Scottish Council on Human Bioethics

21 March 2022

Position Statement on:

The Definition of Embryonic Death

Defining death is not always a simple procedure since different parts of the body cease their activities at different times. In this regard, it is debatable whether it is the process of decline itself or a specific event within that process that can be defined as death. The argument is essentially about defining the point during the gradual decline of biological function within an organism when organismal function *itself* ceases, and therefore a medical declaration of death can be made. Thus, in defining death, one seeks to determine this point accurately and reasonably. Moreover, the definition of death may depend on the development stage and/or age of a particular human being.

In this context, the circumstances under which it is possible to define embryonic death is challenging since no heartbeat and brain yet exist. But, as a first step, the Scottish Council on Human Bioethics (SCHB) would like to suggest the following elements in helping to determine the death of an embryo.

1. Death is not just a medical occurrence.

Defining death is about determining a common understanding of the time of death of an individual that will be relevant on all levels. Persons do not only grieve because of a biological situation, but because death can be socially, psychologically, emotionally, and spiritually very significant. The definition of death is intended to be practical, and guide a person's actions and judgements.

In addition, a particular definition of embryonic death should be based on the best available scientific criteria, rather than utilitarian reasons, such as the desire to provide more cells for research or to save the health service money.

2. An arrested embryo (in which cell division has stopped) may still contain totipotent or pluripotent cells capable of life.

If all the cells in an embryo have permanently and irreversibly lost the ability to divide, then the embryo as a whole can be described as dead. In other words, the permanent and irreversible cessation of all cell division in a whole embryo would indicate that the embryo has died.

However, an arrested whole embryo in which no cell division takes place may still contain some totipotent, plenipotent or pluripotent cells. These living cells may be able to continue dividing to form a whole human embryo even if they can accommodate the presence of other cells which have permanently and irreversibly lost their ability to divide (cells which are dead).[1] Moreover, some living cells can continue to divide if they are separated from those that are dead. This means that if the dead cells are removed from the living totipotent plenipotent or pluripotent cells, an arrested embryo may still have the capacity for life.[2] In other words, it is not because an early embryo has arrested naturally that it is dead (only some cells inside this embryo may be dead). In this regard different, stages can be examined:

> **Before the 4-cell stage (2-3 days after the generation of the one-cell embryo):** All living cells in a human embryo are considered to be totipotent, meaning that they can be regarded as embryos in their own right if they are separated from the original embryo. In other words, in an arrested embryo some of these living totipotent cells may (theoretically) be able to continue forming a whole human embryo if the dead cells are removed or under conditions where the dead cells can be accommodated.
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> **Between the 4-16 cell stage (4-5 days after the generation of the one-cell embryo)**, the cells are plenipotent and remain 'plastic', meaning that they can change their developmental fate based on the

[1] In many cases, embryos with arrested and/or dead cells can resume development if transferred to the supportive environment of the uterus.

[2] Cells that no longer divide for some reason may start dividing again if this reason is removed. For example, a cell which is frozen stops dividing but can begin diving again when thawed.

information they receive. However, they are not able to *independently* form an entire embryo (they are not totipotent). If isolated, they cannot form an organised embryo on their own but exhibit, instead, restricted potency becoming only certain kinds of cells.

Between the 16-cell stage and about 1800-cell stage (5-14 days after the generation of the one-cell embryo): The cells in the embryo are no longer considered to be plenipotent. However, identical twinning can still occur up to 14 days. This means that in an arrested embryo, groups of living cells may (theoretically) be able to form a whole human embryo, even if some of the cells of the embryo are dead.[3]

At about the 2000-cells stage (14-16 days after the generation of the one-cell embryo):
At this stage the process of forming a single embryo has already commenced but conjoined twins are still possible. For example, if the cells of the head region of the embryo split aberrantly, this may result in conjoined twins with two heads.

After about the 2000-cell stage (16 days stage after the generation of the one-cell embryo): the cells in the embryo are still pluripotent but are unable to form an independent living being if they are separated inside the embryo. Isolated groups of cells will be unable to generate a whole embryo after this stage, because cells have become too specialised. This means that, if living pluripotent cells after this stage are separated from a naturally arrested embryo, these cannot become a human being. In this case, living cells may be removed from the dead embryo to be used for transplantation in a similar way to the use of organs from a person who died naturally.

If an organism still has a possibility for continued life, then it cannot be considered dead. It is therefore important to determine whether the irreversible loss of all cell division in an early embryo has occurred before death is certain – something which may be very difficult to establish. In many cases, it may also be difficult to differentiate between a very abnormal and dysfunctional embryo (which is still alive, and therefore from which live cells should not be transplanted) and a dead embryo. Further investigations are necessary, and a precautionary approach may be appropriate, meaning that if uncertainty is present, the embryo should be regarded as still alive.

3. The creation of artificial embryos.

Research, in 2021, has shown that it is possible to create structures which are very similar to human embryos in the laboratory. These are called blastoids or synthetic human early embryo-like entities since they resemble an embryo at the blastocyst stage of development with about 50-120 cells.

