dg-and-is-it-effective-against-covid/articleshow/82567938.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst]
18. https://www.indiatoday.in/coronavirus-outbreak/story/how-india-can-prevent-third-wave-of-covid-19-pandemic-1816077-2021-06-17
19. https://www.thehealthsite.com/news/third-covid-19-wave-may-hit-india-soon-an-epidemiologist-explains-preventive-measures-820205/
20. https://www.insurancedekho.com/health-insurance/news/precautions-to-take-for-third-wave-of-covid-19-1009#popup
21. https://cyware.com/news/the-state-of-cybersecurity-in-the-pharmaceutical-industry-42835bac
22. https://www.isacybersecurity.com/cybersecurity-in-the-pharmaceutical-industry/
23. https://securityscorecard.com/blog/top-5-cyber-threats-impacting-the-pharmaceutical-industry

24. https://www.nozominetworks.com/blog/pharma-cyber-security-how-to-tackle-malware-threats/
25. https://www.1mg.com/articles/are-you-at-risk-of-black-fungus-or-mucormycosis-post-covid-19-read-this/
26. https://www.freepik.com/free-vector/flat-black-fungus-symptoms_14591849.htm
27. https://www.business-standard.com/article/current-affairs/govt-takes-steps-to-enhance-availability-of-drug-amphotericin-b-121061700879_1.html
28. Bharat Biotech denies wrongdoing in Brazil Covaxin controversy; all you need to know (firstpost.com)
29. https://indiabioscience.org/events/lecture-series-on-good-clinical-practice-gcp-1
30. https://www.vectorstock.com/royalty-free-vector/set-medicines-vector-37063260
31. https://www.123rf.com/photo_107239426_stock-illustration-nasal-spray-line-icon-cold-running-nose-rhinitis-medicine-concept-vector-illustration-can-be-used-fo.html
32. https://creativemarket.com/b-s-d/5801555-Rapid-antigen-test-concept-icon
33. Pin on Icon (pinterest.com)
34. https://www.vectorstock.com/royalty-free-vector/injection-vector-31207038
35. https://australiascience.tv/second-wave-of-coronavirus-could-we-see-this-in-australia/

36. https://www.gettyimages.es/ilustraciones/control-de-temperatura
37. https://www.clipartkey.com/view/Jmmihh_clip-black-and-white-stock-oxygen-tank-clipart/
38. Cyber Security Vector 517735 Vector Art at Vecteezy
39. https://www.vectorstock.com/royalty-free-vector/computer-network-cybersecurity-technologies-icon-vector-30385138