

## The Center for Gender-Specific Medicine of the Italian National Institute of Health is facing new challenges: research, training and dissemination

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Last year, on November 1st, almost two years after the Center for Gender-Specific Medicine (MEGE) was established (1 January 2017) as part of the latest reorganization of the Italian National Institute of Health (ISS), I had the honour of being officially appointed director after about a year as acting director.

The Center's main task is to promote health from a gender perspective. If, to date, gender medicine has been neglected and, at times, misinterpreted, awareness of the relevance of this new vision is finally growing and the far-sighted decision to set up a specifically dedicated ISS Center is proof of this.

From its inception, the Center, which has around 60 staff members, has been organised into two sections, Gender-specific physiopathology and Prevention and lifestyles. These, in turn, are divided into units, which, based on the researchers' different yet complementary skills, carry out healthcare and research activities. The actions of these groups therefore cover different areas of biomedical research, such as cardiovascular diseases, immune system diseases and autoimmune diseases, infectious diseases, cancer and toxicology. Other researchers are engaged in studying gender-specific diagnostic and prognostic biomarkers in various diseases. The aspects related to the responses of men and women to different lifestyles and nutritional habits are also studied. Finally, there is a team committed to ensuring correct, comprehensible and validated dissemination, which can guide citizens towards informed choices in the field of health.

The establishment of this Center, in itself an important and far-sighted step, has acquired even greater importance with the approval of Italian law no. 3/2018 "Delegation to the Government on clinical trials of medicines as well as provisions for the reorganization of health professions and for healthcare management at the Ministry of Health, published in the Italian Official Gazette of 31 January 2018. For the first time in Europe, this law guarantees the inclusion of 'gender' in all medical specialties, in clinical trials of drugs (article 1), in the development of diagnostic and therapeutic pathways, and in research, training and dissemination among all health professionals and citizens (article 3 "Application and dissemination of gender medicine in the National Health Service"). The ISS, and in particular the Center

for Gender-Specific Medicine, will be personally involved in monitoring the actions and results obtained at national level by setting up an Observatory. The ISS, together with the other bodies under the oversight of the Ministry of Health, will assure the reliability and appropriateness of the collected data, which will be reported annually by the Ministry of Health to the Italian Parliament.

The drafting of the plan, including the principles, objectives, and governance strategies for its implementation as well as the actions, actors and indicators provided for achieving the specific goals in each of the areas of interest, has required a significant joint effort involving, in the course of 2018, the Center for Gender-Specific Medicine, a number of Directorates of the Ministry of Health, the Italian Medicines Agency (AIFA) and AGENAS, with the collaboration of experts representing some Regions and Italian Scientific Institutes for Research, Hospitalization and Health Care (IRCCS).

Following in the footsteps of the Center's first Director, Walter Malorni, who has been successfully engaged in the field of gender medicine for years, I believe that the first of our institutional tasks is to train and inform health professionals and citizens to promote this new approach to medicine, which, for me, is a new and important challenge. Only few experts know what gender medicine really is.

Some years ago, the ISS, together with the Centro Studi Nazionale su Salute e Medicina di Genere (Italian National Study Center on Health and Gender Medicine) and the Gruppo Italiano Salute e Genere (GISeG) (Italian Group for Health and Gender), created the Italian Network for Gender Medicine with the aim of developing scientific research, promoting the training of physicians and health professionals and informing the public. Many medical federations and societies, scientific associations and some Italian Regions have since joined the network. In addition, the ISS has a scientific collaboration agreement with the University of Ferrara, in particular with the University Center for Gender Medicine Studies, inaugurated in June 2018, of whose board I am an external member.

In order to spread the idea of what gender medicine really is, the Center is strongly committed to training and scientific dissemination.

In particular, several staff members belonging to the Center are involved, as members or collaborators of the Scientific Committee and the Editorial Committee, in developing the project "ISSalute", a portal aimed at spreading scientific knowledge and findings to all citizens to allow informed and appropriate choices to safeguard their health. The portal, the only one in Italy without the participation of private individuals and without sponsors, created by the then President of the ISS, Professor Ricciardi, and for which Professor Malorni is responsible, is achieving important results, as shown by the recent data on access, which confirm the interest aroused by this source of institutional information. This portal, which deals with the issue of health and fake news, emphasizes where appropriate the relevance of gender differences and, more generally, the issue of gender medicine. The Center also coordinates the quarterly publication of a nationwide newsletter on gender medicine and produces information through educational brochures and video productions that are disseminated both via traditional channels and through the press and social media.

The Center is currently involved in numerous projects focused on achieving genuine equality in healthcare for all, including some minority groups, who, for a variety of reasons, may have difficulties in accessing care. In this context, the Gender-Specific Medicine Center has contacted the Tavolo Interreligioso di Roma, an interreligious dialogue association based in Rome, already operating locally for many years now, with which we aim to develop the health project 'System of interventions for gender-specific medicine in multicultural and multi-religious societies'. The pilot study will focus on the analysis of lifestyles by community and gender, on possible critical factors limiting access to national health services, and on information and training interventions. The gender differences and countless effects that can derive from them in terms of fair access to care fit well into the intercultural framework associated with the different religions, faiths and confessions.

Another potentially vulnerable population group is transgender people (400-600,000 people in Italy, although this number is not exactly defined), as indicated by the main international institutions that have included the safeguard of the health of gender minorities among their key objectives, as access to health care is often a challenge for them. To date, there is little data on the health, the long-term effects of hormone treatments, and their possible interactions with other therapies. Through the creation of a national network of clinical and research Centers, together with training and information activities, we will try to obtain a picture of the state of health of the transgender population to identify any critical issues and ensure genuine equality in access to healthcare throughout the country, which, as in many other areas, is not well-balanced.

Lastly, but certainly not least for me considering my thirty years working in the field of molecular oncology, is the commitment to research, because identifying the physiopathological bases underlying biological sex-associated and sociocultural gender differences is a crucial step towards real progress that combines greater therapeutic effectiveness with fewer adverse effects. In the field of oncology, the different responses to therapy (including immunotherapy) found between men and women are already being studied both internationally and at the Center for Gender-Specific Medicine. While to date epidemiological research has provided the hard data on the disparities existing between men and women, today the commitment of researchers and ours in particular is to understand the mechanisms underlying these differences. This approach requires that all new studies, from laboratory research to animal models and clinical trials, are carried out on both sexes. I hope that a gender-based review of the results accumulated over time in the various databases will also produce interesting results, enabling us to re-evaluate the work of many of our colleagues by highlighting similarities and differences in the various fields of research. Working with primary cells derived from male and female subjects and analyzing animal models of both sexes is certainly essential, but it requires the study of twice as many samples to have statistically significant results. Obviously, at least in the initial phase, it will lead to an inevitable increase in costs.

In the future, however, identifying gender-specific diagnostic and prognostic markers and the most appropriate therapies for each individual, improving the health of all, can only represent a strategic goal for the Italian National Health Service, which, through increasingly personalized medicine, together with better results and reduced adverse effects, can also lead to economic benefits.