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Research and Military Health: *disruptive technology anti COVID-19* from early diagnosis to environmental safety

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In scientific research, the relationship with companies, the use of technological and economic resources were the arguments for center of the conference organized by the General Inspectorate of Military Health entitled "**Research and Military Health: anti COVID-19 disruptive technology from early diagnosis to environmental safety**". At the event, held on June 30th 2021 at the prestigious headquarters of the Centro Alti Studi per la Difesa in Palazzo Salviati, the most eminent representatives of the Ministry of Defense took part, first of all the Minister, as well as various exponents of the scientific and industrial world.

In greeting the participants, the Hon. *Giuseppe Fioroni*, Advisor to the Minister of Defense for Military Health, thanked the Dicastery for the important resources allocated to health both to face the pandemic and to progress on the path of innovation and research. And that this path is currently a priority was also reiterated by Gen. CA *Carmine Masiello*, Deputy Chief of Defense Staff. "*The combination of military research and civilian research is now an indispensable requirement*" The general stressed. Similarly, the close collaboration between Military Health and civilian companies must be considered. "*It is necessary* "Continued Masiello" *team up in front of scenarios to seek original solutions for transnational problems. The NATO research project called DIANA, of which Italy is a partner, was conceived in this sense*".

From left: Hon. *Lorenzo Guerini*, Minister of Defense, the Hon. *Giuseppe Fioroni*, Advisor to the Minister of Defense for Military Health and Lt. Gen. *Nicola Sebastiani*, Inspector General of Military Health.

Abstract

Infections, pandemics and antibiotic resistance the effectiveness of non-UV visible light frequencies on bacteria and viruses

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The (post) -antibiotic era and the pandemic era

In four months, COVID-19 has transformed the world.

Thousands of deaths, the entire world population in quarantine and global economic losses quantifiable in trillions of dollars.

There are many lessons we have learned in the last year but what can certainly be considered the most important is that globalization brings not only advantages but also heavy burdens that require adequate interventions: the main global emergencies - from climate change to antibiotic resistance - they are also shared and interconnected and therefore require the need to intervene with equal effort in all countries, especially in developing countries.

The continuous interaction between human beings, the non-respect of the spaces that nature has granted to all the inhabitants of the Earth, the deforestation, the overpopulation have determined a close - but sick - relationship between human beings and nature that created the conditions ideals that allow new - and hitherto unknown - pathogens to pass from animals to humans with the now known phenomenon of *spillover*.

All this led to the beginning of a new era which is now sadly known as the pandemic era.

We should therefore not be surprised if it happens again. There are hundreds of viruses in animals that are ready to "jump" into humans (just think of the H5N8 avian flu) and when this happens there could be an influenza pandemic even much more serious than the one we are experiencing.

And this, albeit with different mechanisms, is not only true for viruses but also for a pandemic that has been with us for many years but which, having not yet had the same impact as Sars-Cov2, is known as a "silent pandemic".

Indeed, well before COVID, the 21st century epidemic was considered - and still is - "antibiotic resistance": a process of genetic mutation of bacteria that leads them to develop a sort of immunity to antibiotics.

Antibiotics have certainly represented one of the most important health discoveries of the past century so much so that Fleming, inventor in 1928 of penicillin which was the first broad-spectrum antibiotic, was awarded the Nobel Prize in 1945 for the enormous impact that his invention would have had for public health (*in truth, the discovery on the bactericidal power of molds is to be attributed to a Doctor of the Health Corps of the Italian Navy, Dr. Vincenzo Tiberio, who already in 1895 had published an article with the results of his experiments in the journal Annali di Igiene Sperimentale).*

With Fleming's penicillin and with the first recovery from a serious infection by a Connecticut nurse in 1942, the so-called "antibiotic era" begins.

From that moment it began to think that humanity would no longer have problems due to bacterial infections because a suitable, more powerful, more effective antibiotic would always be found. But in the following years their excessive use (especially in Italy which is in second place in Europe - after Cyprus - for the deaths from antibiotic resistance) allowed the bacteria to know their enemy better and to develop genetic mutations that make them immune.

