



COVID-19 EMERGING DISEASES AND PUBLIC HEALTH IN CYPRUS What lessons do we have to learn for the future?

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"Παν μέτρον ἄριστον"

'Pan Metron Ariston' 'All in good measure' (Kleobulos from Lindos, Rhodos, Greece).

In this challenging period for all of the world, I would share some thoughts related to the theme entitled "THE IMPACT OF COVID 19 ON OUR LIVES: Socioeconomic and Political Repercussions". Coronavirus disease 2019 (COVID-19), the worst infectious disease (Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2))

Professor Dr Panagiotis Karanis is an anatomist and parasitologist and an internationally recognized expert in parasitic, emerging and tropical infectious diseases. Prof. Karanis is included on the annual list of 100,000 top scientists worldwide and, correspondingly, in the top 2 per cent of scientists in their field, according to a team of researchers at Stanford University in the USA. The updated 2020 list is based on a range of citation metrics that provides standardized data across those fields and subfields, in arriving at the (2019) single year impact result of more than 8,000,000 scientists worldwide. Born in Greece, he did his doctorate and habilitation at the Medical Faculty of Bonn University in Germany. Subsequently, he was Professor at the medical faculties of Bonn and Cologne Universities. He was Professor at the National Research Center of the Obihiro University in Hokkaido in Japan and was the leader of the Unit for Diseases Control and Genetics. He was Professor at the Qinghai University at the Qinghai - Tibetan Plateau in Xining, NW China, after have been selected as Foreign Expert in the 1000 Talent Plan, Recruitment Program of Foreign Experts (RPFE) for non-ethnic Chinese experts, China (2014-2017). In China, he established the Center of Biomedicine and Infectious Diseases in the Tibetan Plateau of North-West China. A small laboratory upgraded inside of three years to the State-Key-Laboratory for infectious diseases dealing with viruses, bacteria, and parasites in China's Qinghai Province. He served as a scientific advisor for the governments in Germany, Japan and China and is acting as international expert and visiting professor in several Universities worldwide. He was the main speaker for the Nobel-Days-Lecture during the Nobel-Days-Festivities at the Örebro University in Sweden in December 10th, 2012, focused on 'Malaria vaccine development'. He taught and researched in Germany, Greece, Australia, Japan, Canada, Thailand and China and now in Cyprus. Professor Karanis is currently the Professor of Anatomy at Nicosia University Medical School. He teaches human Anatomy in the MD6, CS, and MBBS4 courses of the Medical School at Nicosia University in Cyprus and he is the coordinator of the Unit for Anatomy and Morphology coordinator at the Nicosia Medical School. He is an influential scientist, having had fundamental role in triggering the interests of the German, Greek, Japanese, and Chinese governments for research contributions in the biomedical field. He wishes to serve the Republic of Cyprus with knowledge transfer and relevant expertise in the biomedical field on emerging, enteric, parasitic, and tropical pathogens for outbreaks prevention and health care improvements.

that has affected humanity over the past century, is still causing dramatic derangements in healthcare, society and the economy so that nothing will be the same as before. As of March 29th 2020, there have been more than 484,179,897 million confirmed corona virus cases, with over 6.153,536 million deaths. The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is the causative organism responsible for this pandemic. This pandemic is not the first pandemic or epidemic globally, and it will not be the last. Examples abound, and there are many reasons why it is becoming increasingly likely that mass outbreaks and infectious diseases will affect world populations at ever-shorter intervals.

1. Historical aspects on disinfection

In Vienna, Ignaz Philipp Semmelweis (1818-1865) was a Hungarian surgeon and obstetrician. Semmelweis attributed the onset of childbed fever in public clinics to disregard for hygiene for doctors and hospital staff, compared to private births and endeavoured to introduce hygiene regulations. Semmelweis instructed his students to disinfect their hands with a chlorine solution before each examination. Later with the cheaper chlorinated lime - a practical measure, as it turned out: the mortality rate dropped from 12.3% to 2-3% in just a few months. In 1848 the mortality rate fell to 1.3%. Semmelweis recognized that infection could come from living people! Despite this success, Semmelweis' work has not been accepted or recognized for long, particularly inside the medical community and by leading physicians. Many doctors and their students considered hygiene and disinfection unnecessary and did not want to admit that they were the source of the infections and diseases they wished to cure. He was abused during his lifetime and even locked away in a psychiatric ward because hygiene was a waste of time. The theories of the transmission and pathways of the disease prevailing at the time were incompatible. Semmelweis was an early pioneer of antiseptic procedures for proposing handwashing in 1847 and is known as the "saviour of mothers".

