The protagonist of contemporary and emerging nanotechnology-based theranostics and therapeutic approaches in reshaping intensive care unit

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ABSTRACT

يعد الحفاظ على بيئة نظيفة وصحية في وحدة العناية المركزة (ICU) أمرًا ضروريًا لضمان سلامة المرضى، ومنع العدوى، وتقليل المضاعفات المرتبطة بالرعاية الصحية. مع تزايد انتشار العدوى وظهور المقاومة الفيروسية والبكتيرية للمطهرات القياسية، هناك حاجة ملحة لحلول مطهرة مبتكرة. يتم استخدام تكنولوجيا النانو بشكل متزايد في الطب، مع التركيز بشكل خاص على التخفيف من أنشطة مسببات الأمراض المختلفة، بما في ذلك تلك المرتبطة بالعدوى المكتسبة من المستشفيات. نستعرض في هذه الورقة التأثير الحالي لتكنولوجيا النانو، مع التركيز بشكل خاص على الالتهابات البكتيرية وفيروس SARS-CoV-2، الذي يجهد أنظمة الرعاية الصحية بشكل كبير، ثم تناقش كيف يمكن لتكنولوجيا النانو أن تعزز منهجيات العلاج الحالية. نسلط الضوء على فعالية مبيد البكتيريا Bio-Kil القائم على تقنية النانو في تقليل أعداد البكتيريا في وحدة العناية المركزة. الهدف هو تثقيف المتخصصين في الرعاية الصحية حول الدور الحالي وآفاق تكنولوجيا النانو في معالجة الأمراض المعدية السائدة.

To maintain a clean and hygienic environment in the intensive care unit (ICU) is crucial for ensuring patient safety, preventing infections, and reducing healthcare-associated complications. With the increasing prevalence of infections and the emergence of viral and bacterial resistance to standard antiseptics, there is a pressing need for innovative antiseptic solutions. Nanotechnology is increasingly being employed in medicine, particularly focusing on mitigating the activities of various pathogens, including those associated with hospital-acquired infections. This paper explores the current impact of nanotechnology, with a particular focus on bacterial infections and SARS-CoV-2, which significantly strain healthcare systems, and then discusses how nanotechnology can enhance existing treatment methodologies. We highlight the effectiveness of the nanotechnology-based bactericide Bio-Kil in reducing bacterial counts in an ICU. The aim is to educate healthcare professionals on the existing role and prospects of nanotechnology in addressing prevalent infectious diseases.

Keywords: ICU, nanotechnology, SARS-CoV-2, bacterial infection, Bio-Kil

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Some strategies are merely conceived, whilst others are in different phases of testing or are presently in use. Nanotechnology is predicted to make cellular and perhaps subcellular diagnostics possible. At present, full control, monitoring, development, repair, protection, and advancement of all human biological systems are accessible in cancer employing engineered tiny devices and nanomaterials. A wide range of developing nanotechnologies are fast reaching maturity; we expect that during the next 20-30 years, they will become standard operating practices in the intensive care unit (ICU).[1] Conventional medical equipment linked to patients is changing and being changed by the emergence of nanotechnology and nanoscience into smart systems for ongoing rapid assessment and critical care making decision processes.

The first step to enhance patients' prognosis is to assess biomarkers of ailment (nucleic acids, proteins, antibodies, and cells) that occur in abnormally high concentrations in body tissue or fluids when there is disease. Miniaturized "point of care" equipment, which includes the lab-on-a-chip (LOC), is especially useful. Pathogen recognition is critical in the early identification of infection. The major problem. However, the concentration at the beginning of the illness starts and the development cycle is frequently ultralow, for example, in sepsis, 5-10 colony forming units (CFU) per mL.[2] Whereas some advances have

been carried out in point-of-care (POC) gadgets, severe requirements for accuracy and specificity need a centrally located high-quality laboratory and a turnaround time that is too lengthy for clinical applications, such as blood cultures accompanied by amplification and lysis of the component deoxyribonucleic acid (DNA) for identifying pathogens when there is sepsis.[3] This long turnaround implies that ICU physicians must operate without full access to analytical data, normally depending on direct clinical observations. Early diagnosis and treatment have a considerable beneficial influence on patient outcomes.[4] However infection is not always simple to recognize, mostly in patients who are critically sick, and this has resulted in an excessive of antibiotics in hospitals, which has contributed to an elevated rate of resistance to antimicrobial agents.[5]

Accurate pathogen identification is a need for the safety and cure of dangerous and potentially fatal infections in severely unwell patients. Although the latest breakthroughs in biosensors, sepsis is still a prominent cause of illness and death globally. For example, sepsis accounts for more than half of all deaths in countries that are developing. Microfluidic LOCs systems have several benefits for identifying pathogens, including miniaturization, a small specimen volume, mobility, rapid identification time, and POC diagnosis.[6] Using microscale reagent manipulation, effects like quick mixing and heating can be used. It additionally permits less waste and less contact with hazardous chemicals. This review explores the impact of nanotechnology, with a particular emphasis on bacterial infections and SARS-CoV-2, which significantly strain healthcare systems, and then discusses how nanotechnology can enhance existing treatment methodologies. We highlight the effectiveness of the nanotechnology-based bactericide Bio-Kil in reducing bacterial counts in an ICU. The main goal is to educate healthcare professionals on the present role and prospects of nanotechnology in addressing prevalent infectious diseases.

The role of nanotechnology in emergency medicine. In certain clinical conditions, more studies for diagnosis and therapy are progressing slowly due to a scarcity of suitable clinical models. This is especially important in severely unwell individuals. Animal models are now the most popular models. Notably, animal models are considered unsuitable on account of both ethical considerations and the failure of model systems to reflect the complex changes that occur within human responses. Recent work has focused on the translation of laboratory findings into clinical applications that may facilitate the discovery of disease mechanisms and potential therapeutic targets. Accordingly, organ-specific environmental conditions enable the integrated cell biology linked with LOC technology to mimic human physiology and, eventually, support a multicellular human model in vitro. The capability to examine the ailment at a local, even on the nanoscale, level might increase comprehension and reveal profound, frequently specific to the patient insights not possible with animal models that cannot fully mimic clinical circumstances at the level of a single organ. Organs-on-chips could enable the successful modeling of all biological procedures of complete live organs, integrating dynamic mechanical properties and metabolic activity. In particular, projects focused on unmet needs would allow for improved clinical characterization and individualization therapy strategies using new molecules for organ dysfunction identification and regulation at the local level. Using 3D cell-culture models to bring organs-on-chips into studies will include and surpass 2D culture methods by fostering greater degrees of tissue organization and cell differentiation.[7] Certain disorders, including acute respiratory distress syndrome (ARDS), might profit from this technology because we should be able to imitate the cellular properties of an organ in numerous manners, such as tissue-to-tissue interfaces (for instance, vascular endothelium and epithelium), mechanically active microenvironments and chemical gradients in space and time.[8] The use of microfluidics in organs-on-chips allows for the assessment of not only the efficient movement and transport of nutrients but also other soluble signals in real 3D tissue structures. In the next several years, the creation of organs-on-chips and medical instruments on chips is going to be dependent on microfluidic high-throughput technology, which will result in considerable cost and time reductions above traditional platforms for testing. This will be clinically advantageous in disorders involving organ functions, including kidney, lung, heart, and skin (**Figure 1**).[9]

An attractive concept for therapy is the extraction of genetic chemicals from bodily fluids. The elimination of a wide range of infections is currently proven by utilizing the type of extracorporeal dialysis equipment. The interaction duration between the solution and the magnetized beads in these kinds of instruments is restricted to a shorter time. The idea behind magnetic separate-based blood cleaning is that particles of magnetic material equipped with capture moieties

