Small virus, big questions

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Introductory statement

I am a biophysicist, director of research at the laboratory "Matière et Systèmes Complexes" (UMR7057 CNRS & University of Paris). I am the deontologist referent of the Faculty of Sciences to the Committee of Ethics, Deontology and Scientific Integrity and Scientific Integrity (CEDIS) of the University of Paris. In 2021, in order to avoid the freezing of the debate on the origin of the pandemic, I co-signed four open letters that were published by media in different countries 1, as well as a correspondence to The Lancet2 ; and I co-organized an online public conference3. I am collaborating in a joint research project research project entitled "Elucidating the proximal origin(s) of the SARS-Cov2" (Labex WhoAmI, Initiative of Excellence, University of Paris, September 2021-August 2023). The following text does not stem from this research project and does not belong entirely to the domain of my scientific expertise. It does not commit my institutions, nor CEDIS, nor the other co-signatories of the open letters and the correspondence to The Lancet.

To date, questions about the origin of the Covid-19 pandemic have not been answered definitive answer. They have brought to light serious faults in the scientific community, as much scientific community, both in the choice of research conducted and in the debate about it, even though the issue is crucial for the prevention of future pandemics. This first part of this paper traces the failures of the scientists, and analyzes the links between these failures and the and the current functioning of research. It will be followed by a second part, engaging a more general reflection, centered on the lessons to be drawn with regard to scientific research as a whole: its usefulness for society, its dangers, its regulations, and its its dangers, its regulations, and its future.

A debate closed for a year

If a virus emerges that combines the dangers of the AIDS virus, Ebola and Covid-19, that is that it has an initial phase with no visible symptoms, that it is rapidly contagious, and that it is that it is highly lethal, one can imagine the severity of its effects. The question of prevention of future pandemics is crucial. For this it seems essential to understand the origin of the Covid-19 pandemic. Zheng-Li Shi is one of the researchers at the Wuhan Institute of Virology (WIV) most concerned with bat viruses. In a June 20204 interview, she states that on Dec. 30 2019 she was informed of a new outbreak and immediately became concerned about a possible role for her team. She recounts going several days without sleep before absolving herself of any responsibility. To do so, she says she checked that "none of the [SARS-CoV- 2] matched those of the viruses her team had collected from bat caves ". This does not rule out other more plausible scenarios, such as a virus that evolved in his laboratory after he had collected it, or the role of another team in Wuhan. At least, we can say that for her, from that time, it was legitimate to consider that a laboratory could have contributed to the origin of the epidemic that was beginning.

At the beginning of 2020, when few Westerners knew how to place the city of Wuhan on a map, the information that the information that came out seemed distant, exotic, and therefore difficult to

2

dispute. But imagine that an epidemic of a new variant of rabies broke out in the 15th district of Paris; that the list of past scientific publications of the Pasteur Institute shows that researchers there have been conducting research on different Greek variants of rabies for several years Greek variants of rabies; that the Pasteur Institute and the Parisian authorities affirm that this epidemic, without any link with their laboratory, would be due to rabid foxes coming from Greece. Should we take their word for it, that Greek foxes or other rabid animals spread discreetly in Paris, finance new laboratories to monitor foxes and their viruses? foxes and their viruses? Or should we first entrust an investigation to a truly independent team?

In practice, on February 19, 2020, a group of researchers, including the British zoologist Peter Daszak, published an article in the scientific journal The Lancet stating that the Covid-19 pandemic was strictly animal in origin, and that any other hypothesis was "conspiracy".5 The scientific debate then became increasingly tense. From then on, the scientific debate became tense and closed for a year. Two elements raise questions: On the one hand, Daszak chairs the EcoHealth Alliance (EHA), an international organization based in New York that coordinates funding for research programs in various laboratories, including in Wuhan, for the prevention of epidemics of animal origin. The hypothesis of an animal origin of the pandemic would open for him increased prospects of funding and power, while the hypothesis linked to a laboratory would undermine his legitimacy and that of the research model he promotes. Even if, with the benefit of the doubt, one can conceive that he is in good faith, there is objectively a conflict of interest. We will learn later that 26 of the 27 signatories of this letter have connections with the of this letter have connections with the Wuhan Institute of Virology, its researchers or its funding6, and researchers or its funding6, and that they were brought together at the initiative of Daszak, who did not wish to appear too visibly7.

On the other hand, the Lancet article is essentially based on an article8 published online the day before and published shortly afterwards in the journal Nature Medicine. Compared to the article, the article does not bring no significant element: its argument is based mainly on the observation that most emerging epidemics are that most emerging epidemics are of animal origin, without proving this assertion in this case.

The Nature Medicine text, on the other hand, will become particularly influential, and will serve as a reference for many scientific and general public articles. to many scientific and general public articles9. It avoids making a definitive decision but reminds that in the past the coronaviruses have often emerged via an animal host, and puts forward two main arguments:

On the one hand, the authors affirm that they have not detected any indication of artificial manipulation of the sequence of the virus. This statement is correct and may impress non-specialists. In On the other hand, specialists can react10 since they know how to carry out genetic manipulations in the laboratory in the form of genetic manipulations in the form of operations (similar to "copy and paste") that leave no visible trace in the other methods, such as accelerated evolution in living cells, lead to the creation of a cells, result in changes that resemble natural evolution without human intervention.

On the other hand, the authors demonstrate that the virus sequence is not as improved as it probably would have been if researchers had wanted to maximize its dangerousness. Even a non-specialist could easily understand that this argument is not sufficient to assert that the origin of the pandemic is entirely independent of research activities.

In fact, both of these arguments can be questioned and they do not settle the debate because of the lack of direct experimental evidence. More generally, it is inappropriate to frame the debate in such a binary way, as if it were not possible to binary, as if there were only two extreme scenarios: "either entirely natural origin or intentional human origin". Indeed, as we will now see, there is a continuum of possibilities.

Asking the right questions

There is only one consensus: it is that bats living in caves in Southern China on the Tropic of Cancer, harbor many viruses, some of which are similar to SARSCoV-2. The general question of the origin of the pandemic can then be divided into three main, very concrete three main, very concrete questions.

- How did a virus of this type get to Wuhan? How did it get from a tropical cave to the from a tropical cave to the heart of an urban metropolis of 11 million inhabitants, more than a thousand kilometers away? Did it arrive only via animals, which is a plausible hypothesis, but not yet validated? No one responsible for the spread has yet been found. About 80,000 animals, 42,000 wild and 38,000 domestic, have been tested without detection of specific antibodies to SARS-CoV-211. More recent Chinese research specifically targeting 13,000 bats at 700 sites and found numerous coronaviruses in them, but no antibodies to many coronaviruses, but no SARS-CoV-212. Or was its transport linked to a research activity? This too seems plausible, since Wuhan is home to a dozen or so virology laboratories13. Researchers in Wuhan have often collected bat samples themselves on site, and even bat samples, or even live bats, on site14. They could also have brought back to Wuhan a similar virus already passed from bats to humans, which they collected and examined in 201515.

- How did the virus evolve? How did a virus that infects bats without making them sick bats without making them sick become so adapted to humans, being able to transmit between them, and to transmit itself between them, and to be dangerous for them? The hypothesis of a spontaneous evolution during between different animal species (wild or domestic) and humans is plausible, since it is the plausible, since it is extremely common16. However, to date, neither the intermediate hosts of the current However, neither the intermediate hosts of the current pandemic, nor intermediate sequences reflecting progressive stages of virus evolution, have yet been identified. Could SARS-CoV-2 be the result of an evolution that evolution that took place in a laboratory? This is also plausible because, as discussed below various laboratories have conducted and published research on the evolution of this type of virus.

- How was the first human infected? What does a "no laboratory" hypothesis mean? (The word "natural", usual in the media, is inappropriate because by definition an interaction between an animal and a human is never free of human intervention, as an earthquake or an earthquake or a volcanic eruption). Accidental contamination of a human could occur during a visit to a cave by a tourist or a worker, poaching, working in a poaching, working on a farm, or selling in a market, among others. It is certainly plausible; for example, in 2002, this was the case with SARS-CoV, the coronavirus that caused the SARS epidemic. What is a "research-related" hypothesis? (The term "laboratory leak", which is common in the media, is too restrictive as it excludes the collection of samples in the field.) Accidental contamination could occur via an animal that accidental contamination could occur through an animal escaping from its cage, a false maneuver, a failure to follow safety instructions, a lack of lack of proper protective equipment. This is also plausible,17 given the frequency of This is also plausible,17 given the frequency of numerous research incidents that have occurred in the past, some of which are recalled below.

