Jean Hamburger

THE ART OF REASONING IN BIOLOGY AND MEDICINE

The Swiss psychologist Jean Piaget devoted his life to following, step by step and lovingly, the development in children of the art of reasoning. In the course of the successive stages of this development, the child's view of the world changes in nature. Similarly, from its earliest infancy, medicine has viewed living things in successively different manners. For medicine, it is true, the stages overlap; one may still be using an ancient discourse from which another has daringly freed itself. Nevertheless, for the sake of clarity in this analysis, I will try to define successive epistemological attitudes as if they had represented a regular progression of medical thinking.

Those who Reasoned Without Observing and Those who Observed Without Reasoning

The first tentative efforts to understand man and his diseases date to a very distant era. The Sumerian tablet of Nippur,

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undoubtedly the oldest known medical writing, probably dates to 2300 B.C. And from the beginning two lines of thought had two different ways of looking at the medical event.

The Egyptian papyrus of Edwin Smith and the one of Ebers each date to around 1500 B.C. But the former is stamped with the seal of empiricism. It describes what it sees; it is the work of a craftsman. The latter, on the contrary, is inspired by myth and imagination; objectivity is not its strong point. It makes firm decisions. The first one limits itself to describing fractures of the skull, the nose or the arm, just as the unknown author saw them in his practice. The second proclaims, "The spirit is weak within the belly ", or, "The breath of life enters the right ear and the breath of death the left ear."

Greek medicine was born under the same two auspices, distinct but intertwined, hesitating so much between imaginative arrogance and empirical humility that we sometimes see the same author move incontinently from one to the other.

Hippocrates can be classified among the empiricists. It was he who, in the section of the Hexacontabiblos entitled *On ancient medicine*, decreed, "Medicine has no need of an empty supposition, such as occult and doubtful things."[1]

On the other hand, Plato gives more weight to the imagination than to the object when he writes in *Timeus or On Nature*, "Where do diseases come from? I think anyone can see the answer. Just as there are four elements composing bodies (earth, fire, water and air), when they are in excess or when they are lacking, contrary to nature, or if they go from their proper place to another foreign place... this is when disorders and sicknesses are produced."

But where should we classify Aristotle? No one in those distant times was a more rigorous observer than he was. He looked at nature before talking about it. His *History of Animals*[2] is the first model of a zoological treatise born of the methodical examination of numerous living species; his anatomical descriptions of the

[1] Hippocrates. *De l'ancienne médecine*, in *Oeuvres complètes* (French translation of Littré with the Greek text on facing page, t. 1, p. 556-637, Paris 1839, Baillière).
[2] Aristotle, *Natural History of Animals.*

human body are exact with only few errors. And yet he is not at all innocent of flights of interpretative fancy. He remains seized by the demons of the unbridled exercise of his thought. He cannot keep himself from leaving the real to create beautiful images born only of his imagination. "Man," he writes, "has arms and hands instead of forelegs and paws. He is the only one of the animals who holds himself upright because his essence is divine. However, the function of the divine being is thinking and wisdom. But this function would not have been easy to fulfill if the upper part of the body had been heavily weighted. For weight takes away all suppleness of reasoning and common sense. When weightiness dominates, the body must incline itself toward the earth. Consequently, instead of giving quadrupeds hands and feet, nature placed forelegs under their bodies to support them. And this is how animals became quadruped because their soul was incapable of bearing their weight."

Eternal swaying between the pride of mind, indifferent to all objective verification, and the submission of mind, ready to incline itself before observed facts. We will find this swaying movement throughout the following centuries. For example, I would like to cite Descartes, prince of rigor, who called for a clean slate freed of all received ideas, adding his voice to those who in the seventeenth century were struggling to shake off the scholastic yoke, Descartes who still, in his *Treatise on Man*,[3] piled up the most fantastic affirmations drawn completely from his fertile imagination. There we read that, "the Body is nothing but a statue or Earth machine that God forms expressly." Again, "Meat is digested in the stomach by the power of certain liquids, and since these liquids are brought from the heart quite promptly by the arteries, they must be quite hot. And also meat is normally such that it could corrupt and heat by itself, just like new hay in the barn if it is stored before it is dry." Again, "The most subtle parts of meat are unequal and even imperfectly mixed together; they form a liquid that would remain cloudy and whitish if a part of it did not mix with the blood." "The flesh of the heart contains in its pores one of those fires without light that makes it so hot and so burning that as blood enters, it