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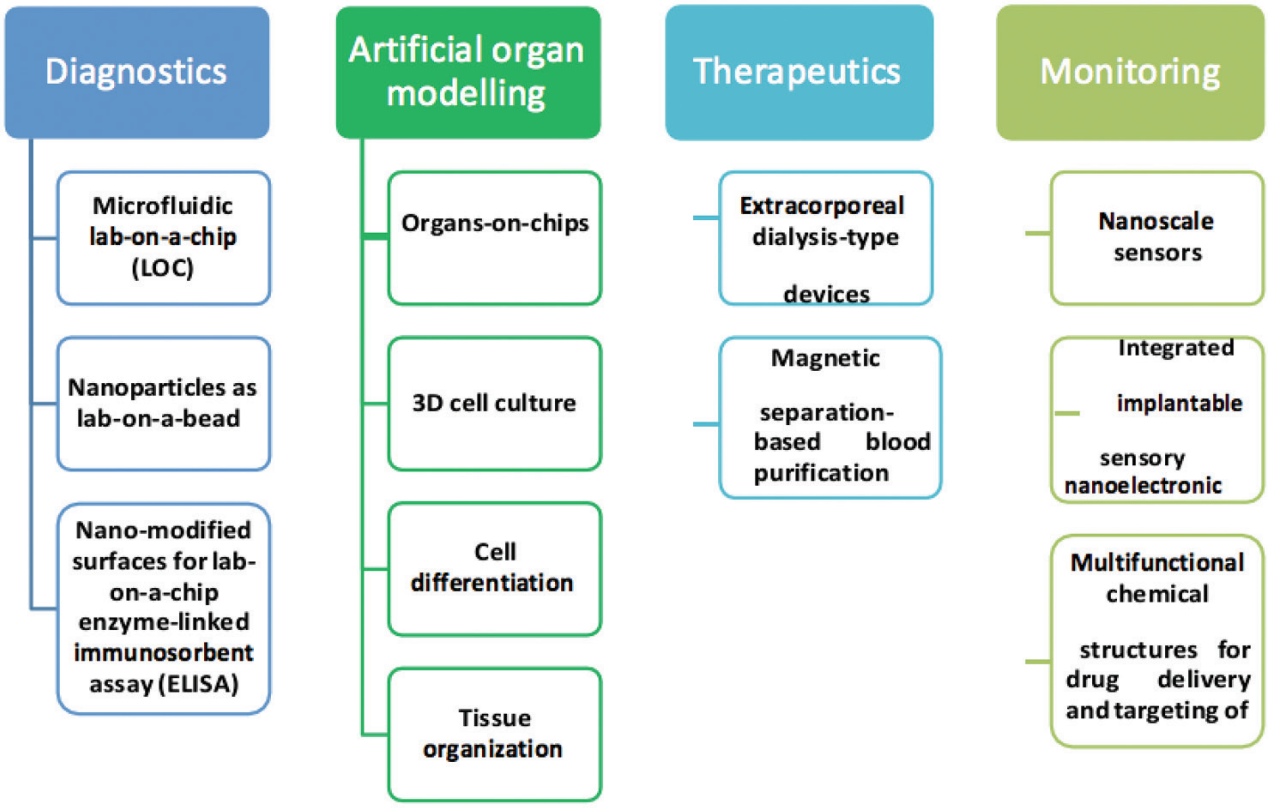

Figure 1 - Future potential for nanotechnology advancement in emergency medicine investigation and practice in the next years.

attach to pathogens and then eliminate them from the blood via a process known as separation by magnetism. The key worry with this technology is its extremely high degree of safety.[10]

Nanoscience and nanotechnology will be at the forefront of this transformation, producing extremely selective customized surfaces that gather and precisely assess ultralow amounts of cellular, nucleic acid, or protein biomarkers.[11] When the chemical data are combined with more typical physical parameters such as respiration, temperature, cell oxygenation, metabolic rate, and microcirculation, they reveal comprehensive insights into the condition of a person at the cellular, tissue, and molecular levels. Closed-loop feedback control systems are coupled to this quantitative analytical data, as well as operational, pharmacological, and "electroceutical" interventions. "Nanobots" circulates in the blood like "Exocet" rockets, delivering their medication payloads to the specific point of action at the appropriate amount while minimizing incidental cell damage caused by the drugs' harmful effects.[12]

Future advancements are envisaged in medication delivery, reparation of cells, artificial organ creation, and so on. There are possible implementation issues since the bulk of the present commercial uses of nanotechnology in medicine are directed towards delivering drugs to allow novel modes of action and also improved targeting and bioavailability of currently available medicinal compounds. As a result, new nanotechnological uses, namely, nanostructures for transportation across biologic obstacles, implanted sensory nanoelectronic devices that are combined, nanoprobe remote control, and multifaceted chemical structures for delivering drugs and ailments targeting, are essential in the near future. Figure 1 illustrates the forecasted development of nanotechnology research and practice in emergency medicine in the coming years.

Nanotechnology in combating hospital bacterial infection. Hospital-acquired bacterial infections pose a grave threat to patients, often due to their resistance to antibiotics and their ability to spread rapidly in healthcare settings. Among the most concerning are *Clostridium difficile*, notorious for causing severe diarrhea and colitis; methicillin-resistant *Staphylococcus aureus* (MRSA), which leads to skin infections, pneumonia, and bloodstream infections; and vancomycin-resistant

Enterococcus (VRE), known for urinary tract infections and bloodstream infections.[13] Vigilant infection control measures and antibiotic stewardship are imperative to combat these formidable pathogens and safeguard patient well-being in hospital settings.[14]

Sepsis is a deadly medical illness, especially now that drug resistance is on the rise. Despite growing awareness of the complicated biology of sepsis, one of the most significant dissatisfactions over the last 30 years has been the inability to translate gains in knowledge into appropriate new therapeutics.[15] Both are extremely selective agents and medications having pleiotropic effects studied, although with varying degrees of achievement. Many people have questioned the present method of developing sepsis therapeutics in light of such dismal outcomes. Preclinical instances of success are being translated into clinics is highly difficult and separates fundamental sepsis study from therapeutic practice.[16] Sepsis is not only tough to cure, but it is also difficult to diagnose. It is frequently hard to distinguish patients who require immediate antibiotic therapy from those who have suffered from systemic non-infectious inflammation caused by other illnesses, where antibiotic therapy can result in undesirable side effects that include *Clostridium difficile* diarrhoea or other adverse effects. Diagnostic ambiguity leads to antibiotic misuse in hospitals and out-of-hospital settings, contributing to increased antimicrobial resistance rates, a major worldwide healthcare concern. Over the last several decades, developments in intensive care and improved awareness have played a role in minimize the risk of imminent mortality linked with sepsis; though, innovative techniques for preventing, diagnosing, and treating sepsis continue to be critical healthcare requirements that may only be fully addressed via the use of innovative technology.

The emergence of nanotechnology has resulted in an astounding number of unique instruments that enable novel technical solutions. Electrical, mechanical, optical, magnetic, and chemical characteristics of systems vary as their size reduces.[17] In the same way, opaque substances can become clear, stable substances can become flammable (bulk iron against iron nanoparticles [NPs]), and insoluble substances can become soluble (AgNPs). Chemically inert substances can become catalytically active when their surface-to-volume ratio increases. Such drastic changes in characteristics open up a completely novel world of material characteristics. By designing systems at the (sub-) nanoscale, we can take advantage of these changing material characteristics and construct systems with outstanding performance from the ground up. Altering the characteristics of components creates an abundance of new chances to develop cutting-edge technology; we may improve systems more robust, durable, sensitive, multipurpose, and so on.

