Impact Objectives

- Clarify the route of infection transmission by screening for drug-resistant bacteria and genetically testing pathogenic microorganism
- Identify effective countermeasures for each route of infection

Chlorine dioxide combats infections

***Professor Kaoru Obinata** leads a project aiming to reduce the risk of nosocomial infections through the development of reliable infection countermeasures*

What issues are you trying to solve with your research?

Nosocomial pneumonia is a form of pneumonia that develops 48 hours after admission and the causative microorganisms include not only general bacteria but also drug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and multi-drug resistant *Pseudomonas aeruginosa* (MDRPA). Nosocomial pneumonia has a high mortality rate and incidence rate, and is a major problem in terms of the medical expenses it incurs for patients. One of the preventive measures for nosocomial pneumonia includes environmental improvement such as disinfection and cleaning of hospital rooms. However, control of infection through the spatial environment is also important, and the establishment of economically healthy and effective infection prevention measures is desired. That is where our work comes in. By screening for drug-resistant bacteria such as MRSA and MDRPA – as well as genetically testing pathogenic microorganism using multiplex polymerase chain reactions (PCR), we can clarify the route of infection transmission and take effective countermeasures for each route of infection. Our team at the Department of Pediatrics, Juntendo University in Japan is focused on doing just this with the aim of helping many patients across Japan and beyond.

From your perspective, what is the ultimate impact of your research?

In this research, in order to examine the efficacy and safety of chlorine dioxide on aerosol infection and contact infection, we will regularly conduct active surveillance for patients admitted in high care rooms or ward. There may be negative and skeptical opinions in the medical field because there is no widespread awareness of the safety and efficacy of low-concentration chlorine dioxide. So, by confirming the preventive efficacy and safety of chlorine dioxide against nosocomial pneumonia, we can expect the establishment of a new nosocomial infection control method with less human and economic burden. Ultimately, it will be beneficial not only for the inpatients but also for the hospitals.

Can you talk about the challenges you have faced in your research?

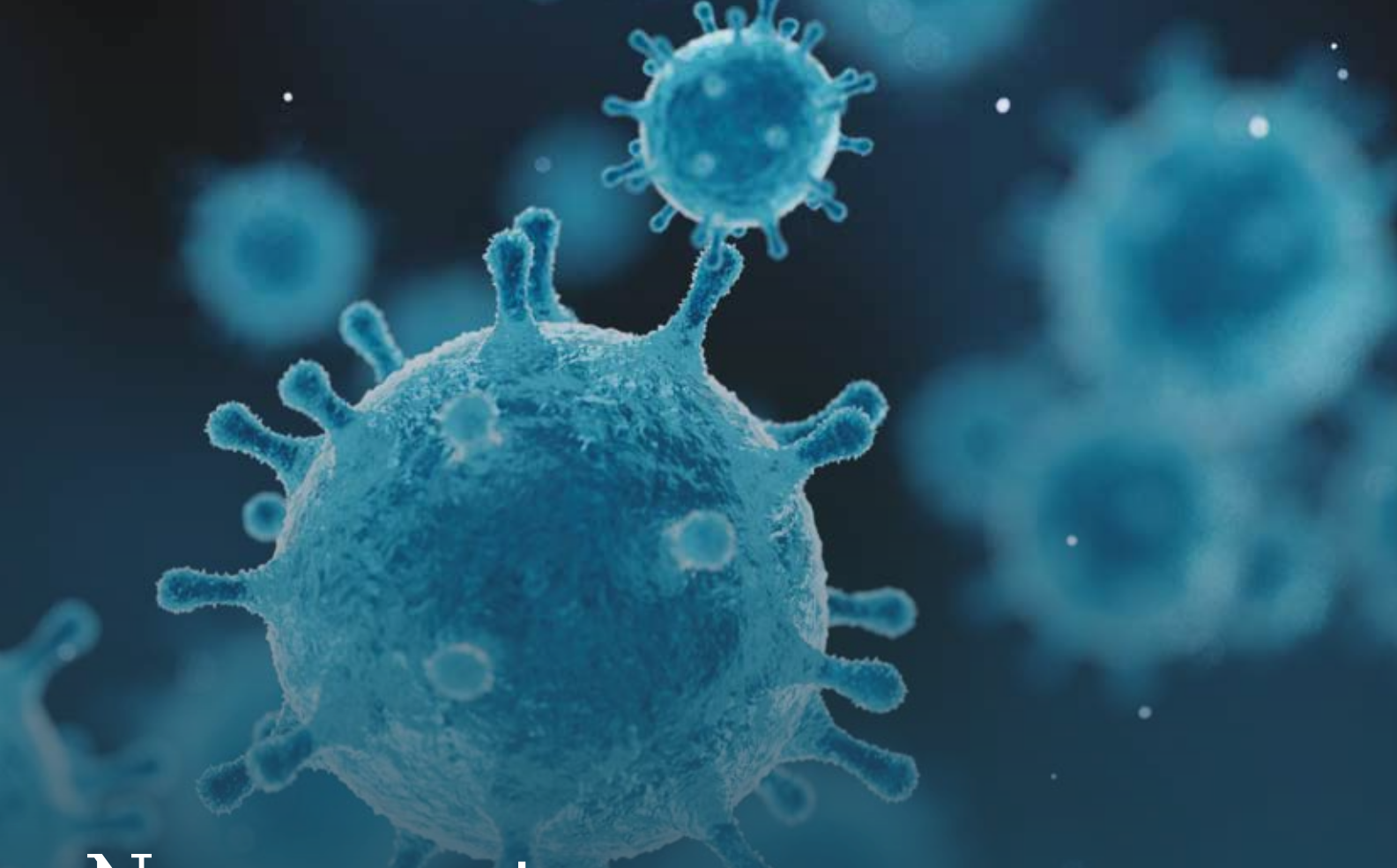
Since ethical support is required when using chlorine dioxide gas in a manned environment, there was a need for us to obtain approval from the ethics committee of each hospital and institution. It can only be installed and applied in an actual hospital environment after careful consideration and discussion by the committee and their approval.