In the early 1980s, therefore, the onset of antibiotic resistance gave rise to the so-called “post-antibiotic era”.

Unlike COVID19, "antibiotic resistance" has never been perceived as a global threat despite the numerous alarms launched by the WHO which classified it as "the Epidemic of the 21st century" and launched in 2017 the*Antimicrobial Resistance*

Campaign, disseminating data that pale even when compared to those of COVID: without effective solutions, the number of deaths from antibiotic resistance will grow every year to reach 10 million a year in 2050.
The problem is that the bacteria not only become resistant, they are also able to pass the resistance on to future bacterial populations. And this means that the population of resistant bacteria grows so fast that we can catch infections from resistant pathogens in places of common life from means of transport, to work and leisure places, to school.
Until now, the problem seemed to be relegated to hospital environments where, especially in Italy, the probability for a patient to acquire infections during hospitalization or following transplants, admission to intensive care or complex surgery becomes increasingly higher. And the "Italian risk" is a perceived problem at European level, so much so that in some European countries, at the time of admission, patients who have had contact with Italian hospitals in the previous six months are screened and immediately isolated.
The problem of resistant bacteria has also assumed an important role during the viral pandemic as many scientists have raised the doubt that the anomalous Italian mortality from Coronavirus is to be attributed to the super-bacteria present in hospitals that have assumed greater aggressiveness due to the greater vulnerability of immune systems as a consequence of Coronavirus. It may seem strange to focus on bacteria during a viral pandemic but it must be considered that already during the global influenza pandemic of 1918-1920 most patients died not from the virus itself, but from secondary bacterial pneumonia that spread easily in hospital wards. crowded with the sick, often malnourished and immunosuppressed.
And the problem is certainly aggravated by two factors: the existing antibiotics are now ineffective on the microorganisms for which they were produced and the pharmaceutical companies have stopped investing in the research of new antibiotic molecules due to the short life cycle that makes them unprofitable. .

The continuous and passive sanitation systems

The debate on the pandemic, especially in recent times, has shifted to a topic that is of little relevance to me if we look in perspective: it is not important whether this virus is transmitted more via aerosol or following contact with surfaces because there will be some. others that will have different modes of transmission against which we will have to be prepared.
Therefore, new solutions must be found.
And if for viruses the discovery of the "universal" vaccine can represent a solution (if and when it arrives) for bacterial infections, it seems clear that the solution cannot be sought in increasingly powerful antibiotics but must be sought in new forms of prevention that are more compatible with normal daily living conditions and hopefully effective on both viruses and bacteria.
The new frontier has moved towards the creation, especially in hospitals, of "biosafe environments" that reduce the presence of pathogens and reduce the risk of acquisition and transmission of bacterial and viral infections. And, thanks to the pandemic, it now seems clear that bio-security will also become a standard in everyday life environments.
And it is now clear that "bio-safety" cannot be the destruction of all existing microbes (especially bacteria) with the massive use of chemical detergents and invasive sanitation systems because bacteria are essential for our survival. The pandemic has forced us to consider them enemies but the time will soon come when we will have to return to live with them in a balanced way.
Also for this reason, during the pandemic, "non-emergency" scientific research focused on new systems of continuous sanitation capable of creating environments in which all living beings and microbes can live together, creating that ecosystem in which equilibrium is the founding element of general well-being.
According to the WHO, the principles on which correct environmental sanitation must be based are:

1. Avoid the sterilization of the environments, since the complete elimination of the populations of microorganisms involves the cancellation of the immune system.

2. Reduce the risk of recontamination, which is what happens when a potentially pathogenic microbial population reactivates in environments previously treated with UV-C decontamination systems or chemical disinfectants.
3. Respect the conditions of competitive antagonism between microorganisms, which is achieved not by eliminating all microorganisms in an uncontrolled way, but by targeting mainly pathogenic microorganisms while protecting the creation of stable colonies of "probiotics".
4. Countering the phenomenon of the "resistome", ie blocking the spread of those groups of genes which, through the exchange between microorganisms, allow the acquisition of genetic information capable of developing resistance to antibiotics and chemical disinfectants in the microorganisms themselves .