In general, the best method to solve an issue is to eradicate its source. Implantable medical equipment and endotracheal tubes are an important cause of infection acquired in the hospital, accounting for more than 40% of all sepsis in a hospital setting. For hundreds of years, silver-based constituents have been used for their therapeutic characteristics; however, with the advent of antibiotics, the usage of silver-based constituents has declined.[18] Unlike prior formulations containing silver, which were quickly deactivated by the environment, silver particles that are nano-sized enable a prolonged release of silver ions with antibacterial action.[19] However, the toxicity of AgNPs is still an issue. Whereas certain research investigations have found AgNPs to be cytotoxic in vitro, toxicity in the body of swallowed AgNPs is uncommon. Wong et al[20] found no overt systemic impacts when administering AgNPs to mice intravenously, even though the comparatively high dosage.[21] However, The whole relevance in vivo and its application to individuals are mainly unidentified.[20] Surprisingly, AgNPs-decorated recyclable tricalcium phosphate particles were used to create silver ion release that is triggered. If there are no bacteria exist, no silver is produced, possibly reducing negative impacts when used in therapeutic settings.[22] Because trigger-dependent methods considerably lower the needed dosage of AgNPs, they might be regarded as a first step towards ensuring the safety of AgNPs-coated surfaces. These self-sterilizing mechanisms might substantially enhance the efficacy of presently employed silver-based coatings, and after protection issues are addressed, they could potentially be utilized on endotracheal tubes, catheters, or grafts.[23]

Primary diagnosis is critical for initiating therapy and influencing the patient's success. Sepsis is a serious medical condition that requires a prompt cure, demanding a swift, early, and correct diagnosis. Sepsis, on the other hand, is hard to identify based merely on clinical signs. Blood cultures sometimes need lengthy incubation durations, and most of them result in false negatives. Whereas over 170 biomarkers have been studied, only some of them have entered clinical practice.[24] There is no one optimal biomarker, and current investigations have concentrated on understanding the diagnostic value of numerous biomarkers when used together.[24,25] However, these types of tests are costly and time-consuming because subtle variations in biomarker amounts must be observed within a few minutes, ideally in a POC setting, posing a significant

obstacle to presently employed routine measurements like polymerase chain reaction or systems enzyme-linked immunoassays. The NPs-based biodetectors can enhance or replace present analytics.[26] Identification systems may be carried out more accurate by using colloidal fluorescent or plasmonic NPs, achieving levels of recognition of single analytes with the naked human eye (**Figure 1**).[26] Plasmonic sensors, for instance, based on gold NPs development in the existence of hydrogen peroxide (H2O2) produced by an enzyme process, were used to recognize single molecules in serum.[27,28] In the same way, Chapman et al[29] described a POC-compatible lateral flow apparatus that can identify one nanomolar quantity of human phospholipase in serum with the naked eye in 10 minutes. Multi-armed polymer release from a liposome substrate by an enzyme, which then aggregates tiny global natural Products social molecular networking (GNPs), is the basis for this assay. The adherence of GNPs networks to the lateral flow manoeuvre causes the development of a red test line as a result of the gold's localized surface plasmon resonance effects.[26] An entire panel of analytes (namely, various enzymes, nucleic acids, or antigens) may be identified in a single specimen at the same time by using orthogonal signal generating and detection techniques.[30,31] Moreover, such devices might eventually enable rapid biomarker panel screening at the patient's bedside.

When sepsis is identified, antibiotics must be administered. Taking care of sepsis patients, on the other hand, is exceedingly difficult, and the efficiency of antibiotic therapy is strongly dependent on the fast and accurate identification of the pathogenic bacteria. Furthermore to diagnostic ambiguity, the antibiotic pharmacokinetics obtained are frequently changed, particularly in individuals with pulmonary illnesses, therefore high doses must be administered over an extended period, which frequently results in the emergence of negative side effects and antimicrobial resistance.[32] Encapsulating antimicrobial medicines into small-sized capsules (namely, polymerosomes and liposomes) enhances pharmacokinetics and tissue delivery, target specificity, (intracellular) administration, and total antimicrobial activity when lowering adverse effects, according to recent research.[32-34] Capsule features (charge, size, and fluidity) can be adjusted to target intracellular or extracellular targets. Intracellular infections like mycobacteria have been proven to be eliminated by employing typical liposomes that phagocytes pick up. Stealth capsules can be constructed to prolong the time for blood circulation, accomplish prolonged medication release, and add specificity to the target.[34,35] Hyaluronidase can cleave the hyaluronic-based capsules, which are produced by bacteria, namely, *Escherichia coli* and *Staphylococcus aureus*, guaranteeing that antibiotics are only released when bacteria are present. Engineered liposomes have been used as decoy targets to trap bacterial toxins in an antibiotic-free method.[36] In a mouse bacterial septicemia model, this greatly enhanced survival. The first clinical trials of this approach on patients with serious *Streptococcal pneumonia* are planned for this year.

However, because identifying the causative germ in time is not always feasible, it is extremely desired to have therapeutic alternatives that operate without the necessity of first recognizing the origin of infection as well as the causing bacteria. Magnetic purification of blood is currently being proven to remove disease-causing components from entire blood quickly.[37,38] Magnetic blood purification involves injecting microscopic magnetic particles customized with capture ligands into the blood as a whole, where they attach to target chemicals. The procedure can be carried out in an extracorporeal environment (akin to hemodialysis) in which cleaned (pathogen-free) blood is circulated again into the body. In recent years, several chemicals have been effectively eliminated from blood in vivo and in vitro (rat model), containing small-molecule medications, heavy metal ions, proteins (namely, cytokines), bacteria and endotoxins.[37-41] Surprisingly, utilizing a mannose-binding lectin, Kang et al[38] exhibited >90% eradication of germs from blood without the necessity for the detection of bacteria in a rodent model before treatment.

Chemically reactive interfaces, as well as the mixture of solid-state characteristics, movement, and changed biodistribution.[42] To reduce negative side effects, therapeutic applications must concentrate on recyclable NPs composed of non-toxic components. Finally, the effective translation of nanotechnology-enabled thought is strongly reliant on tight teamwork between scientists and physicians working in multidisciplinary groups. Collectively, nanotechnology-based techniques provide a plethora of options and enormous potential for enhanced diagnosis and cure of bacterial diseases and beyond. It is now our responsibility to take these advances in technology and safely apply them.

Bio-Kil nanotechnology-based antimicrobial strategies utilized in ICU. Hospitals face escalating costs as more individuals suffer healthcare-associated illnesses (HAI) and hospital admissions lengthen.[43,44] Healthcare-associated illnesses infections are spread by droplets, air, and staff handshake. Droplets, air, and staff hand contact all contribute to the transmission of HAI infections.[45,46] As reported in the previous

studies, surfaces of hospitalized patients infected with or colonized with VRE, these microorganisms are more likely to contaminate MRSA or *Staphylococcus aureus*.[46,47] This demonstrates that patients can spread illnesses like VRE and MRSA to their environments. Even though hand cleaning has been emphasized in hospitals across the globe, additional steps are required to minimize colonization hospital density environment, which is predicted to have a substantial impact on lowering HAI prevalence and breaking the chain of infection.[48,49]

Bio-Kil (Cargico Group, Taiwan) is an antibacterial quaternary ammonium compound (QAC) consisting of inorganic metal elements. Infectious agents are attracted to Bio-Kil molecules because of their strong electric field and excellent attaching structure. Their high electrical charge damages the protein membranes of microorganisms, eradicating microbes.[49] The Bio-Kil forms a covalent, long-lasting bond with the surface of the textile fiber. Despite 50 launderings, the item remains over 90% of its antimicrobial activity.[50] To keep long-lasting bactericidal action, the cure must be repeated every 3-6 months, depending on how frequently textiles are laundered.[50] In the same way, The Bio-Kil® forms a direct covalent bond with ICU device surfaces, such as workplaces, desktops, nurses' areas, keyboards for computers, phones, and surfaces near patients, providing long-lasting bacterial activity. Decreasing the number of microorganisms in the hospital setting decreases the likelihood of bacterial contamination of equipment, surrounds, and linens, lowering the possibility of HAIs as a result of bacterial colonization.[50] When air passes via a Bio-Kil-treated system, it makes contact with the platform, where the germs are killed by a catalytic reaction.[49] As a result, the air as it circulates is constantly cleansed, reducing the amount of bacteria.