[3] René Descartes, *L'Homme*, followed by *De la Formation du Foetus* (New edition with a preface by Louis de la Forge, Paris 1729, Compagnie des Libraires).

promptly expands and dilates. And the fire in the heart serves for nothing other than to dilate and warm and thin the blood that falls continuously, drop by drop through a tube from the vena cava." He states that the liveliest, the strongest and the most subtle parts of the blood go to the brain to "introduce a kind of very subtle wind, or rather a very lively and pure flame that we call Animal Spirits." Nerves, whose outer skin is like "a large tube containing a few other small tubes," enclose in these tubes a marrow that comes from the very substance of the brain; "this marrow does not at all serve for movement of the members," but "it does not fill the little tubes that hold it to such an extent that the Animal Spirits cannot find sufficient room to flow easily from the brain to the muscles." "Depending on the quantity of Animal Spirits entering or leaving, ... they make the body of the muscle expand and shorten ... just as when they leave the muscle contracts and lengthens." If the little nets making up the marrow of the nerves are pulled hard enough so that they break, "the movement they would cause in the brain would cause the Soul to feel *pain*, because it is important for it that its home be preserved. And if they are pulled by a force almost as strong as the preceding but without breaking, (this movement) will cause the soul to feel a certain bodily voluptuousness that we call *tickling*." "When the blood that goes into the heart is purer and thinner, and when it mingles more easily than usual, it has the little nerve which is there in the manner required to cause the feeling of *joy*; and when the blood has the very opposite qualities, it causes the feeling of *sadness*." In his treatise *On the Formation of the Foetus*, Descartes explains in passing why blood is red. A superbly fantastic explanation. Descartes recalls the demonstration in which he proved that seeing light is the result of what he called "little balls of the second Element". However in the "pores of the blood" there passes "sideways and extremely fast" the matter of a certain "first Element" which causes the little balls in question to rotate so quickly that we see "red" (while if they turned less quickly we would see "blue"). It is true that the red pigment which in fact colors the blood was not discovered until two centuries after the death of the famous philosopher.

In this manner the chrysalis of the new scientific spirit had much difficulty in leaving its cocoon. The birth of humility of mind in

front of facts, could not occur without numerous misadventures. The eighteenth century, and even the nineteenth century, still sheltered constructors of theories born of the imagination rather than experience, such as the vitalist theories of Van Helmont, Boissier de Sauvages or Barthez, affirming with authority that a vital principle, totally invented, the grand-nephew of the Animal Spirits of Descartes, is actually responsible for organic functions. Even today I am not sure that the two extreme tendencies I have just described have completely disappeared: the tendency of imaginative persons hardly concerned with a confrontation with reality and, at the opposite extreme, that of rigorous but fearful observers who pile up objective scientific data but who are alarmed by the prospect of any kind of interpretation.

The Age of the Experimental Method

And yet, between these two extremes, was born, little by little and difficultly brought forth, a new scientific algorithm, which quickly proved its value with astonishing results.

In *Le Journal d'Harvey*,[4] I tried to show that the birth of this new scientific spirit dated back to the seventeenth century with men like William Harvey who discovered the circulation of the blood and the true function of the heart.

But for us, biologists and doctors, the text which for the first time states without ambiguity the new rules for the game dates from 1865. It is signed Claude Bernard and is his *Introduction à l'Etude de la Médecine expérimentale*.[5] In the duel between the subject (the researcher) and the object (the human body), the parries and thrusts of the arms are described with a clarity and an authority never before achieved. The enigma provided by the object stimulates reflection by the researcher, inciting him to devise one or more explanatory hypotheses. The researcher imagines the experiment that will prove the hypothesis correct or, on the contrary, that will disprove it by facts. The experiment in

[4] Jean Hamburger, *Le Journal d'Harvey* Paris, Flammarion, 1983, and Gallimard Coll. Folio, 1986.

[5] Claude Bernard, *Introduction à l'étude de la médecine expérimentale* Paris, Delagrave, 1965.

turn provokes the object and forces it to respond. And so forth, from one exchange to another, the solution to the enigma will appear, being born not only from observation as the empiricists would have it, nor simply from imagination alone as the idealists had argued, but from a concordance of the two, where the subjectivity of the researcher and the obstinacy of the objective facts are finally brought into harmony.