Another doctor, the Scottish surgeon Joseph Lister (1827-1912), named himself in antiseptic surgery after recognizing Semmelweis's work. It took almost two decades for his methods to be accepted by the surgical ward. According to Lister's studies, there was a 50 per cent postoperative mortality rate from infectious diseases; antisepsis and good hygiene reduced this mortality rate to 15%.

Like everyone else living today, I was lucky in my life: I've learned to protect myself from infectious diseases. In elementary school in the small village of Chryso/Evritania in central Greece, with about 100 inhabitants, we had to stretch out our hands and fingers every Monday at the school, and the teacher checked whether the fingernails were cut, making 'best practice hygiene' to avoid contamination and infections. We were allowed to pet cats and dogs, but we were obliged to wash our hands immediately afterwards. It was known that human echinococcosis is a parasitic disease caused by tapeworms of the genus *Echinococcus* and at least the eggs of dangerous tapeworms are transmitted from dogs to humans. Today we know that humans are infected by ingesting parasite

eggs in contaminated food, water or soil or after direct contact with animal hosts. More than one million people are affected by echinococcosis, despite echinococcosis is often expensive and complicated to treat and may require extensive surgery and prolonged drug therapy. We had elementary education about nature's basic survival rules, where medical care never existed in such remote environments. The modern urban people not only keep the animals inside their houses, they even often share the bed with their dogs or cat or other animals. However, the fact remains that even these domesticated animals are carriers of pathogens, no matter how much they are loved and 'humanized'. Dogs and cats can usually coexist and survive well with pathogens, but humans cannot.

2. Antiseptics, disinfectants, and social distance

We are all fortunate that anti-septics and disinfectants are used extensively in hospitals and other health care settings for various topical and hard-surface applications. They are an essential part of infection control practices that aid in preventing broad generalizations and nosocomial infections. Microbial contamination and infection control risks would never be possible without antiseptics and disinfectants. Biocides have been used for antisepsis, disinfection, and preservation for hundreds of years, and they are a matter of course. However, we still risk our health and happiness through undisciplined behaviour.

In Japan, the everyday greeting and introduction style was very strange to me at first because the Japanese avoid physical contact in a strict and disciplined manner. In the course of my carrier development and profession, especially during the last two years of the current corona crisis, I appreciate these rules of conduct and know their justification. Especially in Mediterranean countries, where people of both sexes hug and kiss when they meet each other, one should reconsider and refrain from contacting each other.

3. Globalization: Opportunities and threats

In times of globalization, it becomes quickly and standard possible to fly to the most distant places within a day. Globalization offered unique opportunities to get to know the world, but the earth can't take it anymore. In recent years, the number of tourists z. B. in Greece and Cyprus, increased: three times more tourists than the native population in the country. A few years ago, the Minister of Tourism in Greece proudly announced that 30 million tourists a year in Greece achieved and that the government's goal was to increase it to 40 million. I have often asked myself and put the question to the audience of my lectures and presentations at conferences: "What's the point of driving up tourist numbers without sense and measure? What about environmental and water pollution and disturbance of animal's eco-systems?" Fifteen thousand tourists from all over the world visit the island of Santorini every day in the high season. People of different ethnicities and destinations can be carriers with the most diverse flora of pathogenic or non-pathogenic microorganisms, crowded together on cruise ships, on viewing platforms, and in public cafes and restaurants. It is easy for microbial

pathogens (parasites, viruses, bacteria) of different origins to transmit from person to person and adapt to new regions.

In Cyprus, the situation of the tourism business is similar to Greece; tourism and agriculture are the primary industries on the island. Despite no water or foodborne outbreaks that have been reported yet in Cyprus, many infections and diseases are not on the diagnostic focus of clinicians and information about microbial pathogens concerning human disorders is also scarce.

Millions of tourists around the Mediterranean countries accept every year all-inclusive holidays. Hotel businesses are obligated to offer safe food and water, but they will also be affected to compensate for claims in the case of infectious outbreaks. Tourist claims management companies exploit legal loopholes and tout for business at tourist hotspots like beaches and resorts. However, contamination of swimming pools is not excluded, and disinfection procedures are often deficient. Swimming and therapeutic pools are considered a more important transmission route for gastrointestinal illness than drinking water. The primitive nature of background information and the early stage of technological knowledge regarding sampling and analysis of swimming pool samples resulted in a large proportion of negative results, creating distrust between the related research and governmental authorities. In other cases, it takes many years to establish the notion of the pathogenic nature of an organism and recognize it for human infections that cause severe diarrhoea.

