



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com



POSTFACE

Is the drug a scientific, social or political object?

Antihypertensives, hydroxychloroquine, clinical trials, pharmacovigilance, placebo, randomization... The covid-19 pandemic and the search for preventive or curative pharmacological solutions have led to drugs at the heart of current events. Thus, our fellow citizens have discovered many concepts that were, for the most part, foreign to them. For many people, drugs are first and foremost a scientific object in the hands of health professionals, whose work is expected by the public without necessarily taking an interest in their genesis, their mechanism of action or their evaluation, even though concerns about potential risks have been growing in recent years. In fact, drugs are not just a tool for individual use, but are social objects, as defined by Durkheim, as evidenced today by variations in consumption of certain classes and their determinants. Among these determinants, there is a normative part, which confers a political dimension to the drug. So, is drug a scientific, social or political object?

Drugs are first and foremost a scientific object that has oscillated, from the outset, between empiricism and rationalism. Even if the discovery of plants with medicinal virtues was based on the observation of their virtue, pharmacologists in Antiquity and the Middle Ages tried to rationalize their use by conceptualizing it: Hippocrates' "theory of opposites, Paracelsus'" theory of signatures... However, drug and its therapeutic dimension, often considered as an art rather than a science, remained for a long time far from the scientific foundations of innovation and demonstration, either by indulging in a dogmatism ignoring all evolution, so well illustrated by Thomas Diafoirus in the piece of theatre "The imaginary patient" from Molière, or by engaging in experiments, sometimes hazardous (i.e. inoculation of malaria in psychiatric diseases), without evaluation. Many of the drugs still in use were discovered by chance, with a further generalisation of their therapeutic use. Nevertheless, for some successes, many failures are not only linked to inefficiency but, unfortunately, often accompanied by a disproportionate risk compared to a random benefit. It is in this context, and in line with the trend towards scientific positivism, that evidence-based medicine has gradually emerged, with its corollary, the randomized clinical trial (RCT).

Randomized controlled trials are based on two principles: comparison and comparability. These two principles allow dispensing first with the natural evolution of the disease, particularly in infectious diseases, and second the placebo effect, which can now be corroborated by brain imaging studies. Without respect for these two principles, it is impossible to establish the role of the drug in the clinical effects observed when testing a new pharmacological approach. Paradoxically, the methodological rigour inherent to controlled trials and the role of the pharmaceutical industry in promoting these trials have ended up bringing discredit to this approach, which is, however, the best method for establishing the proven effect of a drug, in part of the population. The craze that has arisen for the distribution of hydroxychloroquine, based on a very preliminary study and the analysis of a cohort without a comparator group, was, from this point of view, very emblematic of the fact that belief can quickly replace scientific demonstration. This is not new and already exists for alternative therapeutic methods that refuse to fall under the caudine forks (so named in reference to the battle at the end of which the Romans had to submit to the Samnites) of clinical trial methodology. This attitude has, however, taken an emotional and claiming side in the context of the anxiety and fear generated by the Covid-19 pandemic and its lethal risk.

Empiricism seems to be trying to take again a top position over the rational approach, which some consider too dogmatic, especially in critical situations. Is it necessary, because it is urgent, to abandon all the scientific principles of clinical trials that have previously led to undeniable therapeutic progress? Undoubtedly not, which does not mean that the experimental design of the trials should not be adapted, in an approach reminiscent of Charles Peirce and William James theorising pragmatism as a third way transcending the empiricism/rationalism opposition. For more than thirty years, French medical pharmacologists and therapists have been contributing to an international movement of methodological diversification through a think tank (called "Ateliers de Giens") bringing together the academic, industrial and institutional worlds. Pragmatic trials, adaptive trials using the Bayesian approach, studies with external comparators, trials on small samples, taking into account secondary assessment criteria and the use of biomarkers are all methodological innovations that aim to make the framework of controlled trials more flexible in order to speed up or improve the evaluation of drugs, without abandoning the major and basic principle of comparison [1,2]. The media outburst against methodology rightly clashes with the convictions of the vast majority of health professionals, who have perhaps not sufficiently integrated the fact that drugs, which they consider above all as a scientific object that is their prerogative, have also become an issue that the social body has taken up.