New Ways of Looking at Reality

Nevertheless the *Introduction* does not simply provide a method. It is also an act of faith in a universal determinism. Nothing is without a cause, and by knowing these causes, it is possible to predict everything with certainty. Philosophers have taught us from what depths in man spring the roots of the feeling of causality and of the concept of determinism. For a long time (long before the word existed) determinism fertilized scientific development, while science repaid this service by suggesting through its successes that there is no salvation outside of determinism. And it is apparently true that it is not possible to reason about natural laws without first supposing that these laws exist, uniting causes to effects. In any case, without the premise of determinism, biology and medicine would not have experienced the incredible progress which, from Harvey to Claude Bernard and beyond, has metamorphosed our knowledge of man and life. This explosion of scientific knowledge can be described as the expression of a firm determinist conviction.

This conviction is still just as useful and just as necessary for us today. The work of the researcher, as no doubt the everyday activity of each person, requires that we presume a solid determinist faith. But something extraordinary has occurred since the beginning of this century. Determinism has lost none of its power, but it has allowed its limits to become visible. These limits became apparent on the day on which a new field—immense and unforeseen—was born: the field of *uncertainty*. That was the signal for what, it seems to me, was to become a revolution. And it is this recent revolution in the history of scientific thought that I would now like to analyze.

THE BIRTH OF UNCERTAINTY

It was physicists who first came up against the boundaries of determinism. Ever since the last century when the American Josiah Willard Gibbs opened the chapter on statistical mechanics and the Austrian Ludwig Boltzmann introduced probability into thermodynamics, they created an initial critical passage between a strictly determinist vision of the world and a new probablist perspective, losing in the process a certain immediate determinist style. And then came the great adventure of the atom, where indetermination ruled supreme. "The individual microphysical event is indetermined," wrote the recently deceased Alfred Kastler, Nobel Prize winner in physics, in his book entitled *Cette étrange matière*.[6] The most famous example appeared in the work published by Werner Heisenberg in 1927 in which he showed that it was impossible to know at the same time the position and the speed of an atomic particle with precision exceeding a limit of uncertainty. And this impossibility was linked to the very nature of things and in no way resulting from a technical imperfection on the part of the experimenter.

In a work entitled *La Raison et la Passion*,[7] I have tried to demonstrate that a similar indetermination has now invaded the realm of biology and medicine. In particular I based my demonstration on the analysis of two phenomena with which I am familiar—the allergic accident and rejection of a transplanted kidney. Without going into the technical details of the demonstration, it will be sufficient here to say that, under certain conditions, these phenomena cannot be predicted other than in terms of probability, but not with certitude. And this clinical uncertainty has definitely a very widely generalized application. Despite great progress in molecular biology, the hope for full and complete predictability of clinical occurrences recedes more than it advances; the movement from an infinitely small scale to a macroscopic scale always brings out a certain degree of indetermination. There are so many billions of different molecules in the human body that integrating to the scale of the entire body

[6] Alfred Kastler, *Cette étrange matière* Paris Stock, 1976.
[7] Jean Hamburger, *La Raison et la Passion, réflexion sur les limites de la connaissance*, Paris Le Seuil, 1984.

what we know on the molecular scale would presume a perfectly ideal level of knowledge and of calculations that no research or no computer could ever allow.

May I note in passing that this uncertainty in no way prevents a scientific approach to pathological facts, thanks to widespread use of statistical methods in biology and in medicine. Claude Bernard wrote, "The use of averages or of statistics in medicine and physiology lead necessarily, so to speak, to error... I admit that I do not understand why the results obtained from statistics are called *laws*; for me scientific law can only be based on certitude and on absolute determinism and not on probability... Statistics have never yielded a scientific truth." One hundred years later he would regret having made such a judgment. The statistical method has, with the greatest success, invaded biological research, and it is this which has made possible the astonishing progress of recent years.

