

HISTORICAL EVOLUTION OF MEDICAL KNOWLEDGE IN THE FIELD OF VEGETATIVE STATE

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[Evoluzione storica delle conoscenze mediche in tema di stato vegetativo]

ABSTRACT

The term "vegetative state" refers to a clinical picture characterized by:

- Loss of contents of consciousness (i.e., loss of cognitive functions, and the absence of interaction with the external environment);
- Presence of alertness organized in circadian rhythms of sleep-wake.
- Complete or partial presence of hypothalamic and brainstem functions;
- Cardiac activity, respiration, temperature and blood pressure are normal.

The vegetative state follows, for the most part, a state of coma due to either trauma or non-traumatic events (hemorrhagic or ischemic stroke, cerebral anoxia, encephalitis).

Key words: vegetative state, disturbances of consciousness, bioethics, prognosis, history of medicine

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The etiology that causes brain lesions, the age factor and the duration of the vegetative state are the parameters that affect the prognosis.

The latter, in turn, is less unfavorable due to the vegetative state that follows traumatic events.

However, the prognosis is very poor after anoxic brain damage.

The probability of recovery of consciousness is usually inversely proportional to the duration of the vegetative state and in any case greater in younger individuals.

Several case studies are based on studies often lacking a serious long-term follow-up.

Death is the result of pulmonary complications or urinary infections.

Patients in a vegetative state have a blank stare, open their eyes spontaneously or as a result of acoustic stimuli, make sounds, smile or cry for no reason, breathe on their own and regularly, the pupils react to light, respond to painful stimuli, their motor actions are reduced and aimless, and automatic movements of swallowing, chewing, and sucking may occur.

Sphincter incontinence is always present.

A patient in a coma does not open his eyes spontaneously or in response to an external stimulus, has irregular breathing, does not respond to painful stimuli, has compromised gag reflex, swallowing and cough, and is incontinent.

In a coma, the compromised state of consciousness is due to brainstem involvement.

In a vegetative state, the function of the brainstem is not affected, while there is no interaction between the cortex, thalamus and brainstem.

The vegetative state typically develops after a period of variable duration of coma, although it may directly follow the lesion.

Its evolution can be⁽²⁻⁴⁾:

- 1) death;
- 2) persistent, reversible or permanent vegetative state leading up to death;
- 3) partial, rarely complete recovery.

The vegetative state is persistent if it is present one month after an acute traumatic or non-traumatic brain lesion.

The reversible persistent vegetative state has a variable duration, ranging from a few months to many years.

The physician has a duty: to discuss the “state of consciousness” in terms of rigorous scientific findings and with any doubts that these sometimes cause.

This premise is necessary to introduce the concepts of “vegetative state” and “minimally conscious state”, pathological conditions that most frequently kindle the debate on euthanasia. In this regard, useful data can be found in the final document, issued on December 14, 2005 in Rome, by a Scientific-Technical Commission established by Ministerial Decree dated September 12, 2005. The document drawn up by the members of the committee, at the conclusion of the proceedings, expresses the following considerations in a nutshell:

- In Italy, there are no multidisciplinary studies on diagnosis and therapies with conclusions shared by all with regard to those individuals who no longer possess full autonomy for the primary necessities of life and hence need support and assistance, including for their most basic functions.

- The National Health System provides for the promotion of an integrated network of health and social services for the chronically ill and disabled, in order to achieve an improvement of their quality of life.

- The proceedings of the Technical-Scientific Committee were inspired by the need to come to useful conclusions, based on all the available scientific knowledge, also of an epidemiological nature, to obtain better indications for the continuity of care in diseases with serious clinical conditions.

- The study of the Technical-Scientific

Committee concerned issues of a statistical, scientific and legal nature, in order to obtain better data on:

- Number of subjects in a vegetative or minimally conscious state in Italy.

- Diagnostic course and outcome of the debate in medical, bioethical and legal terms also internationally.

- Effectiveness of Italian public facilities that host subjects in clinical conditions of low responsiveness, with special attention to specialized centers or centers of excellence.

- The committee deemed it appropriate to narrow its field of investigation to the study of vegetative state as a consequence of a traumatic, acute inflammatory, vascular, or anoxic nature, making a distinction with vegetative state secondary to tumors, metabolic or degenerative diseases of the elderly, genetic developmental disorders of childhood.

Metabolic or degenerative diseases of the elderly and genetic diseases of childhood can be overlapped with regard to issues of a bioethical nature, but these require different forms of care. In medicine, it is necessary to share the meaning of a term referring to a particular disease or related problem; otherwise it creates uncertainty and confusion, which are the premises of disinformation. Over recent decades, there has been no full agreement in the international scientific community⁽⁵⁻¹⁰⁾, and, to date, there still is none on the medical terminology regarding individuals with “Low Level Neurological States (LLNS)”, i.e. subjects with low levels of cognition and responsibility with regard to the surroundings.