The sanitizing power of light

Among the systems that seem to have the most promising prospects in this sense, those that use "sanitizing light" must certainly be included.

Light as a sanitizer cannot be considered a real scientific discovery as the sun has always been the sanitizing "tool" par excellence.

Already at the end of the 19th century Niels Ryberg Finsen, Nobel Prize for Medicine in 1903, had discovered that smallpox could be treated with the use of infrared rays, developing his subsequent research for the treatment of *lupus vulgaris* (disease from which he was suffering) using filtered sunlight.

In summary, starting from a perception of greater strength and improvement in his illness and health in general following exposure to sunlight, Finsen was able to demonstrate that these beneficial effects could also be detected in animals. In particular, he attributed these particular abilities to blue and violet rays. Finsen also focused on another very important aspect of light, namely the property of being bactericidal, coming to the conclusion that 95% of the bactericidal action of light comes from blue, violet and ultraviolet rays. Hence the development of one of the first phototherapy systems for the treatment of superficial, localized and parasitic skin diseases, including in particular *lupus vulgaris* on which his attentions were obviously focused.

The limits of ultraviolet rays were already known to Finsen who had understood that to be sensitive to their properties, microbes must be isolated from protective substances and for which their resistance increases considerably if present in a living environment and, above all, that the inflammations caused to healthy skin from such radiations could be very dangerous. It is also for this reason that ultraviolet rays are classified worldwide as a Group 1 carcinogen and dangerous for the inflammations they cause to the visual apparatus.

Simultaneously with Finsen, the Swiss scientist Jacques Louis Sorèt had started his studies on the sensitivity of bacteria to light, managing to identify the peak of maximum absorption of bacterial porphyrins within the frequency range of the visible spectrum (not UV) between 400-420nm . This band, in honor of its discoverer, was called Soret's Band.

Sorèt's studies remained a dead letter for many years for various reasons: certainly because the technologies then existing did not allow to effectively isolate the frequencies of the visible spectrum, so much so that to isolate ultraviolet rays Finsen had used the method used by photographers to filter with the red glasses the photographic plates. And then because the Nobel Prize in Finsen shifted attention to ultraviolet frequencies, in particular UV-C, which were certainly considered more effective.

Furthermore, Fleming's discovery of penicillin in 1928 had generated the belief that antibiotics would be the ultimate solution to bacterial infections.

Sorèt's studies were resumed in a 1954 publication (Shibata et al.) Which analyzed the absorption spectra of some microorganisms through the use of opalescent filters, highlighting how almost all the maximum absorption peaks were located in a neighborhood of 400nm.

A subsequent 2010 study from the Israeli University of Ramat Gan (Lubart et al.) Conducted an analysis of the countless researches that had, with different techniques, demonstrated the ability of bacterial eradication through the emission of light radiation within practically coincident intervals. with the study by Shibata et al.

The discovery of LED diodes in the early 2000s made it possible to create the first devices that emit frequencies of the visible spectrum. Thanks to this, the Scottish University of Strathclyde, having carried out extensive tests and research on disinfection of visible light, has developed its own single frequency disinfection devices which have been in use since 2008 at the Glasgow Royal Infirmary, a managed teaching hospital. by the National Health Service.

Since 2008, this technology - and its effectiveness - have been the subject of dozens of peer-reviewed academic publications and as many presentations at conferences and conferences. All research, however, focused exclusively on narrow power peaks, ignoring the broad absorption spectrum that microorganisms have been shown to possess.

Bacteria, in fact, as already demonstrated by Sorèt, have demonstrated a sensitivity to all frequencies of the visible thanks to the different absorption peaks of bacterial porphyrins and, more generally, of endogenous cellular photo-sensitizers, such as cytochromes, flavins and NADH, in able to trigger an uncontrolled metabolic reaction that is capable of rapidly leading to the definitive eradication of microorganisms irradiated by light, be they bacteria, viruses, spores or bacterial molds.

Biovitae and the microbicidal efficacy of the non-UV visible spectrum frequencies

The efficacy of visible spectrum frequencies on bacteria, in addition to being scientifically established and certified by numerous scientific publications, has been the subject of specific in vivo and in vitro experiments carried out by qualified independent laboratories.

