

Health: You and Your Exposome

By Stephanie Benz, L'Express, Jan,8, 2019

A revolution is underway: scientists are preparing to decipher the precise effects of the environment on health.

Lead, pesticides, bisphenol A, plasticisers ... here is the unhealthy cocktail, with proven or suspected health effects, discovered by European scientists in the blood of 1300 children and their mothers when they were pregnant, according to a study published in November in the journal *Environment International*. In total, of the 45 contaminants sought, two-thirds were found in 90% of participants. "Until now, there has never been data collected for as many substances at a time, in six countries, in the mother and her child," says Rémy Slama, research director at Inserm and coordinator of the study.

Even more complex than genome analysis

This vast work is one of the major projects co - financed in recent years by the Brussels Commission to better understand the " exposome " of the European populations. The exposome ? A concept still unknown to the general public, but destined to become popular. Invented in 2005 by Professor Chris Wild , former director of the International Agency for Research on Cancer , it aims to study the non-genetic risk factors of our diseases of civilization - cancer, diabetes, cardiovascular diseases, asthma .. After the deciphering of the human genome at the turn of the 2000s, scientists thought that they would find in our DNA the causes of these pathologies, and the means to treat them. But understanding the role of our genes has been much more difficult than we imagined then. Hence the idea of exploring the effects of the environment on health: "For a long time in limbo, this concept is now meeting a growing success in the global scientific community," says Dr. Anthony Macherone, co-author of *Unraveling the exposome, a practical view (Decrypt the exposome, a practical view , Springer 2018, untranslated)*. In France, this concept, already included in the preamble of the 2016 health law, should, according to our information, be at the heart of the next National Health and Environment Plan.

Studying the impact on our organizations of all environmental factors is, however, an ambitious project. A little crazy, even. More complex still, in any case, than the study of the genome, which already contains a gigantic amount of data, but whose limits are known. Apprehending the exposome indeed requires taking into account an infinity of variables. Chemical exposures, of course (pollutants, fine particles ...), but also other parameters: radiation, noise, stress, UV, working conditions, standard of living, physical activity, diet, light pollution, microbes, taking medication, traveling, outdoor temperature or even having green spaces close to home ... in other words, our entire physical, biological and social

environment. And this at all ages of life, from conception - and perhaps even before: "Studies show that children who had a smoking grandmother had a higher risk of developing asthma, even if they have not been exposed to tobacco," says Isabella Annesi-Maesano , research director at Inserm.

Discover new interactions

A revolution for specialists in the links between health and the environment, rather used to studying pollutants (asbestos, dioxin, bisphenol A ...) independently of each other. But this change of scale is essential to reduce bias and discover unexpected interactions. "The links already established between noise and cardiovascular disease, or between night work and breast cancer, show the interest of expanding research," says toxicologist Robert Barouki . With the objective of establishing a hierarchy of dangers, far from often irrational fears. "And above all, in the end, to make personalized prevention, according to the risks specific to each", hopes Isabelle Annesi-Maesano.

We are of course still very far, but a lot of progress has already been made. First, to characterize the environmental exposures themselves. "Satellites and many networks of sensors make it possible to cumulate data at very fine scales, on land use (crops, landfills, forests, etc.), temperatures, radiation ..." epidemiologist Alain-Jacques Valleron, Academy of Sciences. In the United States, Google has even equipped some of its Google cars, these cars that crisscross the cities to draw plans in pictures, air pollution detectors. A map of the most contaminated points of cities like Oakland or Houston has already been established, and London will be the next candidate for this exercise.

Individual measurements

"However, this information needs to be supplemented by individual measurements," says Robert Barouki , "For example, in the case of fine particles, we can not be content with atmospheric data, when the population increases from 70% to 80% of its time. inside, where pollution can be very different. " A complex question ... that could find a simple answer. Simple as small silicone bracelets , these plastic strips that teenagers often wear on the wrist. "Silicone absorbs many toxins present in the environment," says epidemiologist Gianluca Severi , who is preparing to test these "sensors" about forty volunteers in the Paris suburbs and the countryside.

At Stanford University (California), Prof. Michael Snyder has developed a more sophisticated handheld device. The size of a matchbox, the device contains air filters capable of capturing bacteria and viruses, fungi and pollen, insecticides, particles and pollutants. After permanently wearing it for nearly two years, he was able to draw up a list of more than 40,000 contaminants with which he was in contact - an experience he has just described in the prestigious journal *Cell*. Next step: to further miniaturize his invention, to go to the size of a big watch, so as to be able to deploy it on a larger scale.

At the same time, scientists are also looking to evaluate exposures directly in our bodies, by analyzing biological samples. Measures that complement each other, because the air sensors can not for example detect what we swallow via our power supply. "Mass spectrometers, always more powerful, now allow thousands of substances to be detected in a few drops of blood, breast milk or urine, on a picogram scale," notes Dr. Jean-Philippe Antignac, scientific leader of the largest French laboratory in this field (LABERCA), located at INRA in Nantes. The challenge now, according to this expert, is to be able to identify with certainty the totality of these traces, an exercise that remains particularly complex.

Find plausible biological mechanisms

But there is even more difficult: to evaluate their precise impact on our health. To see more clearly, researchers must measure contaminants on cohorts, populations monitored over long periods. It is then a question of crossing the evolution of the state of health of the participants with the statement of their environmental exposures, to bring out correlations. "Unfortunately, most of the existing cohorts today have not been designed to encompass so many parameters," regrets Professor Barouki. Faced with this challenge, epidemiologists use complex statistical tools and techniques derived from big data to compile data from different studies. The European Union has also co-financed the setting up of a new cohort dedicated to the study of the totality of the exposome. A project led by Isabella Annesi-Maesano: "We will include 5,000 children, including 600 in France, with many samples from birth, at the maternity, then large questionnaires for parents, all of which will then be repeated very regularly, and supplemented by as many environmental measures as possible."

The correlations unveiled by this type of study are not sufficient to identify with certainty the culprits in this or that disease. For this, plausible biological mechanisms must also be revealed. "The key is probably in epigenetics," says Professor Paolo Vineis of Imperial College London. And this expert decrypts: "In DNA, epigenetic markers surround genes: they can activate them or, on the contrary, extinguish them, but these markers are themselves influenced by the environment." It is now necessary to establish links between environmental factors, modifications of certain epigenetic marks and pathologies. A titanic task. "To date, only one of these variations has been identified with certainty: it is linked to tobacco and would have the effect of amplifying the action of a gene involved in lung cancer," explains Pr Vineis. It is therefore in fact in the interaction between the genome and the exposome that the origin of "multifactorial" diseases will have to be sought.