The Bio-Kil significantly reduced the number of germs in the ICU. Keeping a safe environment and infection-control techniques in hospital settings is critical to avoiding HAI.[51] The majority of HAIs are caused by colonization and illnesses caused by *Endogenous flora*, although outside environmental organisms have been overlooked as a minor HAI risk for decades.[52,53] In the meantime, cross-transmission through direct physician-patient connection has a major impact on HAI caused by exogenous infections.[52] Hands washing has been an important step and preventative action in HAI treatment since Semmelweis' time.[48] In practice, though, achieving a compliance percentage of 30% has always been difficult.[7,51]

Following SARS, the washing of hands campaign was demonstrated to be the most economical and suitable of the numerous disease control packages and imposed a zero-tolerance rule.[51,54] It has also led to a decrease in nosocomial infections triggered by MRSA.[55] The number of occurrences has increased, in current years, of MDR outbreaks, namely, carbapenem or VRE multidrug resistance or *Acinetobacter baumannii*.[46,47,49,52,56] According to the investigation, HAI unintentional communication in relation to the patient's or hospital's environment resulted in transmission from clinicians to patients' surroundings. Ohl et al[57] hypothesized a link between microorganism transfer to patients and medical personnel (HCWs) who avoid washing their hands after handling textiles. In recent times, environmental disinfection has been emphasized to make up for inadequate hand hygiene practices. In addition to reducing the risk of multidrug-resistant organisms (MDRO) spreading from a former inhabitant to a new inhabitant, the space is cleaned when each patient has left.[53,58] Cleaning a patient's bed and surrounds is critical to MDR management.[49,52] However, there is always a threat to quality inconsistency in hand surface cleaning as well as disinfecting due to insufficiently accomplished processes or, perhaps, the untrained hands of domestic workers.[48,49] The use of Bio-Kil nanotechnology or colonization in ICU patients may substantially decrease the number of microorganisms in the surroundings and the incidence of infectious illnesses (which includes surfaces, air, and textiles).

Nanotechnology-based bactericides and SARS-CoV-2 detectors in the healthcare sector. The COVID-19 pandemic, which is still ongoing, has demonstrated to us that we are limited in facing off with respiratory viral diseases. Indeed, SARS-CoV-2 has been spreading around the world to more than 215 countries, resulting in approximately 674,003,861 confirmed cases with 6,862,846 deaths caused by this virus (the Johns Hopkins University Coronavirus Resource Centre). This is where the immune system comes into play, which is highly important for preventing the body from such a disease. However, people who have a weakened immune system and other underlying health problems like heart disease, diabetes, or other major illnesses are at an increased risk. They are dependent upon various measures, like hand sanitizers, immune boosters, face masks, and the dose of recommended medications that are at their priority.[59] Nanotechnology-based antiviral substances and coatings can be used to inhibit the spread of SARS-CoV-2 using infectious substances.[60] Investigators from all around the world have carried out significant advances in the creation of COVID-19 preventive measures. However, the progress of therapies or vaccinations continues to encounter challenges, such

as regulatory issues, production on a large, and public deployments.[61] The global response will take months before an outbreak can be established. Furthermore, we must prepare for the possibility of a 2nd and possibly 3rd wave of the virus, necessitating the growth of different techniques to boost our immune system not just against COVID-19 although additional viral infections are having the ability to cause pandemics. The solution to this problem is the current stage of our technical progress, especially in nanotechnology. Significant effort has been put towards developing nanotechnology-based vaccinations or antiviral medications to combat SARS-CoV-2; though, at the most basic level, none are accessible due to prolonged and demanding regulatory procedures.[62] Given the many mechanisms of coronavirus propagation (via cough, biofluids, or drops of respiratory fluid), one technique for combatting the virus is to sanitize the skin, air, and adjacent surfaces (**Figure 2**).

Chemical disinfectants were used to disinfect and sterilize (namely, alcohols, chlorines, peroxides, and quaternary amines), which are useful against a wide range of disorders.[63] The majority of chemical disinfectants have restrictions, such as the requirement for high concentrations to destroy viruses, a progressive loss in efficacy over time, and major environmental and human health hazards. Similarly, NPs, such as silver, copper and titanium dioxide (TiO2). For this reason, metallic NPs have been the subject of great interest to scientists for many years. They are very useful both in engineering and the field of biology due to the very significant potential derived from the scale of the phenomenon.[64] Nanoparticles are considered substitutes due to their intrinsic versatility of antiviral and antibacterial efficacy, durability, and efficacy at significantly lower doses.[65,66] For instance, preliminary investigations demonstrated that a silver nanocluster/ silica composite face mask covering had antiviral effects against SARS-CoV-2.[67] NanoTechSurface of Italy developed a self-sterilizing disinfecting surface solution based on TiO2 and silver ions. Similarly, FN Nano Inc. developed a photocatalytic coating (light-mediated) based on TiO2 NPs that, when exposed to light, may destroy organic molecules having viral defences on their surface by decomposing the chemical constituents. Nanoparticles might potentially be integrated into respiratory face masks to boost their inhibiting impact.[68] A recyclable cartridge filter made of cellulose nanofibers that can screen particles less than 100 nm was developed by researchers.[69] Graphene NPs might also be employed to adsorb and eliminate SARS-CoV-2 due to their unique chemistry, physical properties, and surface-to-volume ratios.[70] The LIGC

