HISTORICAL NOTES

On death: past, present, and future

Sobre la muerte: pasado, presente y futuro

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Introduction and history

"Being subjected to death" is the definition that the Real Academia Española gives to the adjective "mortal". Greek mythology leaves the rogue Sisyphus as the only mortal who really managed to outwit the winged genie, known as Thanatos, on two occasions. However, since that time of gods, mortals and myths, humans throughout history have considered death as the end of earthly life, continued either in heaven, in Jannah, in Séol, paradise, limbo, hell or in the lake of fire of the Apocalypse. This uncertainty as to whether we will somehow prolong our existence, once we cross the Acheron river, guided by the ferryman Charon, or whether we will pass into "nothingness", plunging us into absolute and eternal darkness, generates an irrational fear in society, as we feel violated one of the primary instincts possessed by almost all species and which has an adaptive purpose: the instinct of survival.

Benjamin Franklin already joked with the idea of death in his book "The Way to Wealth", stating that "In this world nothing can be said to be certain, except death and taxes". This sentence, also reiterated by Woody Allen in his filmography, is somewhat diffuse, given that we could really say that the only thing certain in the sentence, and that they are inescapable and real, are taxes. Death has, at times, a degree of uncertainty that few really know. In his book "Premature Burial", Edgard Allan Poe, a character intermediate in time between the two previous ones, echoed this fact, sowing panic in half of Europe during the 19th century and putting in check anyone who dared to diagnose the death of a person. Especially when the protagonist of the novel narrates in an exhaustive way his terror of waking up after a state of cataplexy inside a coffin. Evidently, other artists through their work also enriched this innate fear in society, as happened with the 1854 painting by Antoine Joseph Wiertz, entitled "L'Inhumation précipitée" in which a hand emerges from the bottom of a coffin of a person presumed dead during a cholera epidemic.

All of these facts have given rise over time to the development of the phobia of being buried alive or taphephobia. In this sense, we can find wealthy lords, such as Count Karnice Karnicki or Duke Ferdinand, who came to design complex warning systems using pulleys and ropes, which allowed to ring a bell from the coffin itself. Therefore, the term "saved by the bell" transcends and surpasses the current concept of the boxer, whose sound allows him to have a respite at the end of each round. This was the best system for alerting from beyond (or in this case below) the existence of an obvious diagnostic discrepancy. Subsequently, different "safety coffins" were designed with mechanisms that activated flags and other more sophisticated systems, which have survived to the present day, in which we find coffins with surveillance cameras, automated opening of the niches after burial and ventilation systems. Many people in our recent history have expressed these concerns, such as, for example, the first president of the United States, George Washington. In fact, his wake was prolonged for 3 days, excusing a massive farewell of the people, when in fact it was intended to fulfill the wish of the person concerned: not to be buried until after a few days, to make sure of the death. Others requested more drastic measures such as those of the Polish-French musician Fréderic Chopin, whose heart was extracted after his death. We even find recent quotes from the Almeria musician Manolo Escobar, in which he told his relatives to prick him to make sure he was really dead.

However, all this compendium of irrational fears acquired a summative aspect when the first societies dedicated to the recovery of "apparently dead" people were established in Europe in the middle of the 18th century. Therefore, it was no longer just a question of being dead or not, but the possibility or not of being able to be resuscitated after death. During this period, the "word of mouth" described by John Fothergill began to be standardized and there is even talk of the first defibrillators that allowed the resuscitation of a young girl who had died in England. As a consequence of all these new data, Jacques Benigne Winslow published in 1751 a book calling for prudence in the management of the deceased entitled "The Uncertainty of the Signs of Death and the Danger of Precipitate Interments and Dissections". It is undeniable that, throughout history, we find different texts dealing with

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these resuscitation techniques separately, as well as their evolution, but it was finally Peter Safar, in the last century, who began to orchestrate the subject of cardiopulmonary resuscitation (CPR) in a basic and systematized manner[1].

Paradoxically, things in life are never simple, and therefore, in death, they could not be less so. If death due to circulatory criteria presented loopholes of doubt, during the consensus conference held at Harvard in 1968, everything became more complicated[2]. The sophistication of medicine led certain patients with severe brain damage subjected to mechanical ventilation to an irreversible situation initially called Coma Depassé and later encephalic death. Thus, people could also die following a series of strict neurological criteria.

