21st Century Publisher

21 ST CENTURY PATHOLOGY

21st Century Pathology

Short Communication

Open Access

The "Nano" Approach to The Future Medicine

Antonietta M. Gatti[1]* **Stefano Montanari**[1]

[1]NewNanodiagnostics, Italy

***Corresponding Author:** Antonietta M. Gatti, NewNanodiagnostics, Italy; E-mail: gatti@nanodiagnostics.it

Received: 27 January 2022; **Accepted:** 25 February 2022; **Published:** 28 February 2022

Abstract

The article deals with a new aspect of medicine, the one that takes into consideration the impact of pollutants of anthropogenic origin and of nano-metric dimensions on health, pollutants in the form of solid and inorganic particles increasingly present in the environment, in food and in drugs. The novel approach requires an interdisciplinary work in which the typical knowledge of medicine is flanked by those of chemistry, physics, and laboratory techniques, the main of which, but certainly not the only one, is that concerning electron microscopy.

Keywords: *Nanopathology; Nanotoxicology; Nano-bio-interaction; Nano-diagnostic operator*

Description

It is widely known that the environment can have a great impact on human and animal health. Already twenty centuries ago, the Latin writer and scientist Pliny the Elder (born 23 CE) reported in his Naturalis Historia that investing money on slaves who had worked in the asbestos mines was not wise, since they did not enjoy a long life. Even observing the facts superficially, as he actually did, he could point out how those slaves suffered from respiratory problems that were nothing but the prelude to an early death.

In short, even then it was clear that breathing dust was a potential source of disease [1, 2]. Today, enjoying the benefits of a far more sophisticated medicine, perhaps something of the simplicity and, perhaps, of the logic of linking symptoms to causes, and causes to effects has changed and something might have been lost. It is a fact that, with some exceptions that may exist, it is very rare for the doctor to ask the patient about the place where he works or where he lives. Working in the countryside or in a factory is a quite different thing, as it is living in a forest or near a waste incinerator. Almost, as a rule, the doctor limits himself to asking if his patient is a smoker or, perhaps, a drug addict. The anamnestic work considers only past illnesses, but it is rare that the series of diseases are listed in a consequential connection. A more accurate anamnesis considers any diseases of the past, but it does not always link the different pathologies coherently. The current symptoms are those that seem to interest, and, in fact, the patient almost always asks to have them disappear, because it is only the manifestations of the disease that bother and worry him. Both because they are often overworked and for legal reasons, doctors find it convenient to receive data generated by equipment, data that they juxtapose like a puzzle. And from that puzzle, a diagnosis will come out and therapy is prescribed. In that way, in many cases, only the symptoms will be treated, without going to the origin of the pathology and to its solution, if a solution can be achieved.

Today we know of an enormous number of diseases, some of which are labeled with the name of those who first dealt with them, but we might ask ourselves how much we know about their etiology? Meanwhile, the list of diseases called with the adjective of "orphan", that is abandoned or set aside, is constantly growing, because there is no economic interest in deepening the knowledge of them or in finding cures. Depending on who counted them, these diseases range from 7,000 to 10,000 [3]. One example among the many is the so-called "frontotemporal dementia" (FTD), where the name offers at best an anatomical localization of the problem. Hastily, a few assumptions and no cure [4]. Beyond any triumphalistic temptation that could turn out to be a dead-end, it is only honest to admit that in many cases medicine needs something different from its tradition and outside its ivory tower where any foreign contribution is considered as an undue invasion. Without claiming anything, our bioengineering approach could give a far from negligible hand to medicine. We cannot fail to realize that today's medicine is missing something, and just by way of example, it would be enough to mention cancer, a pathology, or, perhaps better, a group of pathologies that were once relatively rare but, in any case, have always been known, of

which, in fact, much is ignored about its origin. Today, for some years now, we have been witnessing the rapidly increasing spread of the disease, without having taken a reliable way to deal with it. Taking advantage of the scientific knowledge we have, and which is apparently outside of medicine, we can propose a new point of observation, in a certain way as, overcoming many difficulties that had nothing scientific, did the scientists of the past when they placed the Sun at the center of the solar system. By simply changing the point of view, everything became simpler and easier to interpret.