4. Human evolution and dissemination of diseases

Human history has always been affected by pandemics. Infectious diseases belong to nature, and most will never be eradicated. Since humans began domesticating animals more than 10 thousand years ago, most diseases conditions exist as zoonoses. Dissemination of disease is dependent upon movements between humans and animals. In the long history of human evolution, the importance of the transition from hunter-gatherer to city-dwelling agrarian societies was the presence of domesticated animals raised for meat, work, and long-distance communication. The real threats and the future of infectious diseases in today's communities are influenced by climate change, wild animals, water-, food-, air-borne and biosolid contamination. These factors are critical for the occurrence of pandemics as a natural phenomenon related directly to environmental changes and globalization.

People's curiosity and the urge to own everything in this world allow them to venture into areas where they should have access. Wilderness should remain wild and to itself. We already know that wild animals carry many viruses, bacteria and parasites on and in them that do little or no harm to themselves but can cause terrible and uncontrollable diseases in humans - as we are now seeing with corona. We should learn to live with and respect nature and let nature be nature. Factory farming, deforestation, the introduction of wild animals to markets, mass consumption, tourism, destruction of habitats and much more – everything that we could influence – makes (us) sick.

5. The 'One Health' Concept

We should remember the One Health concept again. The term "One Health" or "One Medicine" has been around for a long time - the idea dates back to 400 BC. It goes back to Hippocrates' On Airs, Waters and Places. In 1948, it was re-introduced to society by an American veterinarian. 'Environment-Animal-Human' - neither can live without the other. No human, no animal, no plant can exist in a sick environment, at least not healthy. Environmental and climate protection is protection against infections or diseases. We have it in our hands whether the egoistic everyone-for-themselves go further or not. The world after the 'Corona lessons' learnt will be different than before, one way or another. In which world, in which society we will live and want to live depends on us. We all know that humans and governments of our time hold in their hands. Life on this small planet is now at risk worldwide and with tragic consequences for its existence. I think that as a result of the "crazy world order," nature has sent us a signal via the pandemic to regulate "our world order" and give us a chance to rethink and rearrange. And it will keep repeating itself until we learn and change. However, we all act as if we are powerless and at the mercy of the "forces" of this earth and cannot do anything.

6. Public health system in Cyprus and the scientific know-how on infectious diseases research

The year 2020 presented us with an enormous challenge – Covid-19. The ongoing epidemiologic situation with Covid-19 continues to challenge us in our everyday lives and work. Now more than ever, we see the need for scientific exchange and investment in biomedical research and the education of the next generation of young biomedical scientists in Cyprus. We need to fill the research gaps and needs in the country in Biomedicine and Public Health. In the case of Cyprus, the public health system was not prepared to deal with the pandemic. The healthcare system needs to transform and expand in surveillance and monitoring to be able to detect and control local outbreaks and pandemics. Cyprus's missing and emerging opportunities for scientific careers and achievements in infectious diseases research are looming. Research and innovation can flourish in the country, and the chances are wide open for the next generation of bio-scientists. Research and innovation should attract researchers and investors from worldwide and create a robust establishment on this island.

Cyprus must rely more on scientific know-how for strategic developments. It is crucial to seek advice from as wide a group of experts as possible. Working closely with these scientists should be the basis of government policy. The putative Board of Experts will be composed of several scientists and experts from all fields. This Independent Council of Experts on Strategic Development in all areas will be established as the epi-centre of capabilities and the main driving force for developing new strategies in Cyprus. Internationally experienced and recognized experts in sciences and research will ensure a high level of know-how. Cyprus and its people cannot depend only on others; they should rely on intelligence from science and technology. The Council of Experts on Strategic Development in Cyprus will be composed of interdisciplinary experts who will develop

transparent criteria and strategies for strategic development in social and public life. The experts will consist of high-ranking and renowned representatives of medicine, law, economics, philosophy, psychology, sociology and social work. They should meet at irregular intervals with the participation of the country's President and governmental authorities, and decision-makers. The council of experts aims to gather the know-how of various scientific disciplines and use the existing knowledge to follow a holistic approach in the country. The developing strategies in critical sectors of the country's economic and social benefits of the developments must be considered.