In short, the declaration of the absence of life in an individual is a matter of low complexity, given that, again based on Greek mythology, the God Chronos, sooner or later by himself, would clear up any doubts that might be present in order to reach this diagnosis unequivocally. In this regard, if we review the clinical practice guidelines and legislation, we can see that the requirements for considering encephalic death vary, and in death by cardiocirculatory criteria, we also find no homogeneous criteria for the minimum observation times for cardiac arrest (they vary between 2 and 20 minutes)[3-35].

Diagnosis of death

As previously discussed, death has different perspectives, ranging from religious, biological, philosophical, anthropological, etc. Therefore, it is not surprising that we find certain divergences in what is considered death today worldwide. These situations are not easy to resolve, and even lead to finding works, such as that of Intensive Care Medicine, 2014, in which a panel of experts tries to bring together all the knowledge and the flow of action that must be developed to reach the diagnosis of death[3]. It is true that, on occasions, there may be different diagnostic criteria or therapeutic approaches for the same nosological entity, although in the case of the death of an individual, there can be no doubt that this is certain and unequivocal and without interobserver variability. There is an interesting editorial, where it is stated that the concrete and exact moment at which life and death are separated is usually insubstantial, given that the clinician has all the time in the world to certify death. Therefore, we must be judicious in certifying death, so that it is conceptually, physiologically and socially acceptable[4].

The death of a person, a purely clinical reason, is again in full swing, not so much for the interest of the event itself, but for the development of end-of-life care, as this phenomenon is closely linked to the possibility of organ and tissue donation for subsequent transplantation. In fact, in Spain the legislation itself that regulates all this aspect related to the death of the individual, is included in the Royal Decree (RD) 1723/2012, of December 28. This RD "regulates the activities of procurement, clinical use and territorial coordination of human organs intended for transplantation and establishes quality and safety requirements". It is therefore somewhat atypical that the legal certification of death is linked by the legislator only to the donation-transplantation process, and is not treated as a matter in itself of high scientific, medical and social interest, in which the possibility of donation could fit, or not, but not the other way around.

Death due to neurological criteria

If the heart stopped and the classic criteria of death by absence of circulation were expressed, together with lividity, rigor mortis, absence of exhalation reflected in a small mirror, it was "almost certain" that the person had really died. However, in August 1968 the outcome of a meeting at Harvard would force society and professionals to have a blind belief in medical information[2]. From that moment on, encephalic death became a reality, which could be difficult to perceive from the outside, or by lay people, given that the patient's situation or, in this case, the appearance of the corpse connected to machines, varied little or nothing with respect to the previous days or hours.

To assimilate the concept of encephalic death from a professional and social point of view

Any new concept taking root in medicine must pass through the criticism and scrutiny of the professionals themselves. In fact, there are several historical references where it is stated that "Doctors should not try to play God". These changes in the way of seeing or considering clinical practice are sometimes linked more to customs and habits than to the conceptual openness of certain justified, objectifiable and scientific facts. Indeed, this new definition of death, 20 years later, motivated Christopher Pallis to describe "Reappraising Death" in the British Medical Journal[4]. In this case, the manuscript reflected a criticism of those physicians who, once death had been certified by neurological criteria, did not accept the disconnection of the cadaver's respirator. The author, making use of a comment by a veteran colleague, indicated that bodies, not patients, were being ventilated in intensive care units that did not withdraw the measures after confirmation of the absence of neurological activity of the central nervous system. This situation becomes even more sensitive for professionals making the diagnosis of encephalic death, given that they know that the repercussion of reaching certainty that the patient has died meeting certain neurological criteria implies the withdrawal of measures or the donation of organs and tissues prior to this[5].

Controversies on how to reach a diagnosis of brain death worldwide

In addition to the lack of credibility per se, which may involve accepting or not the patient's death in this way, there are also legal difficulties between countries,

religions, scientific societies and professionals. Eelco Wijdicks is perhaps one of the authors who has most developed this subject[6-12]. Since his work in Neurology in 2002, in which he exposed the heterogeneity in the diagnosis of brain death, under the article entitled "Brain Death: accepted fact but no global consensus in diagnostic criteria" until the last one published in Neurology 2 years ago, the controversy continues to be open. The justification as to whether or not the atropine test stimulates the tenth cranial nerve may be unnecessary and is always open to debate[13]. In fact, we could emphasize that practically all legislation and clinical practice guidelines coincide in certifying the absence of respiratory stimulation in the presence of increased carbon dioxide in the blood, as irrefutable evidence for the diagnosis of encephalic death in a patient in an active coma[14-16]. Dr. Citerio, in the journal Neuro Critical Care, continues to highlight the differences existing between different European countries[18].