It is not yet clear how closely these new blastoids resemble true embryos formed by fertilisation. Models show that they share gene patterns and respond, in culture, in similar ways to actual embryos, though they still have significant abnormalities, such as unsynchronised growth and cells that are not usually present in a normal embryo.[4] Moreover, thus far, blastoids do not proceed along a normal developmental path to generate a more mature human form.

At this stage, it is difficult to know what would happen if some of the blastoids were allowed to continue developing. Interestingly, in the UK, these entities could be left to develop beyond the current 14-day legal limit for research on embryos since these blastoids may not be considered as embryos.

4. Summary.

- Definitions of early embryonic death must never be influenced by the desire to experiment on or use embryos for scientific or therapeutic reasons.

- Definitions of early embryonic death are not universally accepted. One view is that irreversible cessation of all cell division constitutes death.

- The early embryo is a unique human individual with the full potential to grow and then be born. Therefore, the embryo has the right to be protected from harm.

- The production of early embryos for the purpose of using some for scientific or therapeutic reasons is therefore unethical and, for this reason, the definition of death becomes less important.

[3] If all the cells of the embryo were dead, except for cells of the ICM, twinning could not occur. For twinning to occur, there must be living trophectoderm and Inner Cell Mass cells, and each twin would require some of each cell type.

[4] https://www.bioedge.org/bioethics/several-research-groups-create-artificial-embryos/13743

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1. Definitions and General Information

Death: The ending of a life, which can have biological, social, emotional, psychological, spiritual, and legal facets.

Integration: combination of cells to form a single, functioning, unified whole.[5] The cells communicate to generate a response that is multifaceted, context dependent, and promotes the continued health and function of the whole.

Coordination: the communication of parts in order to achieve an effective outcome. It is the ability to bring cells, tissues or organs into a common action or condition. Coordination can reflect either a single type of response that occurs simultaneously in multiple cells or a set of synchronous but cell-type specific responses.

Organismic death: the irreversible cessation of all the integrated functioning of the organism as a whole.

Clinical death (sometimes defined as cardiac death): Irreversible cessation of heartbeat (cardiac arrest), breathing, and responsiveness.

Embryonic death: the irreversible arrest of the embryo as a whole which does not contain any totipotent, plenipotent or pluripotent cells having the capacity to form a new living being. In this regard, it is impossible to know whether the division of cells in an arrested embryo could be restored in an appropriate environment. For example, many embryos that appear to have arrested will resume development when transferred to the uterus.

Embryoid bodies: Three-dimensional aggregates of pluripotent stem cells.

Arrested embryo: an embryo in which cell division has stopped.

Totipotent cell: A cell which demonstrates the ability to develop into every cell type required for human development, including the embryonic placenta, umbilical cord, and membranes. An individual totipotent cell may (theoretically) be considered as a one-cell embryo. In other words, it is capable of generating a globally coordinated development sequence. Totipotency is believed to be lost by the 4-cell stage in mammals.

Plenipotent cell: The cells of the of a 4-16 cell embryo remain 'plastic' and can change their developmental fate based on the biochemical communication they receive. However, they are not able to *independently* form or organise (on their own) an entire embryo (they are not totipotent). Under some conditions, freshly dissociated plenipotential cells from early embryos (up to the 16-cell stage) can be reaggregated and produce live-born animals.[6]

Pluripotent Stem Cells: after the 16-cell stage, cells in an embryo have the capacity to develop into every cell type of the postnatal human body, but not into the placenta and the umbilical cord. A separation of pluripotent cells inside an embryo during the first 13-14 days of life may give rise to multiple human beings (identical twins or higher-order multiples).

Morula stage of embryonic development: embryo which contains about 16-32 cells (about 4-5 days after the generation of the one-cell embryo).

[5] Merriam-Webster, s.v. "integrate," http://www.merriam-webster.com/dictionary/

[6] Condic ML. Totipotency: what it is and what it is not. *Stem Cells Dev.* 2014 Apr 15;23(8):796-812.

Blastocyst stage of embryonic development: embryo which contains about 50-120 cells (about 6 days after the generation of the one-cell embryo).

Person: A living being to whom full inherent worth and value is recognised.

Cellular Organism: An entity consisting of cooperative and interdependent cellular systems that are united in a harmonious whole. A living biological organism exhibits integrated, self-developing and self-maintaining organisation over both space and time, and therefore must be viewed as an organic whole that precedes and produces its own parts. Consequently, a biological living organism is not merely a sum of biochemical reactions. Instead, it is a dynamic and ordered collection of interdependent, coherent, functional cells and structures which coordinate all their integrated functions for the sake of the organism as a whole. This enables emergent properties to be expressed which are far more complex than the functions exhibited by the substituent parts.

However, although communication between cells can provide a coordinated biologic response to specific signals, it does not provide evidence for integrated function that is characteristic of a human organism.[7]

Trophectoderm: cells forming the outer layer of an embryo at about the 120-cell stage, which provide nutrients to the embryo and develop into a large part of the placenta.

Inner Cell Mass: a group of cells of an embryo at about the 120-cells stage, which eventually develop into the foetus and some of the surrounding membranes.

