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Tailored prevention in occupational and environmental health

Occupational and environmental medicine are now dealing with diseases, e.g., COVID-19, which pose some basic questions: why do only some of the subjects exposed to the same agents develop a severe disease? Should we consider genetically determined traits, as well as gender- and age-related susceptibility to implement more effective prevention programmes? Both in occupational and environmental settings, exposure limits are established to protect the vast majority of subjects, but leave at risk a small minority of susceptible people who might suffer harm if exposed to otherwise acceptable exposure levels. How could we better protect all, including them, without introducing stigma or discrimination?

The article proposed by Bollati et al (1) is an attempt to provide an answer based on recent advances in molecular biology, discussing inter-individual differences in genes and metabolism acting as effect modifiers, and epigenetic changes modulating the impact of environment and lifestyle on human health. A commentary in the first issue of the next volume of the journal (3) also highlights molecular biomarkers of accelerated aging, which may provide surrogate endpoints to test effectiveness of interventions that aim to extend healthy lifespan by slowing biological processes of ageing. Such biomarkers could aid in efforts to mitigate health damage from environmental toxicants, serving as surrogate endpoints in studies evaluating impacts of programs and policies to mitigate environmental toxicant burden (3).

A better understanding of such changes might pave the way towards tailored prevention, promoting a new way to improve the health of the population, within the 'P4' approach of precision public health, which should aim to be Predictive, Preventive, Personalised and Participatory (2). Precision public health promises that a bottom-up approach will result in a more accurate measurement of exposure to environmental pollutants and their effects, perhaps stratifying the population according to their susceptibility. The digital era provides new tools for medical research, which can now rely on advances in analytical chemistry, imaging, bioinformatics applied to several "omic" approaches. Artificial intelligence can also be applied to big data, a huge amount of data coming from different sources and formats, and available to everyone from everywhere. Researchers cannot fully control most such data. As a result, the scientific approach is shifted from the traditional hypothesis-driven design to a sort of agnostic attitude of researchers, delegating powerful software to do their job in a data-driven approach. Results are coming out from data analysis, thereby exposing inference from associations among variables to a possible fallacy of reverse causation. Bottom-up and data-driven approaches based on simple associations might be appropriate for tailored diagnosis and therapy. In contrast, the recognition of a causal relationship between exposure and effect in the frame of complex phenotypes is a pre-requisite of truly personalised prevention.

In occupational and environmental medicine, the population sharing the same exposure could be stratified according to a particular phenotype, into relatively resistant and susceptible groups. Picking out susceptible individuals would be very useful to identify a risk otherwise diluted and overlooked in the general population. Understanding gene-environment interaction might also increase our ability to develop interventions targeted at susceptible people, e.g., removal from exposure, reduced working times, or chemoprevention. However, any intervention should always be ethically acceptable, i.e. not resulting in stigma or discrimination, so that tailored prevention ensures a safe environment not only for the vast majority of people but for all.

There are prominent age- and gender-related differences in medicine regarding the immune system, inflammation, and noncommunicable diseases. Age- and gender-related degenerative changes imply an increased vulnerability and frailty, accounting for dramatic increases in morbidity and mortality after infec-

tion by SARS-CoV-2, and for age-related differences in COVID-19 prevalence and especially outcome. Telemedicine is also expected to benefit from constraints imposed by COVD-19 pandemic. Occupational telemedicine should be worker-centric, and should provide tools for multidisciplinary assessment by occupational health physicians, general practitioners, and specialists as needed by a tailored approach. A safe return to work after a severe infectious disease such as COVID-19 could require a collegial examination, which is easier to organise relying on telemedicine. The need for a multidisciplinary assessment, however, will not reduce the role and the responsibility of occupational physicians, who are expected to be compliant with their ethically binding mandate consisting of workers' health protection.

Mixing exposure settings can give rise to spurious findings, which increase with the number of variables. Extrapolation to individual health will always be challenging, even if assisted by artificial intelligence. Moreover, observed changes in patterns (omics) are transient, and timing is tricky.

For diagnostic purposes, the strength of associations is perhaps more critical than their causality, the probability of a correct classification being more important than the underlying pathophysiological mechanism. On the contrary, primary prevention can only be effective is relevant causal agents are removed. This is why genomics and proteomics and all other "omics" are promising for diagnosis, and perhaps for therapy. For prevention, the recognition of the actual causes of diseases would be crucial for subsequent intervention aimed at removing them, as our primary objective remains ensuring that the workplace and the environment are safe for all.

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