Similarly, we propose to shift the origin of the disease from the body to the outside, with all that the outside means. But let us be clear: this does not at all mean rejecting or abandoning the current studies undertaken since time immemorial, but simply means looking elsewhere for what triggered the changes that are found in the tissues and organs of the patient.

That there are important quantities of diseases originating from external factors is universally known and received. Bacteria, fungi, viruses, parasites, etc. influence our health by penetrating the body through different entrance doors: mouth, nose, ears, eyes, vagina, anus, skin. They settle inside the organism, often proliferate, and, with various mechanisms, cause the state of disease. But another agent has always existed that can trigger a disease: dust. As a matter of fact, Man has always lived with dust: volcanoes, sand, crumbling rocks, burning woods... But its concentration has almost always been relatively modest and, all in all, tolerable for health. At some point in his history on Earth, however, Man learned to light fire. It was roughly half a million years ago, with great time differences from place to place. To understand the impact and consequences of that negligible act, it is necessary to know that both what is burned and fire itself generate pollution, and it is in the moment when Man lights his first fire and then, perhaps centuries later, begins to produce artifacts with its heat that, at first timidly, the phenomenon of pollution of anthropogenic origin begins. Over time, the techniques have refined, the production of goods has increased, and, with them, pollution has inevitably increased as well. A major leap forward was that due to the so-called First Industrial Revolution, which began shortly after the mid-eighteenth century in Great Britain and continued in all the world [5].

What made the situation more critical was the successful search for how to increase the temperature of many industrial processes, thereby making it possible to obtain products that were once unthinkable, and now at affordable prices for an increasing number of people, transformed into consumers. This increased availability increased the production of waste which, somehow, had to be disposed of. At this point, it should be remembered that the higher the combustion temperature, the smaller the particles that are generated. And the smaller the particles, the easier their ability to penetrate the organism, resulting in a different ability to produce diseases or, in not a few cases, syndromes, that is, collections of different symptoms that, at first sight, can also look as mutually unrelated.

Some particles can be naturally degraded both in the environment and in the organism, but there are many, of an inorganic nature, some amorphous, some crystalline, which are extremely stable and are "eternal", if such an adjective may be used. This means that, once formed, they remain forever present in the environment. It is important to remember that the behavior of macro-objects, that is to say those we handle every day, is in many cases very different from that of atoms and molecules [6]. And atoms and molecules on the one hand, and macro-objects on the other, behave differently from micro- and, above all, nanoparticles, that is, following the usual classification, those of a size equal to or less than 100 nm. In many cases nanoparticles have free access inside cells, interacting with organelles and DNA which they can modify in ways that can be irreversible and without the cell being able to remedy [7]. Understanding this phenomenon, it is not difficult to realize how, in this way, cancer can be induced. But nanoparticles can also be responsible for changes in proteins, if only simply by modifying their shape. And proteins also mean enzymes, with all that altering these fundamental catalysts can entail.

Perhaps it is not known to everyone, but it is well known in the industrial field that nanoparticles enjoy very interesting characteristics that can be advantageously exploited for the production of an infinity of products. And this is what is being done at increasing speed. So, now we live in a world where nanotechnology, that is the use of nanoparticles, is becoming more and more present. Thus, inevitably, we are in constant contact with micro- and nanoparticles, some of natural origin as mentioned above; many accidental such as those that derive, for example, from the incineration of waste, from car and air traffic, from domestic heating, and the collateral effects characteristic of many factories; others that come from the use of nanotechnological products such as certain substances for the "purification" of air and water, for the production of cosmetics, or drugs. Not even food is exempt from these presences. With all those particles a nano-bio-interaction [8] with our body components can occur, much of which and many of its consequences have yet to be properly investigated. What we are sure of is that they can cause diseases that are not only serious but of which there is little or no experience and, therefore, there are no effective treatments.