It is above all through the drug risk and its often-mediatized affairs that society has integrated drugs as a social fact [3]. The so-called "Mediator" affair has had a major impact on populations, in this case the French one, with the realization that drugs can be also dangerous, even in the long term. The front pages of newspapers and magazines devoted to medicines and their risks have been booming, like the questions addressed to the Regional Pharmacovigilance Centres. The development of social

networks has had an amplifying effect on the emergence of medicines as a social issue, by bringing it out of the circle of health professionals, previously considered as the only "knowers". Some years ago, several episodes of reporting adverse drug reactions linked to changes in thyroid hormone formulation have emerged as a viral relay on social networks. Social demand may lead regulatory agencies to re-evaluate positions that were initially scientifically based, or to speed up market entry. Recently, the film "120 beats per minute" recalled the interactions, sometimes violent, between patient associations, pharmaceutical industry and regulatory agencies in order to bypass the usual marketing rules, in view of the mortality caused by HIV. This is reminiscent of what we are experiencing today with molecules reputed to be potentially effective against SARS-Cov-2, recalling what we have previously seen with other products, such as baclofen in alcohol use disorders.

While society may request answers from public authorities and healthcare professionals regarding the risks/benefits balance of drugs, social facts may also influence the medical use or diversion of medicines, or even investment in their development. The cult of thinness, advocated year-round in all magazines, was undoubtedly the main factor that triggered the misuse of the Mediator, replacing dexfenfluramine, which, a few years earlier, had been withdrawn from the market because of its valvular risk. Our modern societies, based on the over-emphasis on performance, generate a diversion of drugs, particularly psychotropic ones, for the purpose of cognitive doping. However, anxiety induced by loss of social bearings or by suffering at work linked to the search for profitability at all costs explains the over-consumption of psychotropic tranquillizers or antidepressants. The social context may therefore explain the emergence of a pattern of use or an increase in the prescribing or consumption of a particular drug, which then escapes rational, evidence-based use, necessitating regulatory measures to control prescribing or dispensing. The current health crisis has highlighted the immediate link between the announcement of preliminary or hypothetical results on the efficacy of a particular drug against coronavirus and its dispensing, and often consumption, outside of any regulatory framework.

Taking into account the social dimension of the drug reveals, however, a contradiction in the demand of the social body, which has been amplified during the health crisis. On the one hand, there is an expectation for information that has been scientifically validated by health professionals. In the space of one month, the Pharmacovid site [4] set up on 21 March was consulted nearly 300,000 times, with many questions asked by Internet users. A recent report of a working group on information on medicines, organized by the French government, suggest to create a portal open to the general public. This highlights a fundamental movement to involve patient associations in the therapeutic objectives of medicines, developing the concept of patient-experts. At the same time, there is also a desire for rapid pharmacological and therapeutic responses, even if they are not scientifically substantiated. Reading social networks is also demonstrative here, with its procession of suspicions regarding the merits of drugs based on evidence or the competence of health professionals, not to mention the denunciation of their supposed compromise or submission to the lobbying

of the pharmaceutical industry. This basic trend, which has developed over the last twenty years or so, is exacerbated by fears linked to the risks of coronavirus infection, which itself is seen as an artificial construct designed to increase the system's grip. If drug professionals must respond to this contradictory injunction without contempt, but through education and transparency, it is hardly surprising that the political body is also alerted by these expectations of the social body with regard to medicines.