An interesting and conflicting point occurs when the existence of spinal release movements is detected after encephalic death. These reflexes of the medulla can be quite complex or even complex, making it difficult for inexperienced clinicians to make a diagnosis. These reflexes can be provoked after stimulus in the spinal cord territory, or they can be spontaneous, while the patient remains in bed, or when the aorta is clamped during the process of organ extraction. This phenomenon, secondary to the sudden ischemia of the spinal cord, generates the release of neurotransmitters present in the nerve afferents and gives rise to this type of response. In fact, many authors describe these "movements after death", which are also known as "Lazarus reflex", by analogy to the situation described in the Gospels with the resurrection of Lazarus of Bethany. Evidently, these findings can be the subject of clinical discussion or even should be explained to the family so that they understand why they occur. Information and instruction for professionals and family members is crucial in all these cases[18-20].

In the case of the pediatric population, the inherent associated implications, usually of an emotional or circumstantial nature, make these situations even more complicated for healthcare professionals. On the other hand, although in 2012 the guidelines published by the Task Force in 1987 on the development of diagnosis in this population were revised, it can be said that little or nothing has changed in their systematic approach in recent years.

Finally, with regard to patients connected to extracorporeal devices, the development of the apnea test or its interpretation has been the subject of debate in recent years[11].

Use of complementary tests and observation periods

Our legislation clearly states that in patients with structural neurological damage, an observation period of 6 hours may be sufficient to reach the diagnosis of encephalic death, although in the case of encephalopathy it is advisable to extend the interval up to 24 hours. However, these periods can be reduced by the clinical judgment of the physicians signing the certificate, as long as they refer to a complementary test, which reliably supports the clinical examination performed.

Diagnostic support tests should be used under the idea of what they are intended to measure. One cannot expect a flow test to provide a pattern compatible with cerebral circulatory arrest in the presence of a cranial sealing defect, just as we cannot find an isoelectric line in the electroencephalogram, i.e., the myth of the "flat electroencephalogram" does not exist[21,22]. In these cases, misinterpretation of complementary tests can become a confounding factor in reaching a diagnosis of brain death. Sometimes, their use becomes inexorable, as in the case of neonatal and infant patients, where the use of these tools is repeated over time. In contrast, in adults, their systematic request or unnecessary repetition has been described as a negative element for the patient's family, as well as being recognized as affecting the donation-transplantation process[23-26].

Death due to circulatory criteria

Spanish legislation, dated December 22, 2012, perfectly establishes that the unequivocal absence of cardiac rhythm or pulse can lead to the diagnosis of the patient's death after a minimum observation period of 5 minutes. In all cases, a series of safety requirements must always be met, absence of confounding factors (such as hypothermia or cases of drowning), as well as the judgment of healthcare professionals prevailing above all, as was previously the case with the diagnosis of encephalic death.

However, in the diagnosis of death due to circulatory criteria, the following conflicts arise. First, what observation period (no touch time) should be appropriate[27-32]. Second, what we understand by a permanent and irreversible event within the definition of death by circulatory criteria[33].

Observation period of no circulation

The observation period is crucial in many ways. It assumes that asystole or lack of circulation is maintained over time, life has been extinguished and, therefore, it is already a corpse from the clinical and legal point of view. However, we do not have any cut-off point or any ROC curve that establishes limits of sensitivity and specificity that can make the whole process objective.

In 2013, the prestigious journal Nature, in its Nature Reviews Neurology section, published a review of the observation times considered in different hospitals, universities and health care ethics committees for declaring death due to circulatory criteria, both in the United States and Canada. The University of Pittsburgh protocol, dated 1993, considers asystole of 2 minutes to be sufficient time. Subsequently, in 2001, the recommendations of The Ethics Committee of the Society of Critical Care Medicine were published, indicating that

this period should never be less than 2 minutes, but not more than 5 minutes. In 2006, the report of the National Conference on Donation after Cardiac Death and that of the Canadian Council for Donation and Transplantation were published. In the former, they maintain the possibility of waiting between 2 and 5 minutes, while in the latter they describe 5 minutes as a premise. Finally, and the subject of much editorial controversy and criticism, we find the period of Denver Children's Hospital. In this case, alleging an extraordinary situation, they considered that an interval of between 75 seconds and 2 minutes was sufficient to declare death due to circulatory criteria[27].