Proteins can be arranged in a quaternary structure, i.e., the arrangement of multiple folded protein subunits in a multi-subunit complex. Nanoparticles can interfere with these structures (creating the protein corona) [9, 10], even with a simple unfolding, causing changes in the biochemical functioning of the organism that can lead to serious disorders that medicine is often unable to remedy. An example of a fairly common phenomenon is that which concerns the ability of nanoparticles to transform

fibrinogen into fibrin, thereby initiating the formation of blood thrombi. When the person does not naturally produce plasminogen activators such as urokinase, thrombosis can have severe effects up to pulmonary thromboembolism or stroke.

The question we are often asked is whether the organism can get rid of the particles that enter it. We have an experience of about 5,000 cases of pathologies caused by that type of very small dust that we have identified, photographed, and analyzed in pathological tissues [11, 12]. In all those cases, those particles had remained imprisoned in the tissues to cause the obvious foreign body reaction, manifesting itself in an inflammation which, given the impossibility of degrading the trigger, that is the particle, is chronic. Normally, the particles captured by the tissues are enveloped by a granulation tissue that can transform, even over a long time, into cancer. When the particles are ingested with food, most of them are quickly eliminated in the faeces, but some remain adherent to the walls of the digestive system and remain imprisoned or, in many cases, pass through them to end up elsewhere in the body. When the particles enter the body through breathing, most of them are expelled with exhalation. A part, however, remains in the bronchioles and alveoli, crossing them in a few tens of seconds to end up in the bloodstream which carries them virtually everywhere inside the body. When the conditions exist, the particles are taken up by phagocytes which carry them elsewhere, usually in the lymphatic ganglia. This, however, is only a displacement of the problem, since, while the phagocyte dies and is eliminated, the particle, not being biodegradable, remains in situ. Unfortunately, it is a fact that the normal defenses of the organism can do nothing against nanoparticles.

It should be borne in mind that very often the pathology arises first in a single organ, and all attention is paid to that organ which is often biopsied. But when the particles enter the organism, before they are captured by a tissue they often move rather freely and, therefore, can settle no matter where, where they can trigger a delayed pathological condition, often different from the one that was first noticed. With due experience, by observing the size and shape of the particles under the electron microscope and detecting their elemental chemistry, it is often possible to identify their origin. This is very important because it allows the patient to distance himself from what caused his illness, if only thus avoiding further worsening.

An organism can be polluted directly, for example by the fumes from a factory, from a food or a drug. As an example, we are now working on the brains of children died of Sudden Infant Dead Syndrome (SIDS) and find clear evidence of exogenous particle pollution [13]. But in some cases, the pollution can be of indirect origin. In our experience, for example, we have come across women polluted by their partner's sperm, and fetuses polluted by the content of their mother's blood. It is appropriate to realize that health is undergoing attacks that are decidedly different from those that have been characteristic in the past, and these attacks can be due to entirely new technologies and habits. For this reason, it is essential to modernize medicine, now unable to cope with a completely new situation that requires skills other than medical ones but complementary to them. Limiting ourselves to the observation of biopsy samples and to what is the core of our work, it is important to realize that between what the histopathologist sees through his optical microscope and what can be seen at the electron microscope (and of these there are different types with different characteristics and possibilities of application) there is a gap of 3-4 orders of magnitude, and in that gap the solution of the problem can be hidden or, at least, the possibility of significantly narrowing the margin of diagnostic error can be there.

An interesting application of this approach to medicine is that of forensics. As already briefly described, the presence of particles no matter how introduced into the body can cause illness or death, which can be of particular importance for insurance companies. But equally important, or perhaps more so, is the possibility of discovering whether the particles were used as a kind of "nano-bullets" for criminal purposes [14]. Therefore, in this kind of new whodunnit where the sometimes-unsuspected culprit is to be found out, it is necessary to create a figure with a preparation that includes, beyond biological skills, at least environmental science, materials science, and microscopy techniques. This new figure will immediately prove to be fundamental in helping the doctor in the anamnesis, in the diagnosis and in the possible search for an adequate therapy.