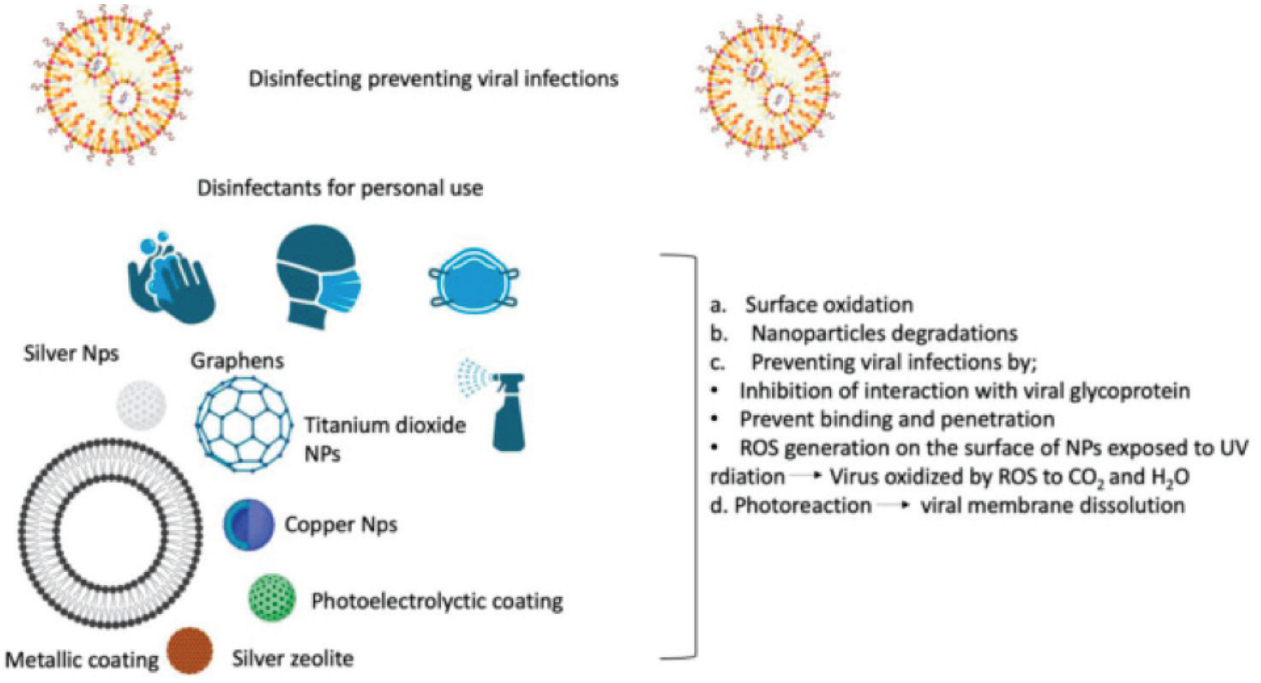

Figure 2 - Nanotechnology-based viral disinfectant safeguards against severe acute respiratory syndrome coronavirus 2 by reducing viral multiplication on surfaces, air, and in preventive devices. Created with Biorender. NPs: nanoparticles ROS: reactive oxygen species, UV: ultraviolet, CO_2: carbon dioxide, H_2O: water

Applications Ltd. developed a recyclable mask with an electrical conductivity that attracts and destroys microorganisms.[71] Graphene-based NPs can be used in biological applications like personal safety devices against the continuing COVID-19 epidemic.[72] Earlier research found that ferroptosis played a role in cell death caused by RAS-selective lethal 3 (RSL3), suggesting ferroptosis might be a common and dynamic type of tumour cell death.[73]

Nanotechnology and surgical applications. According to some, medicine will evolve more in the next 20 years than it has in the previous 2000. This might be due to technological breakthroughs and the current development of nanotechnology. Richard Feynman, a quantum theorist and Nobel winner, developed the idea of nanotechnology. Nanotechnology is concerned with the control and manipulation of NPs with a minimum of one dimension less than 100 nanometers. Nanoparticles have been effectively assimilated into current surgical practice, giving revolutionary less invasive imaging tools, enhanced medication transport systems, and a foundation for the production of designed organs. This paper summarises a few of the most recent developments.[74]

In addition to these, existing uses, the incorporation of nanosized robots into surgical and medical practice has great potential. Nanorobotics involves the creation of smart small devices that may then be used for diagnostic and treatment purposes.[75] Though slightly invasive, image-guided endovascular treatments are well recognized in heart operation, catheterization is confined by the diameter of the artery. Vessels with a diameter in the region of 4-5 m, like those found in capillary beds, are beyond the capabilities of present technology, but nanorobots may be able to access them.[76] Nanoparticles have a high surface area to volume ratio, which deliberates mechanical, optical, magnetic, and chemical capabilities better than the original components. They are classified into 3 types. Fullerenes are carbon allotropes that may take on many forms. Carbon nanotubes, silicones, nanoclays, and innovative artificial nanocomposites that include polyhedral oligomeric silsesquioxane (POSS) are examples of fillers.[77] The latter provides the composite with enhanced physical qualities like as oxidative resistance and mechanical strength. Polyhedral oligomeric silsesquioxane's amphiphilic character enhances the nanocomposite's capacity to facilitate cell adhesion and development making it ideal for tissue engineering.[78] The manufacture of surgical grafts using nanomaterials, imaging, drug delivery, and the development of tissue engineering products like scaffolds with enhanced material-cell interactions are now the most significant applications of nanotechnology for surgeons. One example of this is the development of a scaffold for the transportation of stem cells to replace impaired retinal pigmented epithelium cells in age-related macular degeneration.[79]

There are restrictions to current imaging technology for cancer detection and staging. The emission spectra of fluorescent semiconductor nanocrystals (QDs) range from ultraviolet to near-infrared and are narrow and size-tunable.[80,81] Magnetic resonance imaging (MRI) can be employed using QDs connected to paramagnetic ions. The integration makes use of QD fluorescence's high level of sensitivity and MRI's great spatial resolution, operating synergistically to improve data dependability.[82] Fluorescent semiconductor nanocrystals can be attached to particular peptides to selectively scan cancer cells. This idea might be useful in treatment. In experimental settings, QDs containing bioactive compounds (growth peptides, plasmid DNA) have been demonstrated to extend the survival of stem cells.[83]

Pharmacological substances conjugated to nanocarriers might be employed for targeted medication delivery to increase effectiveness and minimize systemic toxicity. Liposomes and drug-conjugated NPs for cancer therapy are of particular importance among nanoscaled drug delivery technologies.[84]

Nanotechnology has a diverse set of applications in the emerging area of tissue engineering. Stents or artificial bypass implants may be used to treat occlusive vascular disorders. Graft failure is frequently associated with endothelial dysfunction, which results in thrombus development and subsequent consequences.[85] For endothelial renewal, another type of scaffold employs biomimetic nanofibers. Nanofibers have a high tensile strength when linked and offer an axis for endothelial cell movement and accumulation. Carbon nanotubes add conductivity to the scaffold, enabling external electric fields to be used to regulate cell behavior.

Recent scaffolds for bone substitution include drawbacks such as poor mechanical strength, restricted cellular development, and low osseointegration potential.[86] Long-term health ramifications of NPs usage must be properly explored to effectively harness nanotechnology while minimizing any hazardous effects. The size of NPs, for instance, may indicate that the blood-brain barrier might be overcome. The NPs with high surface area-to-volume ratios are physiologically active. This might result in inflammation and an increase in oxidative stress. Moreover, Scaffolds in a position giving the required nutrients and oxygen to

tightly packed cells in complete organs must be designed for effective tissue engineering. Nanotechnological advancements need a multidisciplinary strategy including engineering, chemistry, and biomedicine. Only the surgeon can put these concepts into action.[87]

Challenges and future perspective. Regarding the side effects linked to nanotechnology-based bactericides in healthcare, several studies have highlighted potential issues. Research has shown that certain nanomaterials used in these bactericides could pose toxicological risks, potentially compromising patient safety.[88] The main worries stem from the way NPs may interact with human cells and tissues, which could cause unwanted side effects. Like with conventional antimicrobials, there's also a fear that pathogens may become resistant to treatments derived from nanotechnology, possibly resulting in tougher strains of bacteria and viruses.[89]

Recognition, therapy, and prevention of infectious illnesses have been difficult issues for humanity from its inception. Nanotechnology has substantial implications for tumor diagnosis and cure. With the achievement of NPs in cancer treatment using genes and cellular treatment, investigators are currently focusing on broadening the healing route of NPs beyond malignancies. In this endeavor, one possible field is the employment of nanotechnology in the field of healthcare as an antiseptic for several infectious illnesses. A silver nanocluster silica/face mask with a composite covering, for example, shows antiviral impact against SARS-CoV-2. Different non-metallic and metallic NPs are progressively being employed for injury rehabilitation and infection treatment. The Bio-Kil, an antibacterial composed of inorganic metal and organic elements, has been shown to reduce environmental bacterial load and multidrug-resistant pathogens in ICU.