The efficacy on viruses can be considered a fairly recent discovery whose merit must be attributed to the Scientific Department of the Celio Military Polyclinic which, in collaboration with the Istituto Superiore di Sanità (ISS), conducted the first tests on Sars-Cov2 and on other viruses used a device provided by Nextsense based on Biovitae technology® which is the only one in the world that uses a combination of frequencies between 400-420nm with a peak around 413nm effective on viruses and bacteria (covered by two international patents filed in 2016).

The efficacy tests on SARS-Cov2 were carried out in the midst of the COVID-19 pandemic with replicated trial cycles that evaluated the ability of BIOVITAE technology to eradicate both SARS-Cov-2 and other viral species (including the virus yellow fever and the flu virus).

The results, which were published in preprint in the journal MedRxiv in June 2020, highlighted the ability of BIOVITAE to reduce up to 99.8% of SARS-CoV-2 in less than one hour following exposure to Biovitae light. (***Fig. 1***).

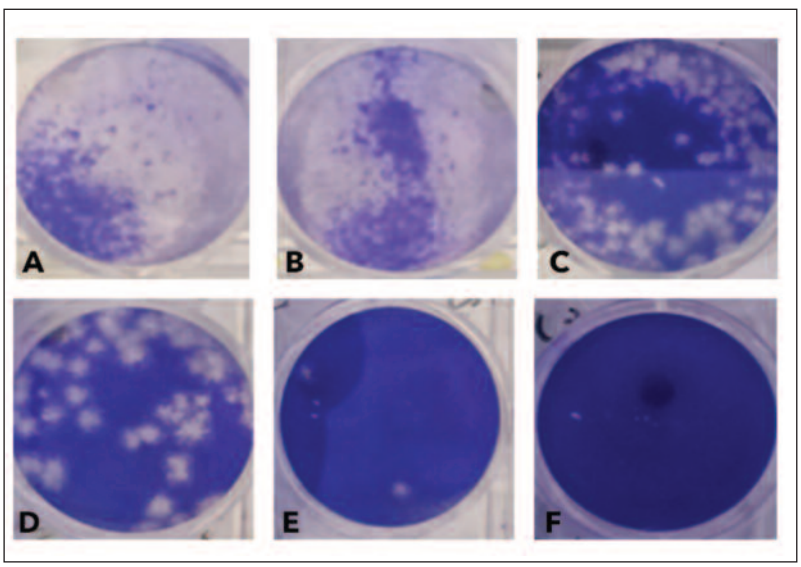


Fig. 1 - Petri dishes used in the Biovitae test.

The second cycle of tests began immediately after the publication of the first article and saw the involvement, in addition to the Scientific Department of the Celio Military Polyclinic as coordinator, of the Scientific Departments of Military Health of Sweden and Germany (all members of EU Biodefense Laboratories Network (https://globalbiodefense.com) and the Sapienza University of Rome. All the experiments concluded with equal efficacy results and the results will be published shortly in a journal in*peer-review*.

In addition to the various studies subsequently conducted using the BIOVITAE technology by various laboratories (only the Commissioner for Atomic Energy and Alternative Energy - CEA - in France and the International Center for Engineering are mentioned

Genetics and Biotechnologies - ICGEB - of Trieste), a mention deserves the recent independent research of the Icahn School of Medicine of Mount Sinai which has confirmed the efficacy of the spectrum frequencies of BIOVITAE on SARS-CoV-2 and other viruses.

The study published in preprint on BioRxiv with the title "*Lighting a better future: the virucidal effects of 405 nm visible light on SARS-CoV-2 and influenza A virus*"Reports the results of tests carried out using a full visible spectrum between 380 and 780nm, with a maximum peak in the 400-420nm range which is reported in ***figure 2***.

This spectrum coincides with that used by the Italian Military Scientific Department in the course of its experiment which is reported in ***figure 3***.

This is an important recognition for the Scientific Department of the Celio Military Polyclinic in Rome, which was the first in the world to make this discovery and to publish the results of its research in June 2020 on MedRxiv.