Conclusion

If we wish to be able to face the needs of a world that we have changed with unusual speed and, perhaps, without considering the consequences of the changes, medicine must accept to become truly interdisciplinary. In 2002, as the title of a European research, we created the name "nanopathology" to define diseases derived from inorganic micro- and nanoparticles, pathogens that are becoming more present day by day and, consequently, more aggressive. In this new discipline, the interaction between the patient and the environment that surrounds him, with this understanding what he breathes, what he eats and what he is currently treated with, assumes a role of absolute pre-eminence. And without there being an approach in which even apparently very different skills work, no progress will be possible.

Conflict of Interest

The authors have no conflict of interest.

Personal Financial Interest

The authors have no personal financial interest regarding publication of this article.

Non-financial Competing Interest

The authors have no non-financial competing interest or personal relationships that could have influenced the work reported in this paper.

Overlapping Publication

This article has not been submitted to any other journal for publication.

References

1. IARC: Outdoor air pollution a leading environmental cause of cancer deaths (2013) International Agency for Research on Cancer. World Health Organization – Press release N° 221.
2. Straif K, Cohen A, Samet J (2013) Air Pollution and cancer.https://www.iarc.fr/wp-content/uploads/2018/07/AirPollutionandCancer161.pdf
3. Eurordis. The voice of rare diseases in Europe. https://www.eurordis.org/
4. Johns Hopkins Medicine. Frontotemporal Dementia. https://www.hopkinsmedicine.org/health/conditions-and-diseases/dementia/frontotemporal-dementia
5. Laden F (2019) A tale of six cities: the landmark Harvard six cities study. Env Epid 3: 221. https://doi.org/10.1097/01.EE9.0000608272.94008.7b
6. Nemmar A, Hoet PH, Vanquickenborne B, et al. (2002) Passage of inhaled particles into the blood circulation in humans. Circulation 105: 411-414. https://doi.org/10.1161/hc0402.104118
7. An H, Jin B (2012) Prospects of nanoparticle-DNA binding and its implications in medical biotechnology. Biotechnol Adv 30: 1721-1732. https://doi.org/10.1016/j.biotechadv.2012.03.007
8. Gatti A, Montanari S (2014) Nanopathology: The Nano-bio-interaction of Nanoparticles Inside the Human Body, M. Lungu et al. (eds.), Nanoparticles' Promises and Risks, Springer International Publishing Switzerland, Part II-5 5 : 70-84.
9. Monopoli MP, Walczyk D, Campbell A, et al. (2011) Physical-chemical aspects of protein corona: relevance to in vitro and in vivo biological impacts of nanoparticles. J Am Chem Soc 133: 2525-2534. https://doi.org/10.1021/ja107583h
10. Ritz S, Schöttler S, Kotman N, et al. (2015) Protein corona of nanoparticles: distinct proteins regulate the cellular uptake. Biomacromolecules 16: 1311-1321. https://doi.org/10.1021/acs.biomac.5b00108
11. Gatti A, Montanari S (2015) Case studies in nanotoxicology and particle toxicology (1st edtn) Elsevier Pub London. 1: 260.
12. Gatti A, Montanari S (2021) Advances in nanopathology from vaccines to food. (1st edtn) Jenny Stanford Pub, New York, 198. https://doi.org/10.1201/9781003056225
13. Gatti A, Lavezzi AM, Stanzani S, et al. (2022) Novel chemical-physical autopsy investigation in sudden infant death (SIDS) and sudden intrauterine (SIUDS) unexplained death syndromes Nanomedicine 17: 275-288. https://doi.org/10.2217/nnm-2021-0203
14. Gatti A, Ristic M (2022) New forensic protocol in the era of sars-cov-2. J Forensic Sci Criminol 9: 2-4.