On the one hand, in order to demonstrate that the origin is research-related, it would be sufficient to show proof of the contribution of a research activity to one of these three stages. On the other hand, to demonstrate that the origin is independent of research, it would be necessary to provide full proof that no researcher has ever intervened at any of the three stages: neither transport, nor evolution, nor contamination. On the level of logic and argumentation, the two hypotheses are therefore not symmetrical.

It is important to continue to examine all the different hypotheses about the origin of the pandemic, and to consider that they remain open18. to consider that they remain open18. They will remain open until there is definitive proof one way or the other, 19 and one way or the other19, and the debate is

lively20. China sometimes promotes the animal hypothesis by the laboratory hypothesis, while at the same time claiming that a leak from a US laboratory is plausible. laboratory is plausible. Despite the order of President Biden, the US intelligence services are unable to intelligence services are unable to make a decision21.

Personally, I have no opinion, and besides, it is not a matter of having an opinion: it is a matter of to establish facts. Of course, this is an unusual debate. Indeed, in the case of a scenario entirely independent of a laboratory, the investigation to be carried out would consist in determining an unknown cause, which would be a scientific investigation. Whereas in a laboratory-related scenario, there would be would be people who would know elements but would not publish them: the investigation to be investigation would be more of a journalistic type.

Risky research

Whatever the scenario that really caused the pandemic, this debate has brought to light an essential fact research in virology constitutes a structural risk. The collection, transport and storage of viruses, as well as experiments, are never done in safe conditions that guarantee safety conditions that guarantee zero risk.

For laboratory rooms, there are different levels of security, depending on the degree of danger of the experiments that are carried out there. Level 2 rooms are clean and sterilized. In level 3 rooms, the air pressure is lower than outside, which protects the environment against possible leaks. Level 4 rooms are also low pressure, and in addition the experimenter wears a high pressure suit which protects him against possible against possible leaks.

Part of the research takes place outdoors. A project coordinated by Peter Daszak, financed by the United States funded by the United States and carried out in China, states that field work "involves the highest risk of exposure to SARS or other CoVs when working in caves with a high density of bats above the density of bats overhead, and the possibility of fecal dust being inhaled. inhaled. There is also a risk of exposure to pathogens or physical injury when handling bats, civets, rodents or other animals, their blood samples or feces.22 22 Yet Zheng-Li Shi's June 2020 interview with Scientific American is illustrated with old photographs that show his colleagues in 2004 collecting bat blood samples bat blood with only gloves, a mask, and a cap on; at the same time,

Shi herself was releasing a bat while wearing only gloves; by comparison, on another trip a group of international scientists wore a full-fledged wet suit from head to toe, including eyes.23

A June 2021 Washington Post article provides details.24 Zheng-Li Shi and another researcher, Junhua Tian of the Wuhan Center for Disease Control (CDC), are competing to collect bats and their droppings. This race for glory sometimes leads to serious compromises with safety. A program in honor of Tian, broadcast by the official channel China Central Television (CCTV) on December 19, 2019, when the pandemic was not yet known to the world, indicates that he has visited dozens of caves. Tian explains that it is during collection that the risk of getting infected is highest, if skin comes in contact with bat droppings or other contaminated materials. Yet the video shows him handling samples without full protective gear. In 2017, he explained to the newspaper Wuhan Evening News that he often received drops of blood from the bats he bats he immobilizes; once when he forgot his protective gear, he was splashed with bat urine and put himself in quarantine at home.

The CDC came under the spotlight when Peter Embarek, the head of the jointly mandated jointly by China and the WHO, noted that this laboratory moved on December 2 2019 to a location 500 meters from the famous market that was soon after considered the as the epicenter of the epidemic. Embarek points out that moving a laboratory, especially one that viruses, is never trivial25; it disrupts its activities, routines, and safety procedures.

Even the Wuhan Institute of Virology's Level 4 laboratory (the safest on the scale) had security alerts by U.S. diplomats in 2018 26. A 2019 Chinese investigation in 2019 also pointed to serious

malfunctions 27. However, for animal viruses including SARS-like coronaviruses, international regulations allow for less stringent to work under less stringent conditions, at level 3; in practice, especially in China sometimes only level 228. When asked about this in July 2020 by the journal Science, Zheng-Li Shi indicated that this was indeed the case for coronavirus research in her laboratory29. However, this is unsuitable for directed selection or mutation experiments that that could make these viruses capable of infecting humans.30

Research-related incidents occur frequently in all countries31 (although they are not systematically recorded and published32). According to Frédéric Tangy, head of vaccine research at the Pasteur Institute: "All it takes is for a researcher to spill a vial. Despite the extractor hood, an aerosol is formed and he is infected without realizing it. At the end of the day, he leaves the laboratory, infecting his entire family and everyone he meets. In 2004, an article in The Lancet reported on incidents of smallpox, polio, and SARS34 . 34 The SARS virus, SARS-CoV, infected researchers on at least six occasions, even after the epidemic ended in July 2003.35 In the United States, the list of incidents is long. In the United States, the list of incidents is long, as China has just reminded us36; for example, between 2004 and 2015, hundreds of shipments of anthrax from one laboratory to another had mistakenly not been inactivated 37. In China, in early 2020, a senior researcher was infected with SARS-CoV-2 in a prestigious laboratory in Beijing38; in 2019, massive brucellosis contaminations were due to discharges from a factory39. In France, on July 27, 2021, the second accidental prion infection in a laboratory of the National Research Institute for Agriculture, Food and the Environment (INRAE) leads to a ban on all research on the subject for three months.40 In the United Kingdom, more than a hundred safety violations in the last 15 years have occurred in laboratories handling pathogens; for example, staff handling Ebola-infected animals with snags in their protective clothing; most importantly, the foot-and-mouth outbreak of 2007 is evidence of the possibility of an outbreak emanating from a leaking Level 4 laboratory.41

Moreover, are these ultra-secure facilities at the mercy of malicious intrusions? A element of answer is provided one evening in 2016 by a harmless incident caused by... a drunk homeless man. Looking for a building where to shelter for the night, thanks to his wire cutter he enters without knowing it a level 4 laboratory containing bacterial strains and extremely dangerous viruses, such as Ebola42. It was this laboratory in Lyon that served as a model for the construction of the one in Wuhan43.

Worrying research

It is in this context that the category of risky experiments must be appreciated: those whose result or at least that can be reasonably anticipated, is the appearance of pathogens that have become more pathogens that have become more dangerous for humans or for an intermediate animal host. For example, by genetic manipulation or accelerated evolution, the pathogen acquires an increased ability to infect a human to infect a human, to affect his or her health, or to spread to other humans. Or, the pathogen acquires an enhanced ability to overcome a human's immune response, to resist a drug or to resist a drug or a vaccine, or to rebuild an eradicated pathogen. eradicated. The comparison between the benefits and risks of such experiments requires determining who can benefit, to what extent who can benefit, to what extent, and who may have to bear the risks, in the short or long term, with what probability, and with what possible consequences.

Following the modification of an influenza virus by researchers in the Netherlands, Japan and the United States, there has been much debate about the potential dangers and even the definition of and even the definition of so-called "gain-of-function research" (GoFRoC) took place during the 2010 decade. This may include the study of cell responses, or the development of a vaccine, with possible vaccine, possibly with defensive or offensive military aims. The benefits expected in terms of a better understanding of how viruses evolve in order to be better prepared to fight them, can better prepare

to fight them, can they justify exposing ourselves to a risk, admittedly unlikely, but with potentially very serious consequences, of a pandemic due to an incident or an act of terrorism44 ?

And in the event of a pandemic, who is supposed to take responsibility for it?

On July 14, 2014, a group of scientists, calling themselves the Cambridge Task Force, said it was deeply concerned about the accelerating frequency of incidents involving regulated pathogens in the best laboratories in the United States: up to two per week! He called for urgent changes in practice45. Two weeks later, virologist Vincent Racaniello responded by collecting signatures for a counter-appeal from "Scientists for Science", according to whom research on pathogens should be encouraged. that research on pathogens is safe and essential for the knowledge, prevention and treatment of knowledge, prevention and treatment of disease.46

In October 2014, in the United States, this debate over detected incidents resulted in a pause on national funding for any new research involving such experiments47. Admittedly, this moratorium was limited to a single country, it only concerned public funding and not other sources of funding, it only prohibited funding and not the research itself, it only concerned new research and not ongoing research, it defined research of concern in a restrictive way research of concern, and above all, at the beginning it only concerned the influenza virus (before being extended to a limited list of other viruses). Moreover, even within this restricted the moratorium provided for numerous possibilities of derogation: 7 of the 18 projects initially blocked were finally projects that were initially blocked were finally funded anyway, on the flimsy grounds that they were urgent and necessary to protect public health or national security". Finally, its audit committee was unable to properly identify all the projects within its scope. But despite these weaknesses, at least this moratorium had an important value, because it sent a strong signal to the international scientific community: this research is really worrying and risky for really worrying and risky for humanity, insofar as laboratory incidents frequently occur. happen frequently. It was associated with an appeal to all the researchers concerned to voluntarily pause their research.