Wanting to give an immediate representation of the importance of the discovery, it is sufficient to analyze the results of the tests on SARS-Cov2 carried out using a full visible spectrum above 400nm both with BIOVITAE technology (CELIO and CEA) and with other devices that emit the same spectrum of frequencies (ICAHN - MOUNT SINAI) which, in summary, are reported in the ***table 1***.

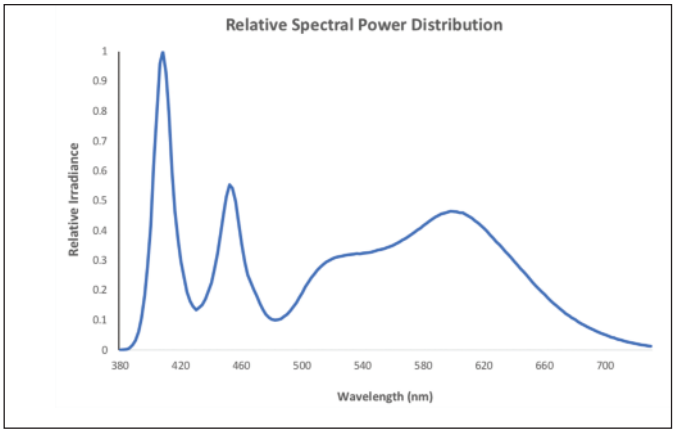


Fig. 2 - Normalized spectral distribution from the study of the Icahn School of Medicine, posted on BioRxiv on April 20, 2021.

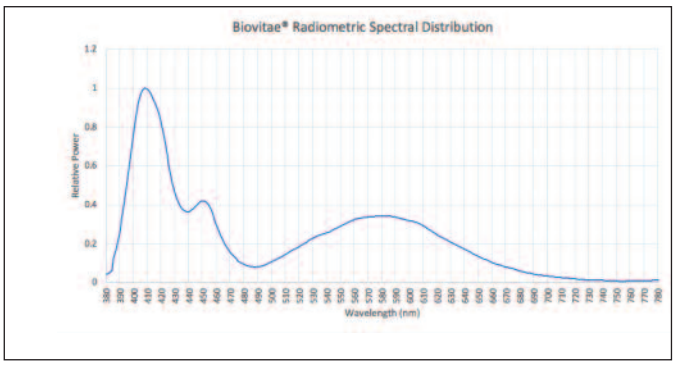


Fig. 3 -Normalized spectral distribution from the TÜV Rheinland test report of January 22, 2021, as made available to

Table relating to tests performed on SARS-Cov2 with BIOVITAE spectrum

	Organism	Medium	Irrad. (mW / cm2)	Time (hours)	Time (minutes)	Results
Mt. Sinai	SARS-CoV-2	PBS (Saline)	0.035	4	N / A	55.08%
				24		90.17%
Mt. Sinai	SARS-CoV-2	Artificial Saliva	0.076	24	N / A	98.22%
Mt. Sinai	SARS-CoV-2	PBS (Saline)	0.15	4	N / A	63.64%
				24		96.21%
Mt. Sinai	SARS-CoV-2	PBS (Saline)	0. 6	1	N / A	71.52%
				8		99.74%
CELIO	SARS-CoV-2	gMEM	4.67	N / A	15	93.25
CELIO	SARS-CoV-2	gMEM	4.67	N / A	30	97.94
CELIO	SARS-CoV-2	gMEM	4.67	N / A	45	99.31
CELIO	SARS-CoV-2	gMEM	4.67	N / A	60	99.64
CEA	SARS-CoV-2	TNE buffer + 0.3g / L BSA	1.04	N / A	30	57.34
CEA	SARS-CoV-2	TNE buffer + 0.3g / L BSA	1.04	N / A	60	98.30
CEA	SARS-CoV-2	TNE buffer + 0.3g / L BSA	1.04	N / A	90	98.65

Could light be a disruptive technology to fight viral and bacterial infections?

What are the prospects after the pandemic?