This evolution is of direct interest to the history of human reasoning, for statistics is not just a set of mathematical techniques. It is instead "a *method of reasoning* that makes it possible to interpret the kind of very particular data especially found in the life sciences."[8]

One example will suffice to show how statistics help advance knowledge in the medical and biological realms. Let us select the model offered by the study of transplant rejections. A great number of elementary factors combines to explain this rejection, and their very number introduces the element of uncertainty into the final result. (We are continuing to call uncertainty that which is impossible to predict with certitude, as it seems correct to do). Among these factors, the respective chemical personality of the donor and the receiver is important. If this personality is identical, as is the case for identical twins, there is no rejection. In other cases this personality is rather usefully represented by a technique of analysis of white blood corpuscles bringing out a certain class of chemical molecules on the surface of the cells, molecules designated by the initials HLA (Human Leukocyte, A, referring to the first system of this class). The problem was to know if

[8] Daniel Schwartz, *Méthodes statistiques à l'usage des médecins et des biologistes*, Paris, Flammarion Médecine-Sciences, 1969.

comparison of the HLAs of the donor and the receiver could have a *certain* value in order to predict the results of the transplant (a certain value and not an absolute value, since it is not certain what other factors might intervene to influence the result). At the beginning of our experiment, we only determined two sub-groups of HLA, and, for a total of 64 cases, with donors and receivers who were brother and sister but not twins, these sub-groups were perfectly identical in 33 cases and partially identical in the other 31 cases. However, four years after the transplant, we noted a total success in 96 percent of the 33 perfectly identical cases and in 68 percent of the partially identical cases. This difference could quite well have been the result of a coincidence or of luck. The person who plays roulette in the casinos knows quite well that even in a series of 64 throws, the red can come up more often than the black or *vice versa*, even though theoretically the chances are equal. But statistical calculation makes it possible in this series of transplants to establish the fact that the probability for the difference observed to be the result of chance is less than one in a hundred, in other words almost none. We were then able to consider that the identity of these HLA groups played a real role in the success of these transplants or, if we prefer, that the non-identity of these groups could be partly responsible for the rejection of transplants.[9] The entire very fruitful history of the discovery and use of these HLA molecules was likewise the result of statistical studies. And the value of such studies could be demonstrated in every area of biology and of medicine.

The Concept of Caesura

Another new epistemological factor, to which I have dedicated a part of my research in the course of recent years, is what I have proposed calling the concept of *caesura*. What I mean by *caesura* is the slicing up into distinct domains the knowledge of reality. The scientific approach to "reality" does not permit unique and homogeneous vision of the universe that surrounds us. There are

[9] Béatrice Descamps, Nicole Hinglais and Jean Crosnier, in *Transplantation Proceedings*, 1973, vol. 5, p. 231.

gaps, obligatorily, in our knowledge of the external world. This is not, of course, a totally original idea, and we could cite any number of ancient philosophical texts that suggest this. But the strength of this concept has increased remarkably in the light of recent scientific events.

To be perfectly clear, I would first of all like to use two absolutely ingenuous examples. The first could be entitled the apologue of the atom and the mountain. A mountain is made up of atoms. Considerable progress has been made in the study of mountains, their erosion, avalanches and volcanic eruptions. And yet it is impossible to predict volcanic eruptions or mountainous erosion from what we know of the atom. And it is probable that we will never achieve this, not because of a technical impossibility but because of a gap, a *caesura* inhibiting an easy passage from the laws governing atoms to those ruling over mountains. Orography cannot be deduced from atomic theory, despite our certainty that mountains are made up only of atoms.

A *caesura* is not restricted to changes of scale. It can also appear within the same scale as soon as we change our method of study. Two different ways of looking at nature can give the same object two images, separated by a certain degree of independence from one another. In Venice, set into the façade of Saint Mark's Basilica, there is a twelfth century relief sculpture generally referred to as *Hercules and the Stag*. There are two ways of studying this sculpture. The first states that it is made of a marble plaque, 164 cm high and 86 cm wide; that this marble is a calcium carbon, formed of attached calcite crystals; that the veins of colored calcite are mixed with white calcite; that each calcium atom is associated with a carbon atom and three atoms of oxygen. This structural analysis could go on for a long time still. But there is also another analysis, one that would discuss the willful, determined and almost brutal expression of the bearded face; the strange confusion depicted by the unknown sculptor as he showed Hercules charging a stag whereas the legend spoke of a cerynite doe; a certain marvelous clumsiness in the harmony of the sculptural masses. There is no contradiction between the physical and chemical analysis on the one hand and the artistic analysis on the other; there is only *caesura*. The reality explored is different because the method is different. The Venetian marble has two distinct realities

because there are two different ways of looking at it.