New assessments from 2016 warn of the dangers of this type of research on coronavirus48. However, scientists like Vincent Racaniello actively promote them 49 ; even if it means minimizing the criticisms, or proposing a restrictive definition of the research for example, an experiment that deliberately aims to make a virus more pathogenic for humans. for humans. The bat coronavirus chimeras that Peter Daszak and Zheng-Li Shi published in PLOS Pathogens in 2017 were not created with an expectation of increased increased50. Should we therefore encourage research that does not anticipate danger to humans, when it is precisely those that may not be safe enough?

In 2017, the joint action of certain biologists who complained about the restrictions placed on their research and their colleagues in high places in the US funding agencies, resulted in the moratorium being emptied of all substance51. the moratorium of any substance51 . Indeed, its scope was reduced to almost nothing. Thus, it only two old and one new project, and the audit committee was unable to detect projects unable to detect projects within its scope, such as EcoHealth/ Wuhan Institute of Virology. of Wuhan. In addition, whereas previously it had the power to block funding, it has become merely advisory.

Perhaps one day we will know whether this 2014-2017 moratorium indirectly and unintentionally contributed to the causes of the Covid-19 pandemic. Indeed, during this moratorium, U.S. laboratories in the United States transferred their research to the laboratories of their Level 3 level 3 or even level 2 laboratories in China52, where the research was subject to less stringent constraints and could be research was subject to less stringent constraints and could be conducted at a rate ten times faster.

The adaptation of a virus to humans can be tested in the laboratory on mice that either express a human gene or have been grafted with human stem cells or tissues (so-called a human gene or have been transplanted with human stem cells or tissues (so-called "humanized" mice). "humanized" mice). Researchers at the Center for Animal Experimentation at Wuhan University have used them to test

three Wuhan University have used them to test three synthetic viruses under Level 3 safety conditions, without reporting them as gain-of-function research of concern.53 Also in Wuhan, at Huazhong University of Science and Technology, humanized mice are still being used in 2021 for 2021 for SARS-CoV-254 experiments.

At the Wuhan Institute of Virology, a bat coronavirus genome is used as a basis for creating different basis for creating different chimeric viruses by adding a different spike protein of different origin. Peter Daszak's idea is to test each time whether the spike protein is human cells in culture, and to check whether the virus thus created has the capacity to infect these cells in the laboratory, assuming that this reflects its ability to cause an epidemic in the to generate an epidemic in the real world55. This type of construction has been achieved, in particular, by using genetic technologies that leave no trace of artificial intervention in the virus genome, in the genome of the virus, in the team of Ralph Baric of the University of North Carolina 56, with a participation of the Wuhan Institute of Virology, which then did the same on its own57.

Thus, in 2015, Peter Daszak preaches about a gain-of-function experiment using a bat virus, which was performed by Zheng-Li Shi, among others, and whose results "move this virus from being a candidate emerging pathogen, to a clear and present danger 58." On February 23, 2016, he detailed, "I didn't do this work, my colleagues in China did. You create pseudo-particles, you insert the spike proteins of these viruses, you see if they bind to human cells. At each step you get closer and closer to the point where this virus can actually become pathogenic in humans. So you narrow the field of study. You reduce the cost. And you end up with a small number of viruses that actually look like killers.59

The weight of the military

This raises the question of possible military involvement in the origin of the virus. The Chinese authorities, both regional and national, have had a heavy hand in controlling and censoring information about the origin of the Covid-19 pandemic; samples from the early days of the pandemic samples from the early days of the pandemic were destroyed by order.60 But this blanket of secrecy does not in itself mean that there is anything to hide. to hide an unmentionable event. Indeed, one could imagine, for example, that at the beginning there was a a minor incident, immediately covered up because it was considered harmless. If this is the case, when the case became more widespread, the information was locked up so as not to lose face, and it seemed impossible to reverse afterwards. More precisely, concerning the contamination of the first human, there does not seem to be any indication that it was linked to the military. The hypothesis that the virus could have been released voluntarily with military (or even terrorist) purposes seems unlikely from a political, psychological or technical point of view. The hypothesis that the virus was deliberately released for military (or even terrorist) purposes seems unlikely from a political point of view, and in view of the first known stages of the spread of the epidemic.

Regarding the transport of the virus to Wuhan, the military does not seem to be involved either.

Their possible role seems to be indirect and not specific: the Summer Military World Games, a sports Summer World Games, a sports competition held in Wuhan from October 18 to 27, 2019, could likely have contribute to the local and global spread of the virus.61 At that time, there was inconclusive but consistent evidence (based on the census of the first known patients and the study of the subsequent evolution of the virus sequence), the epidemic was probably already brewing somewhere, in Wuhan62 or elsewhere63.

On the other hand, the influence of the military on the evolution of the virus is visible. The funding managed by Peter Daszak came largely from the US military (nearly 39 million dollars out of a total of 103 million out of a total of \$103 million64), which supports cooperation with China for biological biological studies of bats.65 In addition, Chinese military personnel have published on this subject66.

Moreover, as of February 2020, the Wuhan Institute of Virology is under military under military control67. And more generally, the 1972 Biological and Toxin Weapons Convention signed by almost all countries, does not provide for any regime of verification of compliance with its the United States: biological warfare is still included in the strategies of the armies of strategies of the armies of various states, first and foremost the United States and China68.

The research carried out was able to combine civilian and military aims simultaneously (this is what is called dual (this is what we call dual research). In fact, research on viruses is the result of several research on viruses is the result of several wills that can coexist in the same laboratory or in the same country. The will to knowledge of humanity and the understanding of epidemics, and to prepare for a future pandemic. to face a future pandemic. But also to be ahead of other countries in the production of a vaccine, to be able to defend ourselves in case of a biological attack by a State or individuals, and eventually to be able to be the attacker, or even to develop more contaminating or more lethal viruses. Is that possesses both a dangerous virus and its vaccine may believe itself to be all-powerful.

In the United States, the "Defense Advanced Research Projects Agency" (DARPA) funds advanced science and technology projects for military use. In January 2018 it launched a call for proposals for the prevention of threats from emerging pathogens, which includes

explicitly includes the possibility of vaccinating wild animals to prevent transmission of viruses to humans.69 On September 20, 2021 an anonymous whistleblower revealed via the Drastic Collective70, without being denied, that a consortium of Peter Daszak, Ralph Baric, Zheng-Li Shi, and others had responded to this RFP in March 2018. Their large-scale, \$14 million application, dubbed "Defuse," sought to, among other things, aerially vaccinate bats in their natural habitat, and synthesize viruses for laboratory testing.

Fortunately, DARPA refused this request: because it was not sure that it could work; because it was "gain-of-function" research, the risk of which was great and poorly controlled, and which could cause an epidemic in humans living near the bats; and because this type of research is dual civil-military, the United States does not want to fund military research in China, and the project did not provide guarantees on this subject.

The lessons to be learned are wide-ranging:

- DARPA funds research on viruses and their animal reservoirs.

- DARPA recognizes that this research has potential military use.

- DARPA recognizes that the Daszak, Baric and Shi application includes research of concern "gain-of-function" research.

- DARPA refuses to fund them because in this case there are insufficient security guarantees, but it does not fundamentally question this type of research.

- The project included work on the Middle East Respiratory Syndrome coronavirus (MERS-CoV), which until now has not caused many victims because it is not very contagious. But this virus has a mortality rate ten times higher than SARS-CoV-2: one in three patients dies.

- The intelligence services solicited by Joe Biden were probably informed of this project. If so, one wonders on what basis they categorically rejected the idea that SARS-CoV-2 could have been made with a military purpose.71 The inadequate response of the scientific community In the context of the existence of worrying research, and its potential to cause future pandemics, it would have been pandemics, it would have seemed crucial to keep the scientific debate on the origin of the the origin of the Covid-19 pandemic. However, for at least one year, from March 2020 to May 2021, in scientific institutions, in scientific journals and among researchers around the world, even in the absence of experimental evidence, the dominant opinion was that the origin was purely animal origin. The corollary has been an increase in the collection of bat virus samples in China and elsewhere,72 and a call for funding to build new laboratories, which increases the risks. It is necessary to investigate by

what mechanisms such a sensitive debate with such consequences could be It is necessary to investigate by what mechanisms such a sensitive debate with such consequences could have been evacuated, and to draw lessons from it.