Have you had any results that you are particularly pleased with?

Chlorine dioxide gas generating gel was installed in each room of the pediatric ward in a city hospital during the winter months when infectious gastroenteritis was prevalent, and we were able to conduct a study on the effect of preventing secondary infections of the infectious gastroenteritis using an aqueous solution of chlorine dioxide. As a result of examination of the four seasons since 2016, it was confirmed that there were no secondary infections of infectious gastroenteritis observed and there were no reported adverse events.

Finally, what are your future plans for this research?

We would like to examine our work's impact on infection prevention against the COVID-19 virus, which is wreaking havoc around the world at present. We are also interested in seeing the effect on the mutant strains that are now appearing on a regular basis ▶



New countermeasures against nosocomial infections

*A team of researchers based within the **Department of Pediatrics** at **Juntendo University** is investigating the efficacy and safety of chlorine dioxide against nosocomial infection to help develop improved infection countermeasures*

Nosocomial is a term used to describe any infection, disease or condition that originated in hospital. Ultimately, this means that a patient was admitted to hospital for one thing and is then afflicted by something else. It is an issue that people around the world have come to be increasingly aware of in recent years with the rise of more resistant bugs, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and multi-drug resistant *Pseudomonas aeruginosa* (MDRPA).

One example of a condition that can occur in patients who have been admitted to hospital is nosocomial pneumonia, which is a type of pneumonia that develops in patients around 48 hours after admission. Unfortunately, this form of pneumonia has a high mortality rate and occurs in a surprisingly large number of patients. For these reasons, researchers are intent on finding new and improved means of preventing nosocomial pneumonia from occurring, but also helping to develop treatments that help combat it in those incidents where it does occur.

One of the chief means of preventing nosocomial pneumonia (and the prevalence of MRSA and MDRPA) is through improving the sanitary conditions of hospitals, where the building undergoes extremely stringent disinfection and cleaning. However, in many ways, this is an uphill battle, as many infections are transmitted through droplets in the air (as we have seen with the recent COVID-19 pandemic), which are extremely difficult to combat, especially when the main preventive method is cleaning surfaces.

NOVEL AVENUES EXPLORED

It is with these challenges in mind that Professor Kaoru Obinata has embarked on a project employing a novel technique to combat nosocomial pneumonia and other conditions contracted in hospital. Based within the Department of Pediatrics at Juntendo University in Japan, Obinata leads a team that is exploring the safe and effective application of chlorine dioxide in medical settings. 'The novel element of the project comes from the fact that, in high concentrations, chlorine dioxide is toxic and can burn and/or severely irritate the skin and eyes of human beings, so it would not be an obvious avenue for exploration - especially in hospital patients, but from our perspective

chlorine dioxide holds a lot of potential,' highlights Obinata.