The real evaluation of the epidemiological status in Cyprus is complex due to the unknown levels of pathogenic contamination in the water supplies, the degree of swimming pools contamination, and the distribution of vectors. The tourism business on the island is a significant pillar of Cyprus's economy. Tourists and immigrants represent a melting pot of human activities that brings many people from all over the world together and potentially serves as a source of contamination that can cause endemic infectious diseases on the island. Control of diseases by constant monitoring of the epidemiological situation of the region can prevent and reduce the incidence of infections. The spread of infectious agents by several hosts (f.e. stray cats, rats, a.o.) appears to be a significant threat to public health in Cyprus. Governmental monitoring and mandatory reporting would be essential for controlling and preventing pathogens outbreaks. These data will help develop national guidelines based on national needs, as defined by changing migration flows and the corresponding change in infectious diseases. The development of suitable protocols will lead to the rational redistribution of financial resources based on the needs. Data collection that is currently lacking at the national and European levels will be crucial. These are actions with interdisciplinary research and routine monitoring character with cross-border co-operations and data exchange with countries on similar migration routes.

Cyprus has not included parasites in the relevant protocols for systematic, pre-symptomatic assessment of newly arrived migrants. There is a lack of systematic collection and analysis of data related to the prevalence of parasites at the national level. Parasitic and emerging infections are not in the diagnostic focus of health care professionals and clinicians; information about parasites and parasitic diseases concerning human infections is also scarce. I alerted on this two years ago. Cyprus is a hub for at least three different migration flows from the MENA region, Africa, Southeast Asia, and Eastern Europe. Due to such instability and geopolitical developments, the country Cyprus is accepting large populations of people with the expected high and heterogeneous prevalence of parasites. The world around Cyprus is rapidly evolving, and the role of Research and Innovation in the health care and the biomedical sector is now more essential than ever before.

7. Emerging diseases teaching and education needed at Universities

As the whole planet turns its attention to the road race to develop and deliver an effective coronavirus vaccine, an equally crucial scientific endeavour should occur: Improve the diagnosis and identify potentially dangerous pathogens that could trigger subsequent pandemics and protect humanity. Like almost all new human viruses, Covid-19-causing Sars-Cov-2 has emerged from animals. In this specific Covid-19-Virus-situation, the virus probably jumped from bats to humans, possibly using a third animal species as a "bridge" as an intermediary host. SARS-CoV-2 is believed to spread predominantly via short-range airborne aerosol, respiratory droplets, and direct or indirect contact with infectious respiratory droplets. Airborne transmission of SARS-CoV-2 has been elegantly demonstrated in the hamster model. In addition, contact with frequently touched surfaces, shared items, and food contaminated by infectious respiratory droplets likely represent another route of transmission of SARS-CoV-2. Other ways of transmission, including faecal-oral and contact with various body fluids, including urine, tears, and breast milk, have been postulated.

Based on elementary facts and clinical case studies, the students of medicine, veterinary medicine, biology, biomedical, pharmaceutical, public health and agricultural studies and related fields should understand that the importance of infectious agents for humans and animals is subject to changes. New human and animal pathogens or pathogens with increasing spread, virulence or resistance to chemotherapeutic agents are called "emerging pathogens". In the sense of the "One Health" concept, the host-pathogen interface is fundamental between animals, and the importance of human pathogens and their host change is to be approved. Various modules and lectures on 'parasites, bacteria and viruses as cellular pathogens', 'climate change and infectious diseases', 'demographic changes and migrants care'. The students and health care professionals should understand the differences between pathogen change and the related factors and can assess their epidemiological and pathogenetic consequences. They should be educated and alerted to the unexpected emergence of dangerous pathogens.

Many of the newly discovered infections have been in existence for a long time, but healthcare providers have not seen them in areas where new outbreaks happen. This year's focus is combating Neglected Tropical Parasitic Diseases under the 2030 Agenda for Sustainable Development Goals (SDGs), infection and immunity, drug development and the 'One Health Concept'.

Advanced knowledge of infectious diseases and their control arises from clinical studies, in vitro culture systems, animal models and new tools for genetic manipulation of the pathogens and simple from their epidemiology. In the sense of the "One Health" concept, the connection between animal and human pathogens is essential, and the importance of the host change of pathogens is shown. The continuation and the initiation of new research on infectious diseases in Cyprus is required, and they will offer new possibilities and investments in the country.