We can note a certain laziness, voluntary or not, on the part of journals and researchers who have avoided to look the arguments in the face. When one examines a claim, the degree of confidence one attributes to it should be When examining a claim, the degree of confidence in it should be judged on the basis of a variety of factors, the first of which is argumentation.

Other elements include the competence and legitimacy of the author, his or her possible conflicts of interest, and the channel interest, and the channel through which he or she expresses himself or herself. One can also take into account the general context, the the ordinary or surprising nature of the statement. In addition, each listener can modulate the trust to their own experiences, opinions, and level of competence.

Yet Peter Daszak, despite his conflict of interest, remained influential during this period.

He was invited to the major conferences on the subject. He was appointed to the two commissions that were supposed to investigate the origin, and that did not dig up the trail of the laboratory, notably because of Chinese resistance73 : that of the scientific journal The Lancet on the origins and initial spread of the pandemic (Daszak was later rejected as an expert on the expert on the question of origins74, and on 25 September 2021 this commission was dissolved in order to cut all ties with EcoHealth75); and the one jointly mandated by China and the World Health Organization Organization (since then, on 26 September 2021, the WHO has announced that it wants to recreate a commission with new scientists, this time with specialists in laboratory biosafety76 and without Daszak laboratories76 and without Daszak).

On the other hand, during this period, correct and important elements could not be heard because they came from non-scientists77 ; or because they were passed on by patent conspiracy theorists conspiracy theorists, supporters of President Donald Trump, anti-Semites, or anti-Asians.

A few ambitious scientists seem to have placed their particular interest above the general interest, which has biased their Some ambitious scientists seem to have put their particular interest above the general interest, which has biased their scientific activities and public statements.78 Some publishers of small79 and large80 scientific journals, research institutes, research funding foundations, and foundations, and the science pages of major media, seem to have played the same game. game. Methods and data have not been published transparently; databases have been altered, partially deleted, or made inaccessible online. Reviewers of articles have been too complacent in the pre-publication critical review process. The motivations of the authors of these acts may be to protect research from the risk of budget cuts, to avoid harming their Chinese collaborators, to show deference to institutions, or to preserve their or to preserve their social status. In any case, this can be called a conflict of interest; from a legal point of view, it would probably be similar to influence peddling or illegal interest taking.

During this period, various information was published, which, without having any evidential value, tended to legitimize tended to legitimize the hypothesis of a role for a laboratory. In particular: (1) An online database of the Wuhan Institute of Virology on bat viruses studied there studied82 has been made inaccessible, officially because since the beginning of the pandemic it has suffered from hacking attempts, but in fact since September 12, 2019 83. (2) In 2012, in a mine where bats nest, six workers became ill and three of them died.

The illness was pneumonia due to a virus that resembled, but was not identical to, SARSCoV (the original SARS virus) and SARS-CoV-284. Samples from these workers were sent to Wuhan for analysis, and at the same time researchers from Wuhan came to the site to collect bats. (3) Zheng-Li Shi's publication on SARS-CoV-2 as well as the bat virus (named "RaTG13") presented as one of the last links in the evolution to SARS-CoV-285, had gaps and inconsistencies, requiring an addendum

Wuhan Institute of Virology may have been sickened by Covid-19 in November 2019 87.

On May 14, 2021, a group of renowned scientists in virology and epidemiology published an article in the journal magazine "Science" in which they asked that the debate on the origin of the pandemic remain open88. From that date on, the debate became admissible again. In a sign of the times, on 26 May, in a terse two-sentence laconic two-sentence statement without any self-criticism, Facebook announced that it would stop censoring "the claim that Covid-19 is synthesized by humans"89.

The failure of the scientific community

It is true that, during this one-year period, many more or less isolated scientists went out of their way to alert or to fight against the abuses, and finally were able to reopen the debate a little. But at that time the scientific community (or more precisely the majority of its institutions, journals and researchers) clearly failed90, with regard to the four pillars of scientific ethics:

- Deontology: the conflicts of interest of some researchers and some institutions led them to bias the to bias the debate.

Integrity: regarding the proofreading of articles, the transparency of methods and the availability of raw data, the scientific norms that international scientific journals are obliged to uphold were violated.
Safety: research aimed at making potentially more dangerous viruses ("gain-of-function research")

was conducted before the intense debate about weighing the expected benefits against the risk taken was resolved.

- The purpose: The search for profit and power, rivalries between nations or between researchers, were mixed with the motivations of collaboration and progress of knowledge.

New questions

The second part of this paper will come back to this purpose of research. Indeed, in view of the foregoing, and with the challenge of preventing the occurrence of even more serious pandemics in the future, it is certainly legitimate to ask questions specifically related to the experiments conducted on viruses. Are they linked to the origin of this Covid-19 pandemic? Do the expected benefits justify the risk of a pandemic due to an unintentional incident or a deliberate act? But it is equally important and important and urgent to ask other questions about scientific research as a whole: about its usefulness to society usefulness for society, its dangers, its regulations, and its future.

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et notamment : Shannon Murray, « Scientists who authored article denying lab engineering of SARS-CoV-2 privately acknowledged possible lab origin, emails show », U.S. Right to Know, August 11, 2021 https://usrtk.org/biohazards/scientists-who-authored-article-denying-lab-engineering-of-sars-cov-2-privatelyacknowledged-possible-lab-origin-emails-show/

79 Sainath Suryanarayanan, « Chinese-linked journal editor sought help to rebut Covid-19 lab origin hypothesis », U.S. Right to Know, April 7, 2021, https://usrtk.org/biohazards/chinese-linked-journal-sought-to-rebut-covid-19-lab-origin-theory/

80 Sur le site de Nature, consulté le 28 septembre 2021, figure toujours le commentaire placé par l'éditeur le 30 mars 2020 sur l'article de Baric de 2015 : « Editors' note, March 2020: We are aware that this article is being used as the basis for unverified theories that the novel coronavirus causing COVID-19 was engineered. There is no evidence that this is true; scientists believe that an animal is the most likely source of the coronavirus. » https://www.nature.com/articles/nm.3985

81 Collectif DRASTIC, « An investigation into the WIV databases that were taken offline », February 2021, https://www.researchgate.net/publication/349073738

82 Base "batvirus.whiov.ac.cn", v1 avril 2019, v2 juin 2019. Cette base de données a pourtant bénéficié d'un soutien à l'accès ouvert aux données scientifiques : deux cent mille euros de financements européens via l'organisation EVAg.

83 Gilles Demaneuf, "The 16 missing databases of the WIV", Sept 16th 2021, <u>https://bit.ly/3nF01M9</u> voir aussi :

https://www.researchgate.net/publication/354647665_The_16_missing_DBs_of_the_WIV, DOI:10.13140/RG.2.2.31193.85600

84 Li Xu, « The analysis of six patients with severe pneumonia caused by unknown viruses », thèse de master en médecine clinique, université de médecine de Kunming, 28 mai 2013.

85 Cette publication a été vue plus d'un million de fois, selon les statistiques de la revue. Zhou, P., Yang, XL., Wang, XG. et al., « A pneumonia outbreak associated with a new coronavirus of probable bat origin. » Nature 579, 270-273 (2020) https://doi.org/10.1038/s41586-020-2012-7

86 Monali Rahalkar, « Criticism for the Addendum: A pneumonia outbreak associated with a novel coronavirus of probable bat origin (Zhou et al 2020) » https://monalirahalkar.wordpress.com/2020/11/27/criticism-for-the-addendum-a-pneumonia-outbreak-associated with-a-novel-coronavirus-of-probable-bat-origin-zhou-et-al-2020

87 M. Gordon, W. Strobel, D. Hinshaw, « Intelligence on Sick Staff at Wuhan Lab Fuels Debate on Covid-19 Origin », The Wall Street Journal, May 23, 2021 https://www.wsj.com/articles/intelligence-on-sick-staff-at-wuhan-lab-fuels-debate-on-covid-19-origin-11621796228

88 Bloom JD, Chan YA, Baric RS, et al. « Investigate the origins of COVID-19 », Science. 372 (6543): 694. https://science.sciencemag.org/content/372/6543/694.1.full

89 « In light of ongoing investigations into the origin of COVID-19 and in consultation with public health experts, we will no longer remove the claim that COVID-19 is man-made or manufactured from our apps. We're continuing to work with health experts to keep pace with the evolving nature of the pandemic and regularly update our policies as new facts and trends emerge. »

Guy Rosen, « An Update on Our Work to Keep People Informed and Limit Misinformation About COVID-19 », May 26, 2021 https://about.fb.com/news/2020/04/covid-19-misinfo-update/

90 Elaine Dewar, « On the Origin of the Deadliest Pandemic in 100 Years - An investigation », Biblioasis, 2021

Viruses and search: 2/2

Should we stop scientific research?