I hope the reader will forgive me these simplistic examples. I selected them for the single purpose of suggesting that our research methods are like so many mirrors, each of which can provide a certain reflection of reality. It is normal that these reflections differ when the mirror changes. Let us come back, then, to our topic, which is to show that similar *caesurae* compartmentalize scientific knowledge like so many room dividers.

For an example I will take the difference of opinion between neurobiologists and psychologists. The former state that thinking is enslaved to cerebral functions and describe, each year with greater precision, the chemical mediators that regulate our behavior. The latter are scandalized by the idea that our mental life could be a simple matter of chemistry and that our freedom of behavior would be only an illusion. The former dream of integrating all of psychiatry into the study of biology, of the brain; the latter rejects this. However, it is evident that a *caesura* separates the approach of the neurologist from that of the psychologist. These are two distinct methods, two different images. No matter how shocking it may seem to our traditional habits of reasoning, it seems to me that the scientific spirit should adjust itself. Here, again, physicists have shown us the way. They too were obliged to accept the violation of their desire for unicity. When non-Euclidian geometries were born, creating the concept of certain new style "spaces," making, for example, Einstein's theory of relativity possible, it was possible to believe that traditional Newtonian mechanics was dead. This was not at all the case. A non-Euclidian geometry is no more "true" than Euclidian geometry. One is effective under certain conditions, the other under other conditions. Likewise it is no more correct to declare that "light is a wave" than to state that it is made up of particles. Light is a wave if we study its propagation, a particle if we look at how it interacts with matter. And the concept of photons then becomes necessary. And all the ondulatory mechanics of Louis de Broglie becomes, like Janus, a two-headed image of a double truth. Following Niels Bohr, physicists became accustomed to this complementarity between wave and particle. Has the time not come when biologists will have to accept the same concept of complementarity, even if it upsets a unitary logic that is deeply

rooted within us? Neurobiologists are certainly correct when they affirm that endomorphines, enkephalines and other cerebral mediators condition our moods and influence our behavior. The psychologists are not wrong when they affirm our freedom to think. A clear idea of the *caesurae* that separate our comprehension of reality keeps me from being shocked when certain people say that my decisions are not free while others tell me that they are fully free. The former are saying, and they are correct, that my mental life is the expression of my cerebral functions. The latter are properly stating that by escaping from my numerous neurons, like the unpredictable poem escapes to the paper which is its medium, my thinking loses a great deal of its determinism. There is no contradiction here but simply a change of analysis, a change of mirror. I am neither free nor enslaved. If I have recourse to the methods of neurobiology, I must recognize the fact that certain physico-chemical events limit my liberty. If I look at myself according to the methods for analyzing the phenomena of thinking and not those of neurobiology, I am free, completely free.

The Inseparable Pair: the Observer – the Object Observed

Scientific reasoning received another warning. The study of the world around us until now supposed that the object should be regarded independently of the observer. All methods of study should necessarily converge in a single, homogeneous description of the object (and by this word I mean everything that is presented to our curiosity, whether it be the human body, living matter or inanimate matter, the universe of astronomers or a specific natural phenomenon whose mechanism intrigues us). The phenomenology of Husserl, this great moment in our conception of knowledge, affirmed the *invariance* of the object. Husserl refused to enter into the eternal discussion of the existence as such of this object; he admitted that we can perceive it differently depending on our angle of vision. But he stated in principle that the object itself does not vary, whatever might be our manner of approach. However, it is precisely this that is brought into question today. It is not certain that there is an invariable object, indifferent to our observation. It is possible, at least on the scale of atomic particles, that *the*

intervention of the observer may change the object. Everything happens as if the object had no permanent existence, its nature depending on the method of exploration. I have already cited the example of light, as wave or particles depending on experimental conditions. In biology, the examination of a tissue section with an optical or electronic microscope never provides an image independent of the method of examination since it requires first of all killing the living matter by plunging it into fixing liquids. The reflection of reality thereby obtained varies according to the technique used. It is only a translation, not to say a betrayal, of the living structures that we are attempting to know. And I could produce many such examples. It is a vain hope to achieve scientific objectivity, independent of the observer and the research methods. It is not the real world that describes scientific research; it is only the result of a dialogue between the observer and reality; a dialogue in which the observer and his methods are as important as reality. In the realm of scientific research, to overlook the intervention of the observer is a grave error in the art of reasoning.