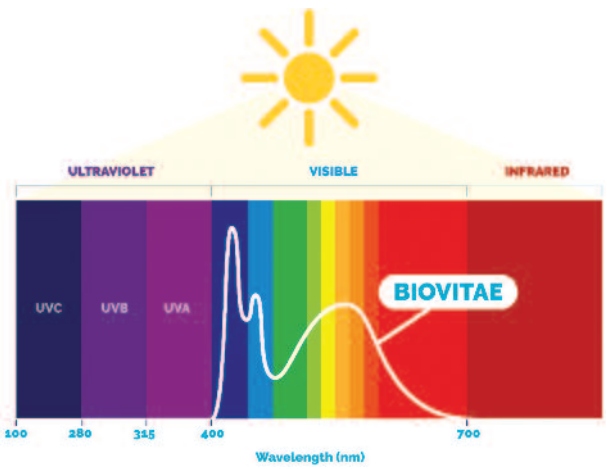
Surely science provides many more tools than those of the past: despite the limitations and concerns related to reduced testing times and real effectiveness, the speed of making vaccines in such a short time is certainly a significant resource as it allows for respond even more quickly than what happened with Sars-CoV-2. But we cannot afford to have millions of deaths a year for each new pandemic and we must therefore invest in tools that allow us to live in a less dangerous way with the new infectious diseases.

Strengthening health systems, instructing the governments of developing countries to deal with health emergencies adequately therefore no longer responds only to solidarity purposes, as we have thought up to now, but is a global need because the safeguarding of health depends on this too. Planet and the health of the entire world population.

Because it is now clear that it is not true that each state is a world apart but all states are part of the world and the planet is everyone's home.

The recovery of control of the situation will depend on our ability to model and implement effective measures that go beyond physical distancing (whose economic impact could not be managed) and mainly concern "less invasive" prevention systems and, obviously, systems of rapid diagnostics and effective therapies.

We cannot predict which direction the world will take once we emerge from the emergency but it now seems clear that the paradigms and standards of health safety will totally change within the environments - not only healthcare but also in offices, schools and private homes - in which the sanitization continues
it will become as important a standard as lighting.



And it is precisely the sanitizing light that uses non-UV visible spectrum frequencies (and therefore not harmful to living beings) can represent the most effective tool for continuous sanitization as it is already used every day in everyday living environments and can guarantee control. of the microbial load when the main vectors of microorganisms are present: humans.

The most immediate use is obviously the general lighting of buildings but other specific applications can be designed to ensure more thorough sanitization, if necessary. And if before the pandemic the most affected segment might have seemed to be that of healthcare facilities, now it is clear that the problem also concerns companies that need to safely resume economic activities, schools but also private individuals, a sign that the need for protection is not only related to business but is becoming a felt and widespread need. And the military environments certainly represent those that most need these systems as the carrying out of ordinary activities inevitably involves gatherings and continuous contacts between people of different origins, especially on the occasion of international missions.

To date, only the BIOVITAE technology on the market is able to offer a patented technology that uses a combination of frequencies of the visible spectrum between 400-420nm (Soret band) (with a peak around 413nm) which has been tested effectively on all bacteria and viruses as it causes damage to the bacterial membrane and the viral capsid through a process of peroxidation. It is clear that BIOVITAE can represent a technology *disruptive* to contribute to the safe resumption of postpandemic activities and to counteract the effects of viral and bacterial infections.

In Italy about 100 million light bulbs are sold (in addition of course to all the other lighting devices of other shapes), we think it could be a logical and natural evolution that of their progressive replacement with sanitizing light systems also because it is a plug and play which, in addition to being part of the ongoing transition already begun a few years ago for the

progressive replacement of outdated halogen and incandescent technologies with LED technology for its greater efficiency from an energy point of view, it does not require any specialized installation and is therefore immediately usable.

Biovitae responds to the new demand generated by a greater awareness of the risk of viral and bacterial infections, the prevention of which will be one of the areas on which the greatest resources will be concentrated in the years to come.

The strength of this technology also lies in its being a "*change without change*": It represents an absolute innovation in the field of bacterial and viral infections without requiring any adaptation or change of habit: to protect yourself, in fact, just turn on the light.