François Graner

Opening statement

I am a biophysicist, research director at the "Matter and Complex Systems" laboratory (UMR7057 CNRS & University of Paris). I am an ethics referent of the Faculty of Science at the Committee of Ethics, Deontology and Scientific Integrity (CEDIS) of the University of Paris. In 2021, to avoid freezing the debate on the origin of the pandemic, I co-authored four open lettersthat were published by media from different countries, as well as correspondence to ¹The Lancet magazine; ² and I cohosted an online public lecture.³ I am collaborating on a joint research project of three laboratories, entitled "Elucidating the proximal origin(s) of the SARS-Cov2" (Labex WhoAmI, ExcellenceInitiative, University of Paris, September 2021-August 2023). The following text is not from this research project and does not belong entirely to the field of my scientific expertise. It does not bind my supervisory institutions, nor CEDIS, nor the other co-signatories of the open letters and correspondence to The Lancet.

To date, questions about the origin of the Covid-19 pandemic have not received definitive answer. They have highlighted serious faults of the scientific community, both in the choices of the research conducted and in the debate on them, even though the stakes are decisive for the prevention of future pandemics. The first flightand traced the shortcomings of scientists, and analyzed the links between these failures and the current functioning of research. This second strand engages in a more general reflection, focusing on the lessons to be drawn from scientific research as awhole: its usefulness for society, its dangers, its regulations, and its future.

As mentioned in the first part, while the real origin of the Covid-19 pandemic is still unknown what is important is what the debateabout it has highlighted, that is to say therisky activity of a few

March 4, 2021: https://doi.org/10.13140/RG.2.2.26695.83368/1 April 7, 2021: https://doi.org/10.13140/RG.2.2.25018.11206/1 April 30, 2021: https://doi.org/10.13140/RG.2.2.18097.51041/2 June 28, 2021: https://doi.org/10.13140/RG.2.2.21927.27042/1

² Jacques of Heroes et al. "An appeal for an objective, open, and transparent scientific debate about the origin of SARS-CoV-2 », The Lancet, September 17, 2021 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02019-5/fulltext https://doi.org/10.1016/ S0140-6736(21)02019-5

³ COVID-19 Origin Webinar, Sept 14th, 2021, https://www.youtube.com/channel/UCrHG9IWjZXLdiWDkf_cBSeg

scientific researchers; for some of them their irresponsibility, greed and power of nuisance; and the profoundly inadequate response of the scientific community. Whether or not the Covid-19 pandemic is linked to research activity, it seems necessary to be cautious, rather than to accelerate the collection of viruses in the field, or the construction of virology laboratorieswhere experiments with poorly assessed risks could be carried out.

This pandemic has generated a shock wave that is not yet extinguished. It is an excellent opportunity to reflect on the challenges of scientific research, its motivations, and the difficulty of itscontrol; as well as the functioning of the community. A historical reminder will make it possible to find resonances with the current situation.

The motivations for research are very diverse

By "scientific research" we mean here approximately academic research in the so-called hard sciences and, for some aspects, also in the so-called human sciences. This activity has extremely diverse and intertwined motivations.

On the part of the public, there is a very concrete demand for improvementsin material welfare and health, and the history of humanity has been largely correlated with the evolution of technology. This demand is also nourished by the thirst for knowledge, the curiosity inherent in the human mind, incessant questions about disciplinessuch as astrophysics, evolution and archaeology. The excellent, exciting and passionate work of the scientific communities over the centuries has enabled superb collective constructions of the human intellect: for example, mathematics, the understanding of the periodic table of the elements, chaos theory or that of relativity. Scientists have sometimes been able to collaborate despite the wars between their respective⁴nations. Above all, there is a real usefulness in havingscientific communities trained in debate and critical thinking, inquestioning certainties, in rejecting arguments of authority; if only to combat political totalitarianism, religious fundamentalism, superstition, all otherthanscientistic dogmatism.⁵

On the researchers' side, the motivations displayed range from personal curiosity to the desire to feel useful, powerful or recognized, to the desire to be paid for an interesting and varied activity in arelatively free environment, not to mention the opportunities to travel, to speak in public or to meet colleagues for stimulating exchanges. Added to this are the pleasure of learning, the challenge of going beyond one's own limits, the wonder of discovering,the jubilation of transmitting, the excitement of clearing a virgin subject, the desire to be quoted in articles and invited to speak in congresses, the desire to join the closed circle of those whose names appear in textbooks.

This idyllic picture very useful for justifying research expenditure and recruiting brains. In reality, precariousness, competition and power relations sometimes completely distance professional life,

⁴ Especially for the measurement of the dimension of the Universe, from 1761 to 1769. See Jean-Pierre Luminet, « Le rendez-vous de Vénus », Lattès, 1989.

⁵ F. Graner, "The scientific spirit: an evolutionary achievement?", Psy Reviewchologie de la Motivation, 23, 98-102, 1997. Revised edition:
F. Graner, "The scientific spirit: an anthropological turning point?", Revue de Psychologie de la Motivation, 40, 129-133, 2005.

http://francois.graner.name/publis/graner esprit sc.pdf

especially of the youngest, from this picture that hashelped to attract them. Those who pass the doctorate, the first rite of entry, then obtain from their supervisors favorable letters of recommendation, win a permanent position, and finally obtain the habilitation to direct research, integrate one by one the concentric circles of which can be described as a real community, with its codes, itslinks of collaboration and itshierarchy.

For centuries, colonial empires sent explorers to identify new lands; taking all the risks, celebrated as heroes, explorers were closely followed by soldiers, merchants, missionaries. For lack of land to discover, it is now the researcher who is assigned this role, and the scheme remains similar. The researcher is pushed to lead the way, and he is closely followed by the army, the company, the advertising. The scientific community works thanks to the contribution of money by funders: national or regional authorities and international agencies, armies, companies, foundations, or associations. These funders have their own motivations, very varied, but with in general the same request: that of benefiting from short- or long-term benefits, especially because understanding aphenomene then makes it possible to act on it.

These funders, as well as the need to regularly publish new results in specialized journals, keep the competition running. Researchers who capture resources early in their careerare in a better position toprogress, apply for new funding and occupy positions of power. Consider two authentic examples. A senior researcher entrusts the same research topic to two precarious young people, warning them that only the one who finds it first will be able to publish; a research institute grants a five-year position to a young person by having him sign the commitment to publish, before the end of the five years, in one of the three most competitive journals (Nature, Science or Cell). This encourages predatory behavior, low blows and fraud.

The need to regulate research activities

When living in society, limitations are erected, based both on a system of more or less wellsharedvalues, and on decisions which concern the community and therefore in essence are political (in the sense of: "which concerns public affairs"). The law and justice are supposed to serve the general interest by setting limits onharmful partic uliers. Research activities are not immune to the need to be regulated, especially since they potentially have major consequences for all of humanity.

At present, the regulation of the content of publications requires the validation of scientific knowledge. It is operated through peer judgment, an internal process within each area of the community. One of the key steps in the verification of a scientific publication is often that it is collected before publication by one or morespecialists in the subject who, protected by their anonymity, can freely list all their criticisms of the text. This system certainly has various disadvantages, such as inter-self, conformism, clientelism or chapel struggles. But it works as best it can, at least when it has proper evidence techniques, space for adversarial debate, and sufficient time. It has a proven track record of distinguishing (at the endof the decade or century) what is or is not a reliable scientific claim, and thus ensuring the continuous increase in knowledge, understanding of the world, and know-how. On the other hand, the validation of scientific knowledge by political decision-makers has a bad press: it is generally ineffective, and above all it evokes memories of interference by religious or totalitarian powers.

The impact on health or the environment

even the very essence of research.

It is not desirable for the research activity itself to have a negative impact on health or the environment, either directly or through the risks it entails. A researcher who wants to carry out an experiment withthe potential for such an impact must justifyit, and generally proposes a comparison of the expected benefits of his research and the possible risks it entails. In principle, it should be possible to make informed choices toregulaterisks. In reality, the analysis can be biased from the outset, because potential beneficiaries (e.g. researchers themselves, or patient associations) are often better able to make their case thanpotential victimes (e.g. poor populations, future generations, or impacted animal or plant species). Finally, it would be necessary in principle to determine in advance who would be responsible in the event of a problem:politically, criminally and financially responsible, which also raises the question of whether a company would agree to carry out risky research.

