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Symposium

SYSTEMS MEDICINE

Models of integration in clinical practice and new therapeutic solutions

THE PATIENT OF THE FUTURE

SATURDAY, MAY 20, 2023

CHARTA DEL SYMPOSIUM 2023

THE PATIENT OF THE FUTURE

FACULTY

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- Alberto Migliore, Director of the UOS of Rheumatology. San Pietro Fatebenefratelli Hospital, Rome
- Valter Santilli, Full Professor of Physical and Rehabilitation Medicine. University of Rome "La Sapienza"

SPEAKERS

- Mariano Bizzarri, Associate Professor of Clinical Pathology. Director of the Systems Biology Laboratory, University of Rome "La Sapienza"
- Laura Boella, former Full Professor of Moral Philosophy at the Department of Philosophy, State University of Milan
- Ernesto Burgio, ECERI - European Cancer and Environment Research Institute, Brussels
- Mario Clerici, Full Professor of Immunology and Immunopathology, University of Milan
- Fabio Esposito, president of the School of Exercise Science, University of Milan
- Stefano Fais, Research Director, Department of Oncology and Molecular Medicine, Istituto Superiore di Sanità
- Vassilios Fanos, Full Professor of Pediatrics, University of Cagliari
- Alessio Fasano, Professor of Pediatrics, Harvard Medical School and Professor of Nutrition, Harvard T.H. Chan School of Public Health - Boston, MA (USA)
- Nicoletta Gagliano, Full Professor of Human Anatomy. Department of Biomedical Sciences for Health, University of Milan, Italy.
- Angelo Gemignani, Full Professor of Psychobiology and Physiological Psychology, University of Pisa
- Jeanette Maier, Full Professor of General and Clinical Pathology, University of Milan
- Marco Paoloni, Associate Professor, Department of Anatomical, Histological, Forensic and Locomotor Sciences, University of Rome "La Sapienza"
- Alberto Priori, Full Professor of Neurology, Department of Health Sciences, University of Milan
- Raoul Saggini, Full Professor of Physical and Rehabilitation Medicine, eCampus University in Novedrate (CO)
- Fabrizio Salvinelli, Full Professor of Otolaryngology and Cervicofacial Surgery, University campus Bio-Medico, Rome
- Luigi Tesio, Director of the Department of Neurorehabilitation Sciences, IRCCS Istituto Auxologico Italiano - Milan. Former Full Professor of Physical and Rehabilitation Medicine, University of Milan
- Gian Vincenzo Zuccotti, Full Professor of Pediatrics, University of Milan. Director Department of Pediatrics Children's Hospital V. Buzzi - ASST Fatebenefratelli - Sacco

THE PATIENT OF THE FUTURE

Humanity is facing an unprecedented population explosion, also supported by a marked extension of average life expectancy. Urbanization seems unstoppable. Rapid communication and migration-often uncontrolled or manipulated-are a source of cultural homogenization but also of serious misunderstandings and conflicts. All this is aggravated by the scenario of dwindling food resources due to dramatic climate change. These phenomena alone explain why the biological and mental life and health of the patient of the future will be increasingly conditioned by socioeconomic context and thus by variables such as cultural level, income, health knowledge network, and relational networks, as well as by epigenetic factors and the genetic characteristics of each individual person.

> The patient of the future will have to contend again and increasingly with *non-communicable diseases*. Cardiovascular, cerebrovascular, neoplastic, metabolic, and especially progressive degenerative diseases, which were less relevant when life expectancy was lower than now, will be responsible for 74% of deaths especially in less developed countries and everywhere in the world among low-income social groups *(*https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases).

Unexpectedly, then, these environment- and age-related diseases will surpass infectious diseases as a cause of death even in developing countries. This hierarchical turnaround among diseases will be even more pronounced when considering not only mortality but the impact on disability, the latter condition to which curable or, conversely, rapidly fatal diseases contribute less and less than chronic-degenerative ones.

The progressive deterioration of *exposome* conditions (diet, stress, environmental pollution, natural and man-made radiation, smoking) and the acceleration imparted to it by *climate change* will contribute to maintaining constant or even increasing the prevalence of diseases such as, for example, myocardial infarction, atherosclerosis, diabetes, and chronic pulmonary diseases.

The "disease of the century," cancer, will remain among the most relevant for at least another 50-80 years despite huge investments and advances in prevention, diagnosis, and treatment *(Kulkova J et al. Medicine of the future: How and who is going to treat us? Futures 2023;146:103097).*

The scenario described does not, unfortunately, represent an equal exchange between types of pathology: rather, it reflects their sum if not an explosive interaction.

The patient of the future will also have to deal with *communicable diseases* and perhaps will have to do so even more in a world that is increasingly globalized and therefore subject to the progressive increase in the circulation of pathogens (proportional to the increase in the movement of people and goods). The situation may be exacerbated by the development and spread of hyper-intensive livestock farms and subverted animal *habitats.*

In the field of infectiology, the patient of the future will face the growing problem of antibiotic resistance, which will evolve as antibiotic therapies advance.