Working with pathogens enables researchers to know the biology and transmission pathways of the pathogens, yield experiences for their control and become experts in a specific field. If experts are available, the government call them from the pool of experts and give them responsibility. If opportunities exist, such as for assisting in understanding the details of various approaches, assisting in the review of alternative proposals, or contributing to the development of strategic alternatives, a larger number of real experts in the field can participate. Rephrasing Aristotle's words, 'In the arena of infectious diseases, the awards for the successful control of pathogens will fall to those, who apply the best strategy in research'.

8. Examples of infectious parasitic diseases

8.1. Toxoplasmosis and stray cats

Most citizens love stray cats and are obviously under protection and free to live outdoor and occupy large landscapes in Cyprus. Pathogens like *Toxoplasma* excreted by stray cats are a potential source of toxoplasmosis for humans and animals in Cyprus. Overpopulation and the proximity of cats as a companion species in human populations play an essential role in transmitting diseases to humans. Humans acquire the infection mainly via the oral route through consumption of raw or undercooked meat of infected animals containing cysts filled with parasites and through the ingestion of oocysts as a result of drinking contaminated water, eating contaminated food or contact with contaminated soil. Thus, the polluted environment may be an essential source of human exposure. Oocysts are excreted to the background only by infected felids, being the definitive hosts of *T. gondii*. Therefore, cats play a significant role in the epidemiology of toxoplasmosis worldwide.

8.2. Cryptosporidiosis and diarrhoea

Cryptosporidium is recognized as an important human enteric pathogen by the occurrence of community outbreaks of gastroenteritis. *Cryptosporidium* has reached the top priority level for funding and research support like malaria and tuberculosis previously have. The Global Strategy has already recognized how a multidimensional approach to disease eradication must also include the general improvement of standards of living. This approach was possible for *Cryptosporidium* due to the invaluable studies thanks to the funding support of governmental organizations and foundations. These were large achievements so far, for a parasite with a short history of recognition due to its water significance and involvement in an environment of political and regulatory forces. The strategy that focuses on is the advancement of the development of safe, affordable and effective vaccines for the leading causes of diarrhoeal and enteric diseases in low- and lower-middle-income earning countries. *Cryptosporidium* was found to be a significant cause of moderate to severe diarrhoea in South Asia and Africa. These perceptions contradict any recent data clearly demonstrating that this pathogen is continuously present and exists in almost any animal (domestic or wild) examined, in any surface waters investigated, in many different food groups and final also in the increase in water- and foodborne outbreaks. This pathogen is prevalent in industrialized countries, not only in the USA, UK, Australia and New

Zealand, where considerable efforts were achieved to establish a surveillance system, but also in North, Central, Eastern and South European countries that have high standards of water quality levels, such as Germany, France, Sweden, etc.. *Cryptosporidium* was one of the four major contributors to moderate-to-severe diarrhoeal disease during the first 5 years of life in the low-to middle income earning countries; it was only second to the Rotavirus as a cause of moderate-to-severe diarrhoea in children younger than 2 years old and it was also associated with a two to three times higher risk of mortality among children aged 12–23 months with moderate-to-severe diarrhoea compared to controls without diarrhoea. *Cryptosporidium* is listed as one of the most important enteric parasites cause of diarrhoea in humans (see paper of Karanis, P: The truth about in vitro culture of *Cryptosporidium* species. Parasitology. 2018 Jun;145(7):855-864. doi: 10.1017/S0031182017001937. Epub 2017 Nov 16. PMID: 29144216.)

9. Scientists must act in ways that serve the public

Though science today is so fast-paced and complex, experienced researchers should take the time or opportunity to explain why a decision made or an action is needed. Young researchers should get the best advice from their supervisors. Adhering to professional standards builds personal integrity in a research career. Understanding the nature and the complex relations of diseases are forces that keep researchers rooted in their laboratory benches—observing or explaining something that no one has ever observed or described before is a personal triumph that earns and deserves individual recognition. Learning something new, the discoverer both draws on and contributes to the body of global knowledge held in common by all researchers and contributes to society should remain the critical motivation standards to serve the public. Irresponsible actions can impede an entire field of research or send it in the wrong direction, and progress in that field may slow. Scientific results greatly influence society, and science is critical for economic and defence upgrades.

Finally, research is based on the same ethical values in everyday life, including honesty, fairness, objectivity, openness, trustworthiness, and respect for others. We are living in a society of confusion and disorientation. Implementing 'Pan metron Ariston' in our lives and passing on this way of thinking to the next generations could improve the life quality of humans, animals and the environment.