A famous example of an attempt at regulation by scientists in a given field took place about fifty years ago. In Asilomar, California, for four days (February 24-27, 1975), 150 researchers from around the world gathered behind closed doors. Faced with the new possibilities of manipulatingorganisms, including pathogens, they debated the choice betweenbanning experiments or regulating them with safety measures. Limited to human health issues, this conference did not address the social, economic, political or environmental impacts of techniques related togenetically modified organisms, nor the question of insurance of the corresponding risks. In the absence of consensus, limited safety recommendations emerged. However, genetically modified organisms, for example for plants grown in the middleof theplant, pose particular problems, because even if they are stopped, they can continue to spread on their own. The question of criminal or financial responsibility arises in a completely new and largely insoluble way.

Concerningresearch in virology, the debates of the 2010s followed a similar path, with as little effectiveness in the end. On 14 July 2014, a group of scientists, entitled "the Cambridge Working Group", launched a call forurgent practice, making explicit reference to Asilomar.⁶ The counter-appeal published two weeks later, by scientists showing their confidence in current practices, also claims to beAsilomar.⁷

The collection, transport and storage of viruses, as well as the experiments involving them, are risky research activities. Yet they are widely supported by the scientific community. This even applies to

⁶ Cambridge Working Group Consensus Statement on the Creation of Potential Pandemic Pathogens (PPPs), July 14, 2014

http://www.cambridgeworkinggroup.org

⁷ Vincent Racaniello, « Scientists for Science », 28 July 2014 https://www.virology.ws/2014/07/28/scientists-for-science/ To see signatories on: http://www.scientistsforscience.org/

"worrying research of gain-de-function" (GoFRoC), whatever the definition given to it, for example: add functions to a virus or accelerate its evolution so that new functions appear, concerning its ability to infect a human, to overcomeits immuneresponse, to affect its health, to spread to other humans, to be resistant to a drug or vaccine. This research of concern is carried out in an informed way by individuals and institutions which are financed by institutional or private actors. It is the scientific community itself that, through its institutions and funding system, tolerates and sometimes encourages the crossing of red lines.

Evenif many researchers behave responsibly, it only takes one whocircumvents the prohibitions for the efforts of all the others to be reduced to nothing. In 2014 the United States decreed a moratorium on the funding of research concerning job gains. Without deterring this type of research, this moratorium has mainly had the effect of exporting it to other countries where this regulation does not apply. Despite assessments in 2016 that warned of the dangers of this coronavirus research, thejoint action of some biologists who complained about the brake on scientific progress, and scientists who led the funding agencies, resulted in 2017 in emptying the moratorium of any substance.⁸

Because it would always work for the "general interest", and pretending to forget the role of each individual, the scientific community seems to assert that it is not subject to law and regulation. It does not even provide for any special measure to prevent the individual de-breeding of a mad, suicidal or malicious scientist. Suggestions to create an international agency for the supervision of biological research, independent of researchers and their funders, and endowed with strong powers of inspection and sanction, on the model of the International Atomic Energy Agency (IAEA), would eventually provide an independent lever to exercise vigilant surveillance.⁹ The analogy between virology and nuclear power is relevant: the existence offisks that are unlikely but have serious consequences, civil-military duality, and the possibility of both accidents and proliferation. Unfortunately, the model is hardly convincing, because in the nuclear sector also many scientists are inclined todeliberately inimize the risks; some countries such as China are almost completely opaque when it comes to publishing incident reports; and even California devotes more effort to convincing that the situation is under control rather than anticipating the problems that may arise.¹⁰

Concerning more specifically the environment, the direct impact that research activity can have, in particular on the climate, is increasingly the subject of public debates and¹¹interpellations. The

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https://www.washingtonpost.com/nation/interactive/2021/a-science-in-the-shadows/

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Rodolphe de Maistre, "For the creation of an international governance on biosafety", L'express, 13 August 2021

10

David Willman and Madison Muller, « A science in the shadows : Controls on 'gain of function' experiments with supercharged pathogens have been undercut despite concerns aend lab leaks », The Washington Post, 26 August 2021

https://www.lexpress.fr/actualite/pour-la-creation-d-une-gouvernance-interationale-sur-la-biosecurite_2156398.html

Kate Mishkin, « 'A combination of failures:' why 3.6m pounds of nuclear waste is buried on a popular California beach », 24 August 2021

https://www.theguardian.com/environment/2021/aug/24/san-onofre-nuclear-power-plant-radioactive-waste-unsafe

¹¹ HorizonTERRE, "Science needs a democratic debate to include ecological and social issues", Reporterre, 19 May 2021

growing industryfor the acquisition, transfer, processing (including through machine learning) and storage of digital data is becoming a concern. They are the subject of quantified indicators in order to help reduce this¹²impact. The same is true for the many trips. But improving the efficiency of a personal computer or replacing a high-carbon-emitting plane trip with a train trip does little to do so when you receive money that needsto be spent andwhen, by definition, research is pushed to go ever harder, faster, higher.

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In particular, exploration directed towards the infinitely large or the infinitely small requires more and more energy and effort, and is accompanied by more and more environmental impacts, to the point that interest in humanity becomes more and more questionable. The European Centre for Nuclear Research (CERN) already consumes half the power of a nuclear reactor in electricity: isit essential to double its consumption during its next expansion, which will also swallow up high-tech materials, while its research tracks are becoming increasingly uncertain? Do we have an imperative need forgiant digital calculations and storage, kilometre astronomical observatories? Is the excessive investment in the International Thermonuclear Experimental Reactor (ITER), spread over a century in the hopeof finally leading to the production of electricity by nuclearfusion, justified, given its risky nature? In another register, in order to study or preserve them, should samples of animals and plants be massively collected, travelling thousandsof kilometres byplane and unintentionally spreading pathogens that could harm these species? To "save the climate", is it necessary to gather tens of thousands of people in congresses and have them write thousands of scientificarticles? Science policy debates, conducted in a national or international context, compare expected benefits and costs, but the latter are often limited to financial costs and it is rarer forenvironmental costs tobe fully taken into account.

Research and competition

The cries of warning about the military uses of advances in science are not new. In 1922, at the end of the First World War and the development of military chemistry, the historian Jules Isaac accused science of manslaughter: "Isit not right to say that science uses it-with regard to humanity exactly like unconscious parents who would leave within the reach of their child a loaded revolver, without even thinking of putting it on the stop? The kid touches it, naturally: the blow leaves; here he lies dead. Willit-be-said that the child alone is responsible, and that the parents are not? ¹³ ». Perhaps it would be more accurate to compare the scientific community to someone who accepts to be paid to constantly invent, simultaneously, innovative revolvers and bulletproof vests.

https://decidim.sciencescitoyennes.ovh/

https://reporterre.net/La-science-a-besoin-d-un-debat-democratique-pour-inclure-les-enjeux-ecologiqueet-social

12 See in particular the work of the collective Labos1point5 https://labos1point5.org/

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Jules Isaac, "Paradoxe sur la science homicide" (1922).

Text taken from Jules Isaac's book, Paradoxe sur la science homicide et autres hérésies, Paris, Rieder, 1936.

Reproduced in Alliage n°52 (2003)

"Science and War," pp. 79-87

http://revel.unice.fr/alliage/index.html?id=3699

The Second World War and the development of nuclear physicsgenerated a new awareness. In 1955 scientists around Russell, Rotblat and Einstein called for a peaceful resolution of international conflicts to prevent a nuclear world war, a source of "universal death".¹⁴

After acentury of nuclear age, the threat has not moved away, and in 1971 a new alert goes through the detour of fiction. The novelist Arthur Koestler imagines a congress of twelve of the world's most brilliant academics, with varied skills, gathered to try to understand the tendency towards aggressiveness andself-destruction of humanity, to propose methods for humanitytourvive, and to influence public authorities.¹⁵ In the novel, the organizer opens the congress by drawing upan assessment of the planet that is stillrelevant. It lists in particular the ability to destroy the atmosphere and almost all living things by nuclear and biochemical weapons; the lack of living space, the rural exodus; pollution; theemotional immurity of humans in relation to their technological successes; the recurrent wars, some of which are accompanied by nuclear threats. Thesesparkling brains separate without proposing anything, except for a few practices probably as nefas they are supposed to cure.