Drugs are also a power issue and fit in well with the concept of "biopower" proposed by Michel Foucault. From an anthropological point of view, there have always been individuals in society who had the power to control suffering and sick bodies. This biopower was for a long time a quasi-mystical power when it was exercised by shamans or sorcerers, before gradually becoming scientific, after the Paracelsus turn, which gradually opened the way to the evaluation of drugs, controlled by health professionals with the knowledge. However, biopower inherent to drug use has also become a power of the state, with the emergence of regulations for the practice of medicine or the dispensing of medicines by the body of pharmacists. It is still crises, particularly due to the emergence of adverse drug reactions, which have led to the creation or development of regulatory agencies, a tool used by States to control drug policy. Intoxication with about a hundred deaths from sulfanilamide, due to a manufacturing error, led F.D. Roosevelt to create the Food and Drug Administration (FDA), the first regulatory agency to be implemented in a country. These agencies, although state power, are based on scientific expertise and independence of political or economic power, even if here again, social body questions reality of this independence, on the occasion of what are mediatized as health scandals or faced with insufficient regulation of some psychotropic drugs that allow a calming of the social body.

The current health crisis may be leading to a turning point, with drugs becoming a political football. It is first of all an object in the international political games, because it is clear that States have lost their sovereignty over the production of medicines, which, like other manufactured products, has become one of the goods of globalized capitalism. The current crisis, however, has made us aware that drugs are above all a common good, since they affect one of the essential elements for humanity, namely health. If tomorrow a vaccine or treatment against coronavirus is found, will we witness a war between states to control supply, as happened with masks? Will the world balance between states be altered? Will the ability to control drug policy in all its aspects (innovation, rapid assessment, production) become a diplomatic weapon or even a propaganda tool for external or internal propaganda? Because drugs have also become a domestic political issue, as we have seen with chloroquine and hydroxychloroquine, with partisan confrontations or positions taken without scientific basis by a head of state announcing his belief in the interest of chloroquine, in a country that was the first to create a regulatory agency. The balance between political power and regulatory agencies may be shifting, as shown by the announcement by the President of the United States of America, in person, of the authorisation of an antiviral by

the FDA, developed by an American company, even though the results of clinical trials are still contradictory. It is the same with a nationalist attitude for the priority delivery of vaccine. Will drug policy tomorrow become a subject of electoral debate, on a par with fiscal or educational policy, and an argument for economic nationalism? How can we reconcile this irruption in the public or political debate and the maintenance of a sufficient level of expertise to avoid falling into the populism we know in other fields, with its share of false or truncated information?

Health professionals must now integrate, perhaps more than they did in the past, that the drug is no longer just a scientific object. The Covid-19 crisis has brutally revealed its social and political dimensions. This must have consequences on the teaching of medicine in the medical, pharmaceutical and paramedical fields in order to arm future professionals to better respond to these social and political issues. This means that medicines must be integrated into education from primary school onwards and that the development of information for the general public must be accelerated, following the example of what pharmacologists and therapists will have initiated during the current crisis. However, the social and political body cannot take over the drug by ignoring its scientific dimension, at the risk of returning to an empiricism, which, although it may be artificially attractive in times of crisis, can only lead, if rigorous evaluation is not maintained, to dangerous adventures in terms of the benefits/risks balance of the drugs. Pharmacological research must, more than it is now, become interdisciplinary, in form of university chairs that make it possible to combine medical, pharmaceutical, political, human and social sciences.

Disclosure of interest

The author declares that he has no competing interest.

References

- [1] Cucherat M, Laporte S, Delaitre O, Béhier JM. the participants of Giens XXXV Round Table Clinical Research. From single-arm studies to externally controlled studies. Methodological considerations and guidelines. *Thérapies* 2020;75:21–7.
- [2] Laporte S, Diviné M, Girault D. Quelle utilisation et quelle hiérarchisation pour les critères de jugement secondaires? *Thérapie* 2016;71:34–7.
- [3] Montastruc JL. Social pharmacology: a new topic in clinical pharmacology. *Thérapie* 2002;57(5):420–6.
- [4] Société française de pharmacologie et de thérapeutique. Pharmacovid platform: questions and answers for the public about drugs in the context of the COVID-19; 2020 <https://sfpt-fr.org/covid19-presentation> [Accessed May 20, 2020].

Régis Bordet

Université de Lille, CHU de Lille, département de Pharmacologie Médicale, 1, place de Verdun, 59000 Lille, France

E-mail address: regis.bordet@univ-lille.fr

Available online 23 May 2020