So far, several dialysis procedures have been used in the ICU and hospitals to eliminate hazardous compounds from the body. The primary goal of this method is great protection with little toxicity.[90] Surfaces with very selective functionalization developed by nanotechnologies will be at the heart of this revolution to gather and precisely analyze small amounts of nucleic acid, cellular, or protein biomarkers.[91] Nanoscale sensors have high spatial and temporal resolutions and inserted microfluidic gadgets function as "liquid biopsies" quickly and give the doctor the information required to change therapy. When these chemical discoveries are combined with more common physical data such as the rate of respiration, temperature, breathing, cell oxygenation, and microcirculation, they give an extraordinary insight into an individual's status at the molecular, tissue, and cellular levels. Such quantitative information regarding investigation linkages is carried out possible by closed-loop feedback control systems, the operational, anesthesia, and "electro pharmaceutical" interruption.

To accurately target the region of activity and transport their treatment payload there at the required pace, "Nanobots" circulate in the bloodstream like "Exocet" rockets, minimizing cell collateral harm triggered by the negative effects of pharmaceuticals.[49] This supply is originally determined by the location and quantity of a relevant biomarker. This capacity is offered in a unique technique by the use of nanostructured, "biofunctionalized" lines built of "smart" 4D ingredients.[56] These boundaries are completely biocompatible and have features that can alter over time in response to environmental factors. A single instance is the development of surfaces containing NPs that modulate the biocompatibility of extracorporeal circulation of blood.[92] Future improvements in drug transport, cell regeneration, artificial organ production, and other fields are expected. The majority of the already commercialized applications of nanotechnology in medicine are oriented at drug delivery, permitting novel modes of action increased bioavailability, and targeting of established medicinal ingredients, and implementation concerns abound. Unique nanotechnological uses, containing nanostructures that let transport across biological barriers, completely inserted nanoelectronic sensing systems, nanoprobe remote control, and multifunctional chemical structures for delivering medications and disease targeting, will be needed in the coming years.

The degree of interest and speed of NPs investigations, along with the biophysical modification of visible surfaces of live tissue to limit infection transmission, is cause for hope. To more fully comprehend the relationships between coated biofilms, hosts, and surfaces, further information on the toxicity and NPs pharmacokinetics in vivo applications are now necessary. Before any clinical application, more research is needed. Microbiologists and nanoengineers must work together to produce more efficient and broadly acceptable MDR treatment solutions. Once completed, it will open the door for larger-scale successful implementation in the hospital sector. Furthermore, economic approaches for the welfare of humanity must be devised. This literature review intends to increase alertness of the magnitude of the issues faced by nosocomial infections, as well as the potential role of nanotechnology in combatting them.

In conclusion, the latest publications have emphasized the advancement of several nanotechnologies in nanotherapeutic therapies and the healing of wounds,

which are impressively multifunctional. Understanding the physical and chemical features of systems on the nanoscale, their anticipated behavior, and their hazardous consequences on the human body is complicated. Moreover, because massive synthesis and NPs and polymer refinement are often difficult, the Food and Drug Administration's need for scaffolds of great purity and NPs allowed for human use creates a difficulty. Therefore, innovative methods of analysis and artificial devices are always needed to integrate nanotechnology-based procedures into clinical practice. Various efforts are also necessary to equip chronic injury treatment in terms of area and targeted effectiveness to avoid unwanted occurrences and interventions that might hamper the biological behavior of nanotechnologies in the human body.

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References

1. Wong HR. Intensive care medicine in 2050: precision medicine. *Intensive Care Med* 2017; 43: 1507-1509.
2. Martin-Loeches I, Perner A. Focus on infection and sepsis in intensive care patients. *Intensive Care Med* 2016; 42: 491-493.
3. Zilahi G, Artigas A, Martin-Loeches I. What's new in multidrug-resistant pathogens in the ICU? *Ann Intensive Care* 2016; 6: 96.
4. Perner A, Rhodes A, Venkatesh B, Angus DC, Martin-Loeches I, Preiser JC, et al. Sepsis: frontiers in supportive care, organisation and research. *Intensive Care Med* 2017; 43: 496-508.
5. Martin-Loeches I, Deja M, Koulenti D, Dimopoulos G, Marsh B, Torres A, et al. Potentially resistant microorganisms in intubated patients with hospital-acquired pneumonia: the interaction of ecology, shock and risk factors. *Intensive Care Med* 2013; 39: 672-681.
6. Nwankire CE, Venkatanarayanan A, Glennon T, Keyes TE, Forster RJ, Ducrée J. Label-free impedance detection of cancer cells from whole blood on an integrated centrifugal microfluidic platform. *Biosens Bioelectron* 2015; 68: 382-389.
7. Singh M, Tong Y, Webster K, Cesewski E, Haring AP, Laheri S, et al. 3D printed conformal microfluidics for isolation and profiling of biomarkers from whole organs. *Lab Chip* 2017; 17: 2561-2571.
8. Beitler JR, Goligher EC, Schmidt M, Spieth PM, Zanella A, Martin-Loeches I, et al. Personalized medicine for ARDS: the 2035 research agenda. *Intensive Care Med* 2016; 42: 756-767.
9. Sakr Y, Lobo SM, Moreno RP, Gerlach H, Ranieri VM, Michalopoulos A, et al. Patterns and early evolution of organ failure in the intensive care unit and their relation to outcome. *Crit Care* 2012; 16: R222.
10. Bohmer N, Demarmels N, Tsolaki E, Gerken L, Keevend K, Bertazzo S, et al. Removal of cells from body fluids by magnetic separation in batch and continuous mode: influence of bead size, concentration, and contact time. *ACS Appl Mater Interfaces* 2017; 9: 29571-29579.
11. Basit H, Maher S, Forster RJ, Keyes TE. Electrochemically triggered release of reagent to the proximal leaflet of a microcavity supported lipid bilayer. *Langmuir* 2017; 33: 6691-6700.
12. Gobbo OL, Sjaastad K, Radomski MW, Volkov Y, Prina-Mello A. Magnetic nanoparticles in cancer theranostics. *Theranostics* 2015; 5: 1249-1263.
13. Haque M, Sartelli M, McKimm J, Abu Bakar M. Health care-associated infections - an overview. *Infect Drug Resist* 2018; 11: 2321-2333.
14. Revelas A. Healthcare - associated infections: a public health problem. *Niger Med J* 2012; 53: 59-64.
15. Angus DC, van der Poll T. Severe sepsis and septic shock. *N Engl J Med* 2013; 369: 840-851.
16. Rittirsch D, Hoesel LM, Ward PA. The disconnect between animal models of sepsis and human sepsis. *J Leukoc Biol* 2007; 81: 137-143.
17. Kelly KL, Coronado E, Zhao LL, Schatz GC. The optical properties of metal nanoparticles: the influence of size, shape, and dielectric environment. *ACS Publications* 2003: 668-677.
18. Atiyeh BS, Costagliola M, Hayek SN, Dibo SA. Effect of silver on burn wound infection control and healing: review of the literature. *Burns* 2007; 33: 139-148.
19. Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. *Biotechnol Adv* 2009; 27: 76-83.
20. Wong KK, Liu X. Silver nanoparticles - the real "silver bullet" in clinical medicine? *MedChemComm* 2010; 1: 125-131.
21. Munger MA, Radwanski P, Hadlock GC, Stoddard G, Shaaban A, Falconer J, et al. In vivo human time-exposure study of orally dosed commercial silver nanoparticles. *Nanomedicine* 2014; 10: 1-9.
22. Loher S, Schneider OD, Maienfisch T, Bokorny S, Stark WJ. Micro-organism-triggered release of silver nanoparticles from biodegradable oxide carriers allows preparation of self-sterilizing polymer surfaces. *Small* 2008; 4: 824-832.
23. Kollef MH, Afessa B, Anzueto A, Veremakis C, Kerr KM, Margolis BD, et al. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. *JAMA* 2008; 300: 805-813.
24. Pierrakos C, Vincent JL. Sepsis biomarkers: a review. *Crit Care* 2010; 14: R15.
25. Vincent JL, Teixeira L. Sepsis biomarkers. Value and limitations. *Am J Respir Crit Care Med* 2014; 190: 1081-1082.
26. Howes PD, Chandrawati R, Stevens MM. Bionanotechnology. Colloidal nanoparticles as advanced biological sensors. *Science* 2014; 346: 1247390.
27. Wang S, Bi S, Wang Z, Xia J, Zhang F, Yang M, et al. A plasmonic aptasensor for ultrasensitive detection of thrombin via arrested rolling circle amplification. *Chem Commun (Camb)* 2015; 51: 7927-7930.
28. De la Rica R, Stevens MM. Plasmonic ELISA for the ultrasensitive detection of disease biomarkers with the naked eye. *Nat Nanotechnol* 2012; 7: 821-824.
29. Chapman R, Lin Y, Burnapp M, Bentham A, Hillier D, Zabron A, et al. Multivalent nanoparticle networks enable point-of-care detection of human phospholipase-A2 in serum. *ACS Nano* 2015; 9: 2565-2573.
30. Geissler D, Charbonnière LJ, Ziessel RF, Butlin NG, Löhmannsröben HG, Hildebrandt N. Quantum dot biosensors for ultrasensitive multiplexed diagnostics. *Angew Chem Int Ed Engl* 2010; 49: 1396-1401.