Around the same time, on May 25, 1970, the mathematician Alexandre Grothendieck resigned from the Institute of Advanced Scientific Studies (which had been created twelve years earlier almost tailor-made for him) because this institute received a few percent of its budget from the Ministry of Defense.¹⁶ Grothendieck then called for radically decoupling science from any military application, and even from any military-related funding.¹⁷

When asked about this, several of my colleagues replied: "I use military money for good research, and if it is not me others will take this money to do worse." This argument seems to be mainly intended to give itself goodcon cience. It is by weighing politically to dry up military budgets that it would be possible to redirect these funds for real freedom of research or for more socially useful activities. Because by definition of their profession, the military aimsat defensive or offensive combat, and not at being philanthropists. Military research contributes to competition and inequality, particularly between different states or between different regions of the world.

Even primarily civil research contributes to competition between individuals, companies and peoples, nurturing economic and political domination. Strengthening competitiveness, expanding its power of influence, controlling patents, perfecting its methods, securing a few years ahead of its opponents, are some of the motivations of funders, and the strongest can hope for the best return on investment.

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16 Allyn Jackson, « Like Called of Néant - As If Summoned from the Void: The Life of Alexandre Grothendieck »,

https://www.ams.org/notices/200409/fea-grothendieck-part1.pdf

¹⁴

https://pugwash.org/1955/07/09/audio-bertand-russell-joseph-rotblat-manifesto-press-conference-9-july-1955/

Arthur Koestler, "The Call Girls", 1971-1972; ed. Frenchwoman Calmann-Lévy, trad. Georges Fradier, 1973.

AMS Opinion 51 (4). pp. 1038-1056 (part 1) and pp. 1106-1212 (part 2).

https://www.ams.org/notices/200410/fea-grothendieck-part2.pdf

¹⁷

Alexandre Grothendieck, "Responsabilité du savant dans le monde d'aujourd'hui: le savant et l'appareil militaire", lectures at the Faculté des Sciences d'Orsay, June 26, 1970 and at the Université de Montréal, 8 July 1970, drafted a posteriori by Grothendieck (date not specified, between July and September 1970), http://francois.graner.name/publis/Grothendieck_la_responsabilite_du_savant.pdf

A small contribution to the budget of a laboratory, whose researchers have salaries paid by the taxpayer, can allow a funder to expect profitable results at low cost.

In addition, the most innocuous research can, once published, be used for applications that have not beenanticipated. As far as I am concerned, or around me, I have seen a large telecommunications company take advantage of a social science dissertation on groups of opponents of nanotechnologies, or the explosives services of the French army be the first to be interested in work on soap foams. A multinational agrochemical company can take advantage of agronomic techniques put in place precisely to help small farmers resist competition.

War in the living

The site "Pièces et Main d'Oeuvre", in a text written to accompany the republication of a conference by Alexander Grothendieck, points out that in addition to competition between humans, research also provides the means for the war that humans wage against he rest of life, domesticating species and suppressing others.¹⁸ Since the highly publicized birth of dolly the sheep in 1996, the creation of mammalian twins ("cloning") has been part of this effort to control life. Now, compared with genetically modified organisms in the open field, the possibility that an introduced gene is able to quickly take the place of the existing one (so-called "gene forcing" technique) makes the risks even greater; even researchers in this field recognize that many ethical problems are not solved.¹⁹

On the human level too, advances in knowledge due to research offer increased opportunities for action. Eugenics was highly developed in Occident before the Second World War, on the basis of values giving priority to the improvement of the human species. After the Second World War it was largely banished from the West by the decision to place the dignity of the individual asthe dominantvalue, priority over the progress of science that it is necessary to frame.²⁰ However, forced sterilization laws persisted in Sweden until 1976, in the Swiss canton of Vaud until 1985. And eugenics is coming back via detours. Thus, thetechniques developed by research make it possible todetermine whether an embryo is a carrier of trisomy before implanting it in a mother. The ethics committee of the National Institute of Health and Medical Research (Inserm) considers that this detection of trisomy is part of the evaluation of the viability of an embryo, an evaluation that is encouraged (while the choice of genetic characteristics is not).²¹ In addition, in many of today's

¹⁸ Parts and Labor, "Will we continue the research ? », introduction to the text by Alexandre Grothendieck,4 August 2021

https://www.piecesetmaindoeuvre.com/spip.php?page=resume&id_article=1535 19 « Unsettled ethical issues in gene drive research », Gene Drive Research Forum

http:/www.fnih.org/UnsettledEthicalIssues

²⁰

Halioua Bruno, "From the Trial to the Nuremberg Code: Principles of Biomedical Ethics", in: Emmanuel Hirsch ed., Traité de bioéthique. I - Foundations, principles, benchmarks, Sheres, 2010, p. 233-248.

https://www.cairn.info/traite-de-bioethique-1--9782749213057-page-233.htm

²¹ Bernard BaerchiBertrand Bed'him, Christine Dosquet, Marie Grosset, Anne Dubart-Kupperschmittand to the.. Evaluation of PReimplantation embryo Aptitude for DEvelopment (EPRADE). 2021. inserm-03328662

https://www.hal.inserm.fr/inserm-03328662/document

societies, with new technologies resulting from research and the promotion of a healthy right to the child, selection is practised at the stage of gametes, embryo or even foetus.

A European colleague has suggested that I collaborate on research on human embryos, which is being initiated in his country as well as in mine, through the use of a laboratory in a third country where this practice is possible. Human cloning, which is also not currently part of institutionally supported practices, is addressed through a variety of means. As for the artificial manipulation of human genetic information ("genome editing"), it is also in an intermediate situation. The first announcement of the birth of a human baby after genome editing took place in China in 2018. Following the shock of this announcement, the author was sanctioned and marginalized. However, since then, far from wanting to ban genome editing, the World Health Organization set out in July 2021 "good practices" based largelyon the goodwill of the actors themselves. They limit themselves to regulating for three years the "premature" use of this technology.²²

In the longer term, concerns may legitimately arise from synthetic biology, which is strongly supportedby institutions and governments (especially French).²³ It covers a wide variety of fields, from medicine to food, the creation of new materials, digital data storage, energy and reproduction. It includes the assembly of ingredients to make a cell, the assembly of cells to make a tissue or an organ, or the assembly of materials to develop a living-machine interface (prosthesis, exoskeleton, neurone-computer interface). The boundary between humans and animal species is also gradually blurred. In2021, two different teams of researchers, one in France, the other in collaboration between China and the United States, announce the manufactureofchimeric embryos combining man and monkey.²⁴

Is research reformable, or problematic in essence?

More generally, whether it takes the form of collaboration or competition, research, which in essence must constantly produce novelties, is a perpetual headlong rush. The main reason why research is currently funded is that research and development activities in the broad sense are the driving force behind the observed increase ineconomicoutput, consumption, population and profits. However, all living things, human and non-human, and more generally the habitability of our planet and its general state, suffer from the disproportionate growthof the consumption of energy and materials, the accumulation of waste and the resulting degradation.

Each funder sets a cursor between the freedom necessary for the academic world, and the management of research. This involves different types offinancing: between financing, either permanent or

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See also:

https://www.who.int/publications/i/item/9789240030381

https://www.who.int/publications/i/item/9789240030404

World Health Organization, « Human genome editing: a framework for governance », Technical document, 12 July 2021

https://www.who.int/publications/i/item/9789240030060

²³ http://www.biologiedesynthese.fr/

²⁴ Florence Rosier, "The first chimeric human-ape embryos have been created", Le Monde, 15 April 2021 https://www.lemonde.fr/sciences/article/2021/04/15/de-premiers-embryons-chimeriques-homme-singeont-ete-crees_6076911_1650684.html

punctual; between financing that is either open or targeted at fixed subjects. Is it necessary to carry out this sorting before starting a search, for example at the stage of recruitment and allocation of funding, whichallows a more precise management? Or, in order to give researchers more latitude, but at the risk of much less effective control, should research be sorted only once it has been completed, and before it is implemented a large scale? There is no obvious single solution to place this cursor.

In principle, the management of research, particularly through calls for projects, could lead to the encouragement of reflection, critical thinking andenergy-efficient intellectual productions aimed at better understanding the world and human beings, as well as preventing the difficulties that await humanity. However, the trend in today's societies is towards increased application-oriented steering, especially those that are profitable in the short term. The impression that emerges is that everything that we know how to do technically ends up being realized. In other words, that the richest societies today, those that carry out research activities, do not have a system of collective moral and psychological values that is sufficient to spontaneously put the brakes on.