The relentless acceleration of environmental and social change will conflict with the timing of the natural adaptive capacity of the "human system" punctuated by its biological evolutionary history, whose slow Darwinian timescales contrast with tumultuous cultural evolution. This dis-chronometry will make adaptive behaviors increasingly difficult in favor of mal-adaptive behaviors.

The patient of the future will increasingly be a biological system at risk of maladaptation, which may gradually lose its inherent capacities for robustness and resilience and will be increasingly unable to maintain its stability and dynamic reciprocity with its surroundings.

Mental suffering will require more attention: already, while framing it in formal psychiatric diagnoses and statistics, it afflicts at least one in eight people according to the WHO *(https://www.who.int/news-room/fact-sheets/detail/mental-disorders).*

Changes in the *exposome* (also daughters of *climate change*) will reverberate at the psychic level by drawing new nosographic entities such a s eco-anxiety and will also be reflected, in an average time span of 5-10 years, at the organic level.

New patterns of *interactome* (set of relationships of each human with other humans and other living things) will lead to a condition of collective neurosis in 30-50 years *(Kulkova J et al. Medicine of the future: How and who is going to treat us? Futures 2023;146:103097).*

The bidirectionality between progressive virtualization of relationships and the tendency toward isolation will lead to the development of a virtual *interactome*, itself dysfunctional, which, in the presence of a real *exposome* will worsen the "toxic" *burden of* the "human-system," with a maladaptive psycho-neuro-endocrine-immunological response.

A steady rise in indices of inflammation and inflammatory lesions will be observed as also well documented by studies on the correlation between *early stage adversity* and susceptibility to inflammatory diseases in adulthood, or on the direct relationship between negative emotions and increased cytokine *markers* of inflammation.

The patient of the future will be an increasingly inflamed and neuroinflamed patient whose multiple comorbidities will recognize this condition as their common matrix.

It is in this scenario that, in order to meet the needs of the patient of the future, a paradigm shift in Medicine and Health Care Systems as postulated and recommended *in* the *Milan Declaration 2022-New Goals for Medicine* is required.

And it is on the basis of these premises that Systems Medicine will be able to make its valuable contribution as Medicine that is the result of the hybridization of knowledge and whose perspective hinges on the 4 fundamental elements for managing the health and well-being of the patient of the future:

- Prevention
- Customization
- Predictivity
- Accuracy

In this context, *Low Dose Medicine* deserves specific attention, which enters fully within Systems Medicine and, related to it, *Low Dose Pharmacology* (characterized by the use of physiological sub-nanomolar dosages of biological molecules) as they represent coherent application solutions of a Medicine that identifies as a crucial etio-pathogenetic moment of disease the alteration of *cross-talks* between cells and between *networks* operated by signal molecules.

In fact, only a Medicine that can consider the *Whole* and not the single molecule or single cell can unravel and understand the pathogenesis of diseases and act on them in depth.

Great new challenges await the patient of the future and one great challenge in particular awaits the Medicine of the future. To meet the growing and complex health needs of the community and offer viable solutions to emerging clinical and health problems, Medicine will have to redesign itself to become:

1. A Medicine that makes use of *big data* and virtual interactions to facilitate interpretation of patient uniqueness without reducing the physician to a *data doctor*, allowing more time for empathy and *concordance* relationship building
2. A Medicine that knows how to benefit from the results of Research in every field of knowledge without becoming a passive application gymnasium. So, a Medicine also capable of original Research, specific in its objectives, methods and clinical results
3. Medicine that is predictive but free from predictive anxiety
4. Medicine that is precision but does not lead to fragmentation of the systemic view of the patient in his or her being a "body-mind-spirit" *unicuum*
5. A Medicine that also makes use of the integration between different diagnostic and therapeutic approaches (*overlapping*), and between different Pharmacologies (synthetic and natural-biological, of high and low dosages) and *person-system* interventions such as, for example, those of psychiatric, physiatric, thermal or such as movement
6. A Medicine that prioritizes a preventive and not just a therapeutic approach and provides for increasing accessibility and efficiency of diagnosis and treatment, optimizing the human and economic burden of pharmacological, physical, and surgical methods, and also enhancing rehabilitative techniques
7. A Medicine that provides, for a patient who is increasingly chronic, with comorbidities, poly-treated, and in need of treatment for his or her disabilities, treatments with low impact on both the individual microcosm and the environmental macrocosm through the reduction of the pharmacological *burden*, drug dosages, and concentrations of their active ingredients, while also capitalizing on the opportunities offered by *Low Dose Medicine*
8. A Medicine capable of primary and secondary prevention and able to act in the early stages (early phases) of disease
9. A Medicine that favors keeping the patient in *low* disease activity once

brought into remission

10. A Medicine that considers that *"an ounce of prevention is worth a pound of treatment"*