However, on the European continent the criteria are not homogeneous either, with an even more complicated panorama, given that certain observation times are, in my opinion, excessive. Domínguez-Gil et al., in the journal of the European Society for Organ Transplantation, report the observation times established in each country[28]. Specifically, Spain, the United Kingdom, the Netherlands, France and Belgium accept an observation period (no touch period) of 5 minutes. On the other hand, we find that 10 minutes are required in Austria, Czech Republic and Switzerland. In the case of Latvia, 15 minutes are required. Finally, the longest period is in Italy, where 20 minutes are required to consider the observation time completed.

The main concern that leads to this divergence is when the patient ceases to be a patient and we are certain that his or her heart will not regain a pulse and, therefore, effective circulation. The term self-resuscitation has been described by different authors, in isolated cases or short series of cases[30-32]. In this regard, Hornby et al. published a review in Critical Care Medicine in 2010, in which they evaluated all these publications dealing with patients who had self-resuscitated[30]. Although the authors plot the different times at which cases of self-resuscitation have been described, which ranged from one minute to 2 cases that occurred at 15 minutes and one isolated case at 20 minutes, they themselves acknowledge the existence of serious failures in patient monitoring, which could have been considered deceased when in fact they were not. They also indicate that these cases were always described after cardiopulmonary resuscitation maneuvers had been performed, not when the disease had been allowed to evolve in a monitored manner and cardiac arrest had been detected and precisely timed.

A subsequent study, aimed at evaluating the process of controlled asystole type III donation, was published in 2012 in Critical Care Medicine[31]. In this study, all patients were exhaustively monitored with invasive blood pressure by means of catheters inserted at the arterial level, and the periods from withdrawal of measurements and absence of pulse were recorded. The authors describe that an average of 22 minutes elapsed from the limitation of life support to the patient's death. At the same time, no episodes of self-resuscitation were detected after 2 minutes of observation. In this regard, in Spain, the legislation provides for twice as long plus one minute of observation (5 in total), so that this period can be considered adequate. However, at the present time, we must recognize that the evidence that exists in this respect is poor and it will be difficult to resolve this research question. Nevertheless, another aspect that should not be underestimated is that prolonging these observation times beyond what is reasonable and legally established, either due to ignorance, uncertainty or lack of determination, can be considered maleficent if a possible organ donation is being considered, since the recipient will be offered a suboptimal organ, unnecessarily assaulted during the entire donation process[32-34]. In this regard, there are a number of open research studies evaluating how to alleviate the oxidative stress associated with these phenomena.

Circulatory death as an irreversible and permanent situation

In an article published in the Journal of Medicine Philosophy in 2010, the differences between irreversible and permanent are discussed. In it they indicate that a situation is irreversible (cannot reverse) when function will not be restored, not even by applying measures aimed at doing so. The permanent state (will not reverse) occurs when function will not be restored on its own or when measures to restore function will not be applied[35].

Two years ago, the journal Intensive Care Medicine published the article "International guideline development for the determination of death"[3]. This work, sponsored by the World Health Organization, includes different concepts: cessation of circulation and respiration, cessation of circulation and respiration without the possibility of spontaneous recovery and, finally, cessation of circulation and respiration without any possibility of recovery. The different scenarios are broken down according to whether or not resuscitation maneuvers are applied, as well as stating that the observation time should be between 2 and 5 minutes. They reflect that between 2 and 10 minutes the impossibility of recovery is reached, and leave, to close the scheme, the presence of biological data established after cell death.

Nevertheless, we are witnessing a historic moment regarding assisted cardiorespiratory arrest care using extracorporeal devices. In fact, a clinical case of a hypothermic patient resuscitated after 6 hours without pulse has recently been reported in the press. It is evident that the multidisciplinary effort, both in the out-of-hospital, emergency and critical phases, together with the peculiarities of the case (severe hypothermia), open a door to a field that was unknown years ago. Under the principle that "a patient is not dead until he or she is warm and dead", we are faced with a change in the paradigm of action, which must be deeply studied, analyzed and reasoned, in order to be able to apply all the necessary efforts in those patients in whom the measures are not expected to be futile a priori[35]. We will therefore have to begin to adapt to these new scenarios, progressively and in accordance with the scientific evidence.

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