Some researchers are fighting the desire for regulation; they argue in the name of freedom of research, teachingand expression.²⁵ Faced with the real attacks they suffer, they defend the freedom "to think, to inform, to seek, to say, to reveal, to go against or elsewhere, to take crossroads, to think on the margins or outside, to create without dogma, to imagine without orthodoxy".²⁶ They add thatthere can be varied and unpredictable positive impacts of all research activities, whether labeled as applied or as fundamental. We can distinguish two types of research: those that are launched with, or not having, already in mind a precise expected impact. But once research is launched, the interweaving is so strong between increasing knowledge and increasing opportunities to act on the world that it becomes impossible to place a clear demarcation between the two.

It is true that any research can have unpredictable positive effects (regardless of the meaning attributed to this word). But the argument goesagainst immediately, because then there is just as much chance that the same research will also have unpredictable negative consequences. And because the unexpected is the rule in research, it is also impossible to predict whether the positive spilloverswill be negative. Any research is a gamble made without having complete information. Only past experience can guide us in determining whether research activity is globally beneficial to all of humanity. However, such an evaluation necessarily subjective, it varies according to the person; moreover, it differs according to whether one is placed on the scale of a few years or a few thousand years.

For example, while research in virology increases both the risk of pandemicand the capacity to produce vaccines, it seems difficult to state categorically that the overall picture will be positive, both in the short and long term, for humanity as a whole. Total freedom of research, coupled with regulation that would be entrusted solely to scientists themselves, would have potentially devastating consequences, and virology is just one of the many disciplines that this problem concerns.

^{25 &}quot;We are RogueESR », https://rogueesr.fr/

²⁶ Edwy Plenel, "Defending and Illustrating Academic Freedom: A eBook free", Mediapart blog, 23 Sept. 2021,

https://blogs.mediapart.fr/edwy-plenel/blog/230921/defense-et-illustration-des-libertes-academiques-un-ebook-gratuit

Attempts at co-management between scientists and politicians are also rapidly reaching their limits. Ethics committees were born in the United States in response to medical experiments on uninformed humans.²⁷ Faced with the difficulty of defining in a sustainable and international way, and especially to anticipate, what is desirable or what is not, these committees are often led to "run after" researchers. A ban is sometimes lifted quickly. The opinion of a committee is oftenconsultative, and may not be followed by any effect; sometimes the committee even plays a purely cosmetic role.

The issue of science responsibility is politically²⁸important. On March 11, 2020, French researchers who are members of the Ateliers d'Ecologie Politique expressed in "Le Monde" their fears that research, as organized by government policy, contributes to aggravating the ecological crisis, not to reducing it.²⁹ The next day, on his blog, the journalist Sylvestre Huet told themthat it would be more effective to attack the real places of political power and private companies, and to oppose their decisions such as the agricultural policy of the European Union, the choices of the automobile industry or the extensiveand segregationist urbanisms.³⁰ However, it is possible to oppose both these concrete choices and the research that has provided the means.

The same journalist adds that "advanced technologies from science" can allow "energy selfsufficiency" and "a drastic saving of raw materials and natural spaces, minimizing pollutant emissions" in order to "ensure decent living conditions for more than seven billion human beings, more than half of whom live in cities and hundreds of millions in megacities". But predicting that science and technology will find ways to compensate for the damage created by science and technology is perhaps more naïve, supersition or deception than an observation of concrete reality: nothing has yet proven that "green growth" or "sustainable development" is achievable.³¹ The growth of profit, the improvement of material well-being, the creation jobs, the increase in lifespan, sustainable development or other comparable considerations are not sufficient justifications for any scientific research activity.

Faced with the current excess, humanity needsto collectively identify how to intelligently reduce inequalities, the extraction and consumption of energy and material resources, scales of size and power, and impacts on the surrounding environment. It is a challenge. Political commitmentin this

29 Ateliers d'Écologie Politique de Toulouse, Dijon et d'Ile de France, "Public research must no longer be used to destroy the planet", Le Monde, 11 March 2020 https://www.lemonde.fr/sciences/article/2020/03/11/la-recherche-publique-ne-doit-plus-servir-a-detruirela-planete 6032632 1650684.html

31

https://eeb.org/library/decoupling-debunked/

²⁷ Henry K. Beecher, « Ethical and Clinical Research », New England Journal of Medicine, 274, p. 1354-1360 (1966).

Shana Alexandra, « They Decide Who Lives Who Days », Life Magazine, 9 November 1962. Albert Jonsen, « The Birth of Bioethics », Special Supplement, Hastings Center Report, 23, p. S1-S4 (1993).

²⁸ Isabelle Stengers, "What would a responsible science be?", Critical Sciences, 10 April 2017, https://sciences-critiques.fr/que-serait-une-science-responsable/

³⁰ Sylvestre Huet, "Science against the planet? The major mistake. ", blog {Sciences²}, 13 March 2020, https://www.lemonde.fr/blog/huet/2020/03/13/science-against-the-planet-major-mistake/

Parrique T., Barth J., Briens F., C. Kerschner, Kraus-Polk A., Kuokkanen A., Spangenberg J.H., « Decoupling debunked - Evidence and arguments against green growth as a sole strategy for sustainability », European Environmental Bureau, report, 8 July 2019

direction can usefully be supported by the analytical tools and solutions that research would be able to provide, provided that it itself breaks with excess and competition.

Many governments believe that if their pays slows down its research, it runs the risk of being overtaken by other countries. At the international level, this would require cooperation agreements: the example of disarmament agreements shows that this is not inconceivable. One of the levers of actionavailable is to reduce the overall volume of activities in the research sector in the same way as that of other sectors (e.g. industry, the army, advertising). It is certainly very difficult socially, politicallyand psychologically; ³² but this does not come up against any material impossibility or physical law. This would require lower, recurrent, non-competitive funding for research and development activities as a whole, withperhaps fewer but more stable jobs.

To want to reduce research activityglobally, is it to oppose the creation of knowledge, to play the game of obscurantism, to promote ignorance and subjectivity, to believe that everythingis the same, or even to pretend that we already knoweverything? No, it's none of anyone. It means taking note that limits exist, recalling that infinity is not accessible, reacting with moderation to excess, asking oneself essential questions, sorting, carrying out a real reversal of values, and precisely not leaving this reaction to obscurantists alone. We can cultivate critical thinking, curiosity, debate, evaluation of knowledge: for this, there is no need for a perpetual flight forward, no need to want to know everything about everything.

And now, where are we going?

The year after his resignation from the Institut des Hautes Etudes Scientifiques, having pushed his analysis to the root, Grothendieck uses his course at the Collège de France as a platform and questions: in what way does scientific research serve society, will we continue to do it? ³³

To try to answer him, let's summarize the above. It is indeed the prerogative of scientists to *validate theresults* of their research, far from any interference from politicians. Conversely, the *amount of effort* that society devotes to research, and therefore the eventual choice of degrowth, is a decision that must be taken outside the scientific community. Between the two, the most difficult thing is to regulate the choice of research *tracks* while preserving the freedom that gives efficiency to researchers.

While retaining its undeniable advantages and qualities, scientific researchis beginning to accumulate disadvantages, whether directly through the course of the activity itself, or indirectly through the application of its results. The dangers associated with research come from the community and its

33

http://www.fabriquedesens.net/Allons-nous-continuer-la-recherche https://sciences-critiques.fr/allwe-continue-scientific-research/

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Roland Lehoucq, "Facing the Wall of Exponential Growth," The Conversation, April 18, 2020, https://theconversation.com/face-au-mur-of-exponential-growth-135331

Alexandre Grothendieck, "Science and technology in the current evolutionary crisis: will we continue scientific research?", Collège de France, 3 November 1971. He develops this question in sa conference at CERN on 27 January 1972. Several recordings, transcripts and explanations of the context can be found on the Web, for example:

structure, which the Covid-19 pandemic has just highlighted. Many areas of research, of which virology is just one example, are advancing faster than our collective regulatory capabilities. Almost everything we know how to do technically isdone is done without knowing how to evaluate the future advantages and disadvantages. No politician, no insurance company will assume the future consequences of the current choices. Research, which in essence must produce newlifepermanently, is a perpetual headlong rush, which leads to excess.

We urgently need to determine and impose a framework of values that will make it possible to anticipate and sort both the lines of research and their applications, to curball their excess, to cut all the links not only with the war of humans against each other, but also with the war of humans against the living; and to commit humanity towards the reduction of the global research effort and inequalities.

Are we capable of it? If not, Grothendieck's lucid question arises seriously: should we stop doing scientific research?

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