Many heads of communication bodies, i.e., the mass media, often speak of medical discoveries as if they were “certainties”, “conclusions”.

This fuels beliefs in public opinion that are not always in line with the true meaning of official medical terminology.

The term “vegetative pathways” was coined by the Frenchman Arnaud and his collaborators in 1963 and a few years later it was renamed “vegetative survival” by Vapalahti and Trupp.

In 1972, Jennet and Plum defined “persistent vegetative state” the condition of apparent wakefulness without awareness of subjects that emerged from a coma. In 1989, the World Medical Association defined persistent vegetative state as the chronic loss of consciousness caused by “a lack of consciousness for at least twelve months.”

In 1994, the Multi-Society Task Force (MSTF)

published a document that defined persistent vegetative state a state of “wakeful unconscious state that lasts longer than a few weeks” in the prestigious journal “New England Journal of Medicine”.

In 1995, the American Academy of Neurology published a document of guidelines on the evaluation and management of patients in persistent and permanent vegetative state.

In 1996, the British Medical Association, in disagreement with the American Academy of Neurology, published other guidelines, using the term “persistent” rather than “permanent” used by the MSTF, to define the condition of irreversibility.

In 2003, the Royal College of Physicians in London called persistent vegetative state a persistent vegetative state lasting for several weeks⁽¹⁰⁾.

In Italian, the term “vegetative state” takes on at times a conceptual meaning other than the scientific one⁽¹⁰⁾.

In current medical language, words like “apallic syndrome”, “wakeful coma”, and “akinetic mutism” still resist. One of the first terms coined for individuals who woke up from a deep coma, without regaining an apparent awareness of self and their environment, was that of apallic syndrome, first used by Kretschmer in 1940, to mean that clinical picture of loss of cortical function in both hemispheres, yet with preserved function of the brainstem. Other improper terms used are “decortication”, “decerebrate rigidity”, and “state of decerebration.”

The recent term of “cortical death” is also improper and incorrect. In 1941 Cairns and collaborators adopted the term of “akinetic mutism”, describing a patient suffering from cystic tumor of the third ventricle. These patients showed a significant reduction of movements and speech, in the presence of a state of adequate alertness and ability to follow others with their eyes.

For a long time, Anglo-Saxon literature used the term “akinetic mutism” also for subjects whose clinical picture was similar to Cairns’ original concept and, currently, many continue to use this term referring it to a subcategory of so-called “minimally conscious state.” Subjects with significant post-traumatic neurodisabilities and even minimal signs of purposeful behavior, labeled as patients with “severe post-traumatic dementia” are considered in a minimally conscious state.

In 2003, the National Health and Medical Research Council of Australia published a document in which the term “vegetative state” has been replaced

with that of “post-coma unresponsiveness” to indicate a prolonged disturbance of responsiveness.

The Italian Technical-Scientific Committee, while expressing the hope for a change in terminology, continued to use the currently most used term of “vegetative state” in its document. In terms of terminology, the vegetative state (VS) must be distinguished from the minimally conscious state (MCS), both included in the group of conditions of “low-level neurological state” (LLNS). This group comprises those subjects, not quite fully conscious, that do not meet the diagnostic criteria of vegetative state, as they have a state of minimal and not always wakeful consciousness.

The term “minimally conscious state” was introduced by the Aspen Consensus Group to indicate the nosographic category of subjects with a clinical picture following a vegetative state. Patients included in this group show a severe impairment of consciousness, with the presence of a minimal behavioral manifestation of relationship with the surrounding environment.

In these cases, patients execute simple orders, albeit inconstantly. In the scientific community there is still controversy over the term “permanent vegetative state”, formulated first by the MSTF in 1994, to indicate the maximum possible limit of recovery of patients who could awaken from a post-anoxic or post-traumatic vegetative state. Both the MSTF and Italian Technical-Scientific Committee agree in emphasizing the value “probabilistic” when it comes to the term “permanent” applied to a vegetative state. In fact, the MSTF, in its document issued in 1994, specified that the term permanent “is based on probabilities, not absolutes.” However, this probability is, in fact, equated by the MSTF to a diagnosis of irreversibility when it is stressed that “...the persistent vegetative state becomes permanent that is, when a physician can tell the patient's family or surrogate with a high degree of medical certainty that there is no further hope for recovery of consciousness or that, if consciousness were recovered, the patient would be left severely disabled.”

The Multi Society Task Force (MSTF) reached its conclusions on the basis of a retrospective review of clinical cases dating back to the period between 1972 and 1993, but with no strictly controlled clinical studies.

Furthermore, the study of the possibility of recovery of patients was carried out, regardless of their type of pathology and duration of rehabilita-

tion treatment performed. It can therefore be noted that the conclusions of the MSTF do not rest on a large case history, and are based on retrospective surveys of non-controlled clinical cases with follow-up (study in progress) of no more than twelve months.

For the MSTF, post-traumatic vegetative state is defined as “permanent” after twelve months.