The team of researchers have identified the potential success of chlorine dioxide as a countermeasure against nosocomial infections. 'In nosocomial infections, contact infections such as drug resistant bacteria and viruses become a problem. Furthermore, measures such as ventilation of air-conditioning and prevention of aerosol spread by shielding are being taken as measures against aerosol infection and air infection, which are also the problems we are seeing with the new COVID-19 virus,' observes Obinata. 'However, standard infection prevention measures alone leave viruses and bacteria in the environment. Secondary infections also occur in actual medical settings, making it difficult for clusters to occur.' He says they believe that it is possible to further reduce the risk of nosocomial infections by adding a more reliable infection countermeasure in spatial disinfection and virus removal using chlorine dioxide gas to the conventional infection countermeasures.

IMPROVING EXISTING MEASURES

Of course, measures already exist within hospitals to prevent or counteract air and droplet infections. One of the chief methods is the use of high-efficiency particulate air (HEPA) filters, but even if the pathogenic microorganisms are captured by the filter, they are not sterilised or killed - meaning that the problems are not really solved in any meaningful way. There are also problems with the associated costs of HEPA filters, as well as the issues they cause regarding the need for secure spaces in hospitals - something difficult to achieve when HEPA filters are installed.

On the other hand, chlorine dioxide exists as a gas at room temperature and dissolves in water to form an aqueous solution. Chlorine dioxide gas and aqueous solution are known to have a sufficient effect on aerosol infection of the causative microorganism for nosocomial pneumonia and an improvement of its efficacy can be expected by using it in combination with the conventionally used HEPA filter. 'The infection route for nosocomial pneumonia is associated with aerosol infection when performing endotracheal suction operation in cases of respiratory management,' points out Obinata. He explains that as a preventive measure, the use of negative pressure and positive pressure chambers to prevent the diffusion and inflow of microorganisms are being carried out, in addition to the use of a closed suction system, the disinfection of hospital rooms, cleaning of the environment, ventilation and the use of HEPA filters. 'However, the installation of a negative pressure chamber is expensive and the HEPA filter cannot sterilise or kill the pathogenic organisms even if it can capture them. Alcohol is not effective for the disinfection of objects against norovirus and adenovirus while sodium hypochlorite has a problem in terms of producing carcinogens such as trihalomethane,' he outlines.

The low concentration of chlorine dioxide gas and aqueous solution are considered to be sufficiently effective against aerosol infection for the causative microorganism of nosocomial infection, and it is expected that when it is used in combination with a HEPA filter, it will be highly safe with good prevention effect and cost effectiveness.

FINDINGS TRANSLATED

So far, the team's investigations have shown that chlorine dioxide aqueous solution is effective against various bacteria, viruses and fungi at a lower concentration than sodium hypochlorite solution. However, it has also been found that low-concentration of chlorine dioxide gas is effective against airborne bacteria and viruses, as well as adherent bacteria and viruses. In mouse models, the team has shown that it is effective against aerosol infection for the influenza virus and against influenza-like illness in humans.

Chlorine dioxide aqueous solution has been proven to be effective against MRSA and MDRPA too - which seems to support its use against other nosocomial infections. 'Interestingly, the team's research has also found that it is effective against the new coronavirus (SARS-CoV-2) and the mechanisms of action that inhibits the binding of the spike protein of the SARS-CoV-2 on ACE2 through the action of chlorine dioxide has been verified,' confirms Obinata. 'Based on these results, it appears that chlorine dioxide aqueous solution can be applied in hospital settings for the prevention of a wide range of nosocomial infections.'

The next stage is for the researcher to find a means of ensuring that the concentration of chlorine dioxide can be kept to safe and constant levels so that the effects are beneficial and not harmful. Thus, they are working to clarify the installation location of the chlorine dioxide generating gel in hospital rooms, as well as the time at which the mechanism should be replaced. If these final pieces of the puzzle can be put together, there is a genuine chance that the findings can be translated into real-world settings, thereby saving the lives of patients around the world.

> *'It appears that chlorine dioxide aqueous solution can be applied in hospital settings for the prevention of a wide range of nosocomial infections'*

Project Insights

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