31. Lowe SB, Dick JA, Cohen BE, Stevens MM. Multiplex sensing of protease and kinase enzyme activity via orthogonal coupling of quantum dot-peptide conjugates. *ACS Nano* 2012; 6: 851-857.
32. Omri A, Suntres ZE, Shek PN. Enhanced activity of liposomal polymyxin B against *Pseudomonas aeruginosa* in a rat model of lung infection. *Biochem Pharmacol* 2002; 64: 1407-1413.
33. Walsh TJ, Finberg RW, Arndt C, Hiemenz J, Schwartz C, Bodensteiner D, et al. Liposomal amphotericin B for empirical therapy in patients with persistent fever and neutropenia. National Institute of Allergy and Infectious Diseases Mycoses Study Group. *N Engl J Med* 1999; 340: 764-771.
34. Drulis-Kawa Z, Dorotkiewicz-Jach A. Liposomes as delivery systems for antibiotics. *Int J Pharm* 2010; 387: 187-198.
35. Baier G, Cavallaro A, Vasilev K, Mailänder V, Musyanovych A, Landfester K. Enzyme responsive hyaluronic acid nanocapsules containing polyhexanide and their exposure to bacteria to prevent infection. *Biomacromolecules* 2013; 14: 1103-1112.
36. Henry BD, Neill DR, Becker KA, Gore S, Bricio-Moreno L, Ziobro R, et al. Engineered liposomes sequester bacterial exotoxins and protect from severe invasive infections in mice. *Nat Biotechnol* 2015; 33: 81-88.
37. Herrmann IK, Urner M, Koehler FM, Hasler M, Roth-Z'graggen B, Grass RN, et al. Blood purification using functionalized core/shell nanomagnets. *Small* 2010; 6: 1388-1392.
38. Kang JH, Super M, Yung CW, Cooper RM, Domansky K, Graveline AR, et al. An extracorporeal blood-cleansing device for sepsis therapy. *Nat Med* 2014; 20: 1211-1216.
39. Lee HY, Bae DR, Park JC, Song H, Han WS, Jung JH. A selective fluoroionophore based on BODIPY-functionalized magnetic silica nanoparticles: removal of Pb2+ from human blood. *Angew Chem Int Ed Engl* 2009; 48: 1239-1243.
40. Herrmann IK, Schlegel A, Graf R, Schumacher CM, Senn N, Hasler M, et al. Nanomagnet-based removal of lead and digoxin from living rats. *Nanoscale* 2013; 5: 8718-8723.
41. Lee JJ, Jeong KJ, Hashimoto M, Kwon AH, Rwei A, Shankarappa SA, et al. Synthetic ligand-coated magnetic nanoparticles for microfluidic bacterial separation from blood. *Nano Lett* 2014; 14: 1-5.
42. Stark WJ. Nanoparticles in biological systems. *Angew Chem Int Ed Engl* 2011; 50: 1242-1258.
43. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol* 1985; 121: 182-205.
44. Haley RW, White JW, Culver DH, Hughes JM. The financial incentive for hospitals to prevent nosocomial infections under the prospective payment system. An empirical determination from a nationally representative sample. *JAMA* 1987; 257: 1611-1614.
45. Boyce JM. Environmental contamination makes an important contribution to hospital infection. *J Hosp Infect* 2007; 65: 50-54.
46. Oie S, Suenaga S, Sawa A, Kamiya A. Association between isolation sites of methicillin-resistant *Staphylococcus aureus* (MRSA) in patients with MRSA-positive body sites and MRSA contamination in their surrounding environmental surfaces. *Jpn J Infect Dis* 2007; 60: 367-369.
47. Hardy KJ, Oppenheim BA, Gossain S, Gao F, Hawkey PM. A study of the relationship between environmental contamination with methicillin-resistant *Staphylococcus aureus* (MRSA) and patients' acquisition of MRSA. *Infect Control Hosp Epidemiol* 2006; 27: 127-132.
48. Pritchard RC, Raper RF. Doctors and handwashing: instilling Semmelweis' message. *Med J Aust* 1996; 164: 389-390.
49. Hsueh PR, Huang HC, Young TG, Su CY, Liu CS, Yen MY. Bacteria killing nanotechnology Bio-Kil effectively reduces bacterial burden in intensive care units. *Eur J Clin Microbiol Infect Dis* 2014; 33: 591-597.
50. Chen YL, Yeh MY, Huang SY, Liu CM, Sun CC, Lu HF, et al. Feasibility study for epidemic prevention and control in a regional hospital. *Mol Med Rep* 2012; 5: 859-865.
51. Yang L, Yu S, Lin H, Chang Y, Wang L, Chun C, et al. The effect of applying quality control circle in reducing nosocomial infections. *Nosocom Infect Control J* 2001; 11: 137-147.
52. Weber DJ, Rutala WA, Miller MB, Huslage K, Sickbert-Bennett E. Role of hospital surfaces in the transmission of emerging health care-associated pathogens: norovirus, *Clostridium difficile*, and *Acinetobacter species*. *Am J Infect Control* 2010; 38: S25-S33.
53. Passaretti CL, Otter JA, Reich NG, Myers J, Shepard J, Ross T, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. *Clin Infect Dis* 2013; 56: 27-35.
54. Haley RW, Morgan WM, Culver DH, White JW, Emori TG, Mosser J, et al. Update from the SENIC project. Hospital infection control: recent progress and opportunities under prospective payment. *Am J Infect Control* 1985; 13: 97-108.
55. Tseng SH, Lee CM, Lin TY, Chang SC, Chuang YC, Yen MY, et al. Combating antimicrobial resistance: antimicrobial stewardship program in Taiwan. *J Microbiol Immunol Infect* 2012; 45: 79-89.
56. Hsueh PR, Teng LJ, Chen CY, Chen WH, Yu CJ, Ho SW, et al. Pandrug-resistant *Acinetobacter baumannii* causing nosocomial infections in a university hospital, Taiwan. *Emerg Infect Dis* 2002; 8: 827-832.
57. Ohl M, Schweizer M, Graham M, Heilmann K, Boyken L, Diekema D. Hospital privacy curtains are frequently and rapidly contaminated with potentially pathogenic bacteria. *Am J Infect Control* 2012; 40: 904-906.
58. Nseir S, Blazejewski C, Lubret R, Wallet F, Courcol R, Durocher A. Risk of acquiring multidrug-resistant Gram-negative bacilli from prior room occupants in the intensive care unit. *Clin Microbiol Infect* 2011; 17: 1201-1208.
59. Hu TY, Frieman M, Wolfram J. Insights from nanomedicine into chloroquine efficacy against COVID-19. *Nat Nanotechnol* 2020; 15: 247-249.
60. Imani SM, Ladouceur L, Marshall T, Maclachlan R, Soleymani L, Didar TF. Antimicrobial nanomaterials and coatings: current mechanisms and future perspectives to control the spread of viruses including SARS-CoV-2. *ACS Nano* 2020; 14: 12341-12369.
61. Dourado E. Accelerating availability of vaccine candidates for COVID-19. [Updated 2020; accessed 3 Feb 2024]. Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3564664
62. Itani R, Tobaiqy M, Al Faraj A. Optimizing use of theranostic nanoparticles as a life-saving strategy for treating COVID-19 patients. *Theranostics* 2020; 10: 5932-5942.