The researcher in this way creates reality as much as he discovers it; that is to say, he is constantly exposed to an ultimate trap, one that today appears clearly evident: the sin of anthropomorphism.

The Sin of Anthropomorphism

The *Vocabulaire de la philosophie* by André Lalande[10] defines anthropomorphism as reasoning which, in order to explain what is not human, applies notions borrowed from human conduct. The scientific researcher today would no doubt like to give this word a broader scope. Human reasoning is valid for that which man observes through his senses alone, at his everyday scale. However, the exploration of the infinitely small reveals to him that it is not possible to reason about micro-particles in the same manner in which we reason about billiard balls. Compared to our usual images, the world of microphysics appears as a surrealist world where the concepts of identity, permanence and causality undergo

[10] André Lalande, *Vocabulaire technique et critique de la philosophie*, 12th ed., Paris, Presses Universitaires de France, 1976.

strange transformations. In the same manner, in the infinitely large, astrophysicists present us with a world that is finite and yet without limits, an image unacceptable on our scale where there is no boundary without something beyond. It is, therefore, an anthropomorphic attitude to apply our customary logic to scales infinitely different from that of our immediate surroundings.

Another anthropomorphic temptation is to forget the original premises. The researcher has discovered a scientific law and has carefully verified it under specific conditions of observation. He has completely penetrated it. And, without realizing it, he extends the field of application beyond the boundaries delimiting the situation in which the law has been demonstrated. He extrapolates. The oldest example is that of Euclidian geometry, which was considered for more than twenty centuries to be evident truth, whereas Euclid had based it on undemonstrable postulates. Those who had the audacity to change these postulates at the same time changed the image of the world. Scientific truth is never an absolute truth; it is relative, the slave to the conditions, explicit or tacit, in which it was established.

The researcher at the end of our century has become conscious of the series of traps that I have just pointed out. Science has not only made progress through observations and new tools, it has made progress through the art of reasoning.

And, to come to the heart of my thinking, I ask myself if every man who reasons should not be concerned about the logical traps to which recent scientific experiments have given such force. Should not the risk of anthropomorphism make us careful about extrapolating from our common logic to scales of space and time that are quite different from our ordinary little world. In fact we find in the works of many philosophers—Nietzsche, Stuart Mill and others, a foreboding of the danger that exists in incorrectly applying our reasoning habits to areas to which they are not proper. At our level from childhood on we cannot restrain ourselves from asking the why of things. This is legitimate, for events that we witness always have one or more causes. But do we have the right to ask the same question to cosmic scales? Is it legitimate to ask ourselves about the causes and the significance of the world, under the pretext that in our daily life everything seems to have a cause and a meaning? For supposing that the world has a significance in

itself means supposing that the very structure of the concept of signification is not limited to human logic, that it is applied to the world and would continue having a meaning if men disappeared.

In the same way, we play with spatial infinity and cannot imagine that the question about the boundaries of the world is a false question, as the astrophysicists invite us to do. Apparently we are playing with temporal infinity and cannot imagine that the world did not have a beginning, although the question of the beginning of the world may be as absurd as that of its boundaries. However, if the word beginning, applied to the world, is nothing more than an illicit extrapolation, born of the fact that on our human scale everything has a beginning and nothing appears that has not been created, do I need to say what a revolution this could represent in our thinking habits?

Naturally these troubling ideas, this awareness of the possible weaknesses of our rational thinking are perhaps not new. Many philosophers have been able to see them. But for the first time in the history of human thinking, these limits to knowledge appear in full evidence because of recent scientific progress. Science, a sumptuous adventure, allows itself the luxury of announcing that it will never provide the key to the cage.

To those who might feel frustrated, we can only answer that scientific knowledge of the world is certainly not the only pathway for our thinking. There are others, for example that of the feeling for beauty, passion, faith, moral guidelines, thirst for justice, the internal kingdom in which the requirements and the limits of scientific knowledge are no longer valid.

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