Again, it should be emphasized that scientific papers have been published based on well-documented case studies of delayed recovery (Andrews 1993, 1996).

Even today no one, for sure, can be able to distinguish between those who recover within twelve months and those who do not. The same limit of twelve could be moved, if taking into account larger case histories of better therapies and more prolonged rehabilitation interventions. Moreover, the most qualified Anglo-Saxons researchers do not all agree with the concept of “recovery window”. A recent publication of the Royal College of Medicine in England suggests an observation period of six months in order to better evaluate the possible emergence from the post-anoxic vegetative state.

The Technical-Scientific Committee fully agrees with the conclusions of Prof. ND Zasler in the prestigious journal *Neurorehabilitation*, (19:285-292, 2004): “... The MSTF has reached a coarse synthesis lacking a sound scientific foundation when it stated that in the diagnosis of permanent vegetative state a physician can tell the patient’s family or surrogate with a high degree of medical certainty that there is no further hope for recovery of consciousness or that, if consciousness were recovered, the patient would be left severely disabled.” First of all, what exactly is a high degree of “medical certainty”?

Does it mean that you are really sure but you are not sure at all?

So what is the difference between “medical certainty” and medical “probability”? Moreover, how can we, as clinicians, label a condition of unconsciousness as “permanent” and then have the “scientific audacity” to state that this definition also includes a condition in which the patient is conscious, but since he is also seriously disabled, we should not bother to change the diagnosis and/or prognosis?

In our opinion and in that of many other authors, the extension of the concept is dangerous and scientifically irresponsible.

Prof. Nathan D. Zasler has introduced useful

elements of discussion and analysis for everyone. We are quoting him because we are convinced that, in the absence of “ancient and Christian piety”, many would do well to reflect further and gain greater insight into alleged certainties, which, however, scientists do not dare to affirm.

It is important to know the diagnostic criteria to define “vegetative state”. These have been formulated and accepted by the scientific community (American Congress of Rehabilitation of Medicine, *Arch. Phys. Med. Rehabil.* 1995; 76: 205-9).

The vegetative state consists⁽¹⁰⁻¹¹⁾ in a clinical condition characterized by complete loss of consciousness of the self and contact with the external environment, a preservation, even partial, of hypothalamic and brainstem functions and recovery of the sleep-wake cycle. The correct diagnosis of a vegetative state must be correlated with specific diagnostic criteria.

These are the following:

- No evidence of consciousness or awareness of the self and environment;
- No evidence of lasting reactions in response to stimulation;
- No verbal activity;
- The presence of eye opening;
- Rudimentary sleep-wake EEG pattern;
- Independent vital functions;
- Deficit of cranial nerves;
- Variable presence of brainstem and spinal reflexes;
- No ocular motility;
- Rarity of the blink reflex and primitive motor patterns;
- Stiffness-spasticity;
- Pathological postures.

The patient in a vegetative state lies, apparently unconscious, even with his eyes open, but with preserved respiratory, cardiovascular, thermoregulation, kidney and gastrointestinal functions.

The subject does not require support technologies and shows signs of focal or diffuse damage on CT and MRI. Brain perfusion on SPECT is reduced as is glucose metabolism on PET. In addition, EEG activity shows variable alterations.

The following clarifications need to be made:

- 1) the clinical characteristics of the vegetative state have a duration that is at times variable, with extremely transient conditions;
- 2) it is necessary that the conditions correlated with a vegetative state are still present after one month from brain damage and with the presence of

metabolic or degenerative disorders;

3) EEG and techniques anatomical and functional neuroimaging cannot predict with absolute certainty a possible unfavorable prognostic outcome;

4) in no way can the patient in a vegetative state be understood terminally ill;

5) the diagnosis of vegetative state is mainly clinical and it is not easy even in highly specialized centers; moreover, it features spaces of doubt or clinical uncertainty involving the possibility of diagnostic error;

6) the vegetative state is burdened by high rates of misdiagnosis even in specialized centers.

For the “minimally conscious state” the diagnostic criteria, formulated by the Aspen Consensus Group, are as follows: spontaneous opening of the eyes, sleep-wake cycle, range of dulled to normal wakefulness, present but inconsistent perception, reproducible but inconsistent communication, inconsistent yes/no replies, tracking with eyes, intentional attitudes and gestures (not reflex activity) to environmental stimuli. Therefore, a favorable evolution from vegetative state to that of minimally conscious state is determined when minimum cognitive behaviors can be distinguished from reflex behaviors.

The Aspen Consensus Group has clarified that “the exit from the MCS and recovery of a higher state occurs along a continuum whose upper limit is necessarily arbitrary.”

The correct diagnosis of vegetative state is important for a correct and appropriate rehabilitation and an effective choice of correct models of care. A person in a “vegetative state” or in “minimally conscious state” gives rise to the following important considerations: an advanced and civil society and culture should always consider human life as non-negotiable and essential good, even in the presence of serious diseases, which should neither alter nor diminish the rights of an individual.

This is our opinion, in science and consciousness.

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