63. Fathizadeh H, Maroufi P, Momen-Heravi M, Dao S, Köse Ş, Ganbarov K, et al. Protection and disinfection policies against SARS-CoV-2 (COVID-19). ***Infez Med*** 2020; 28: 185-191.
64. Mody VV, Siwale R, Singh A, Mody HR. Introduction to metallic nanoparticles. ***J Pharm Bioallied Sci*** 2010; 2: 282-289.
65. Shahzadi S, Zafar N, Sharif R. Antibacterial activity of metallic nanoparticles. [Updated 2018; accessed 5 Feb 2024]. Available from: https://www.intechopen.com/chapters/59058
66. Sportelli MC, Izzi M, Kukushkina EA, Hossain SI, Picca RA, Ditaranto N, et al. Can nanotechnology and materials science help the fight against SARS-CoV-2? ***Nanomaterials (Basel)*** 2020; 10: 802.
67. Balagna C, Perero S, Percivalle E, Nepita EV, Ferraris M. Virucidal effect against coronavirus SARS-CoV-2 of a silver nanocluster/silica composite sputtered coating. ***Open Ceramics*** 2020; 1: 100006.
68. Weiss C, Carriere M, Fusco L, Capua I, Regla-Nava JA, Pasquali M, et al. Toward nanotechnology-enabled approaches against the COVID-19 pandemic. ***ACS Nano*** 2020; 14: 6383-6406.
69. Widdowson N. New mask material can remove virus-size nanoparticles. [Updated 2020; accessed 05 Feb 2024]. Available from: https://phys.org/news/2020-04-mask-material-virus-size-nanoparticles.html
70. Palmieri V, Papi M. Can graphene take part in the fight against COVID-19? ***Nano Today*** 2020; 33: 100883.
71. Talebian S, Wallace GG, Schroeder A, Stellacci F, Conde J. Nanotechnology-based disinfectants and sensors for SARS-CoV-2. ***Nat Nanotechnol*** 2020; 15: 618-621.
72. Gungordu Er S, Tabish TA, Edirisinghe M, Matharu RK. Antiviral properties of porous graphene, graphene oxide and graphene foam ultrafine fibers against Phi6 bacteriophage. ***Front Med (Lausanne)*** 2022; 9: 1032899.
73. Sui X, Zhang R, Liu S, Duan T, Zhai L, Zhang M, et al. RSL3 drives ferroptosis through GPX4 inactivation and ROS production in colorectal cancer. ***Front Pharmacol*** 2018; 9: 1371.
74. Singh S, Singh A. Current status of nanomedicine and nanosurgery. ***Anesth Essays Res*** 2013; 7: 237-242.
75. Chang TM. 50th anniversary of artificial cells: their role in biotechnology, nanomedicine, regenerative medicine, blood substitutes, bioencapsulation, cell/stem cell therapy and nanorobotics. ***Artif Cells Blood Substit Immobil Biotechnol*** 2007; 35: 545-554.
76. Martel S, Felfoul O, Mathieu JB, Chanu A, Tamaz S, Mohammadi M, et al. MRI-based medical nanorobotic platform for the control of magnetic nanoparticles and flagellated bacteria for target interventions in human capillaries. ***Int J Rob Res*** 2009; 28: 1169-1182.
77. Al Sheheri SZ, Al-Amshany ZM, Al Sulami QA, Tashkandi NY, Hussein MA, El-Shishtawy RM. The preparation of carbon nanofillers and their role on the performance of variable polymer nanocomposites. ***Des Monomers Polym*** 2019; 22: 8-53.
78. Ayandele E, Sarkar B, Alexandridis P. Polyhedral oligomeric silsesquioxane (POSS)-containing polymer nanocomposites. ***Nanomaterials (Basel)*** 2012; 2: 445-475.
79. Hasan A, Morshed M, Memic A, Hassan S, Webster TJ, Marei HE. Nanoparticles in tissue engineering: applications, challenges and prospects. ***Int J Nanomedicine*** 2018; 13: 5637-5655.
80. Yaghini E, Seifalian AM, MacRobert AJ. Quantum dots and their potential biomedical applications in photosensitization for photodynamic therapy. ***Nanomedicine (Lond)*** 2009; 4: 353-363.
81. Mahmoud W, Sukhanova A, Oleinikov V, Rakovich YP, Donegan JF, Pluot M, et al. Emerging applications of fluorescent nanocrystals quantum dots for micrometastases detection. ***Proteomics*** 2010; 10: 700-716.
82. Jennings LE, Long NJ. 'Two is better than one'--probes for dual-modality molecular imaging. ***Chem Commun (Camb)*** 2009: 3511-3524.
83. Ferreira L, Karp JM, Nobre L, Langer R. New opportunities: the use of nanotechnologies to manipulate and track stem cells. ***Cell Stem Cell*** 2008; 3: 136-146.
84. Malam Y, Loizidou M, Seifalian AM. Liposomes and nanoparticles: nanosized vehicles for drug delivery in cancer. ***Trends Pharmacol*** Sci 2009; 30: 592-599.
85. De Mel A, Jell G, Stevens MM, Seifalian AM. Biofunctionalization of biomaterials for accelerated in situ endothelialization: a review. ***Biomacromolecules*** 2008; 9: 2969-2979.
86. Zawadzak E, Bil M, Ryszkowska J, Nazhat SN, Cho J, Bretcanu O, et al. Polyurethane foams electrophoretically coated with carbon nanotubes for tissue engineering scaffolds. ***Biomed Mater*** 2009; 4: 015008.
87. Waheed S, Li Z, Zhang F, Chiarini A, Armato U, Wu J. Engineering nano-drug biointerface to overcome biological barriers toward precision drug delivery. ***J Nanobiotechnology*** 2022; 20: 395.
88. Bruna T, Maldonado-Bravo F, Jara P, Caro N. Silver nanoparticles and their antibacterial applications. ***Int J Mol Sci*** 2021; 22: 7202.
89. Mubeen B, Ansar AN, Rasool R, Ullah I, Imam SS, Alshehri S, et al. Nanotechnology as a novel approach in combating microbes providing an alternative to antibiotics. ***Antibiotics (Basel)*** 2021; 10: 1473.
90. Wu MJ, Feng YS, Sung WP, Surampalli RY. Quantification and analysis of airborne bacterial characteristics in a nursing care institution. ***J Air Waste Manag Assoc*** 2011; 61: 732-739.
91. Wong V, Staniforth K, Boswell TC. Environmental contamination and airborne microbial counts: a role for hydroxyl radical disinfection units? ***J Hosp Infect*** 2011; 78: 194-199.
92. Wang JL, Chen ML, Lin YE, Chang SC, Chen YC. Association between contaminated faucets and colonization or infection by nonfermenting gram-negative bacteria in intensive care units in Taiwan. ***J Clin Microbiol*** 2009; 47: 3226-3230.