Zygote: a one cell embryo resulting from the fertilisation of an egg by a sperm cell.

Normal Embryonic Development

When a maturing egg of a woman is released, about every month, into her fallopian tubes it measures just about 0.1 mm in size and is surrounded by a trans-lucid membrane layer called the zona pellucida. After penetrating the zona pellucida, the sperm cell binds to the surface of the egg and the two cells fuse into a single cell; this fusion takes less than a second to complete and produces the one-cell zygote.

As soon as this happens, biochemical changes take place (within the first 1–3 minutes) and the zona pellucida is modified by the zygote so that other sperm cells cannot get through. Inside the one-cell embryo (zygote) the pronuclei (with only one set of chromosomes) derived from the sperm and egg cells, respectively, are still separated and generally remain distinct and visible entities until 20 hours after the sperm cell has fused with the egg; this is called the pronuclear stage.[8] However, they have by this time duplicated their number of chromosomes in preparation for cell division in a coordinated pattern of development. Interestingly, the entire process up to this stage and including the pronuclear stage can be disrupted in humans, while not eliminating the potential for development. Indeed, the process is believed to be 'reversible' in humans in that the pronuclei can be taken out of the zygote and, subsequently, put back in without affecting future development.[9]

By approximately 20–24 hours, the two pronuclei of the egg and the sperm cells begin to come together in a gradual process and the nuclear membranes dissolve. It is only at the end of this stage (called syngamy) that fertilization is considered to be complete, and a one-cell embryo is obtained. This one-cell embryo can no longer be compared to a fertilized egg or the sum total of a sperm and egg cell since, from a molecular perspective and its developmental behavioural pathway, it is totally new. In some countries, such as Germany, it is only when fertilization is complete that a new human embryo, as such, is recognised in law as having come into existence. It should be noted, however, that there is no actual fusion of the pronuclei at this one-cell zygotic stage in human beings to form a single clearly defined cell nucleus with 46 chromosomes since, at syngamy, the cell immediately begins to divide to form a two-cell embryo.

After division of this one-cell embryo, which is the end of the first cycle, a two-cell embryo is formed in which both cells normally contain 46 chromosomes in their nucleus of which 23 come from the father and the other

[7] Condic ML. Determination of Death: A Scientific Perspective on Biological Integration. *J Med Philos*. 2016;41(3):257-278.

[8] The cell produced by sperm-egg fusion can no longer be considered an 'egg' in any meaningful sense. The process of producing a zygote cannot be 'reversed' (meiosis II has been completed and a number of other irreversible changes have taken place) but it can be disrupted by removing the pronuclei, leaving a cellular cytoplasm that, while significantly different from that of an egg, is still sufficient to support development if new pronuclei are transplanted.

[9] For example, it is because of this reversibility in the first 24 hrs of fertilisation that the Pronuclear Transfer procedure was developed. See: https://www.newcastle-hospitals.nhs.uk/services/fertility-treatment/mitochondrial-donation/

23 from the mother. This means that it is only at this two-cell embryonic stage that paternal and maternal chromosomes are present together in the nucleus of each of the two cells.

Once the two-cell embryo is obtained, animal research suggests that each one of the cells of the two-cell embryo may already be slightly different in that they may be biased to develop into specific elements of the future animal body. But science shows that these early cells are relatively 'plastic' in that they can change their developmental direction without any negative consequences if they are disturbed for some reason.

By the 4-cell stage of the developing embryo, distinct molecular and developmental variations among the cells already exist. At this point, if one of the cells is removed, the embryo may not always recover to normal growth, which means that the removed cell may have started to specialize in the coordinated matrix of development which is important for survival.

The subsequent normal development of the embryo in the fallopian tubes of the woman takes place with a division of the cells about every 12–36 hours without the embryo really growing in size, which means that the cells in the embryo become smaller. Unless a problem occurs, all these cells have exactly the same genetic composition.

In most animal models, if one cell is removed from an embryo at the two-cell stage, in an appropriately supportive environment, the isolated cell can develop on its own into a second embryo. Because of this, the cells are defined as totipotent, a property that is believed to be lost after the 4-cell stage (2-3 days after sperm-egg fusion) in humans.[10] Since this second embryo would have exactly the same genetic composition in its chromosomes as the first, it would be genetically identical to the original zygote. While identical twins can be produced in this way in the laboratory, natural identical twins are likely to result from of a group of several cells detaching themselves together (not just a single cell) at the blastocyst stage.

At the 8-cell stage (about 3 days after the generation of the one-cell embryo), a normal human embryo can continue to develop after the removal of one of its cells, indicating that the embryo has adaptively replaced the missing body parts.

At the 16-cell stage (3-4 days after the generation of the one-cell embryo) the structure of the embryo (now called a morula, which is Latin for a mulberry since it resembles such a berry) changes and cells begin to tightly adhere to each other in a process known as 'compaction', causing the morula to become smoother in appearance.

Between about 4-6 days, when further divisions have taken place and the embryo (now called a blastocyst) reaches about the 120-cell stage, an internal fluid-filled cavity appears, and two different parts are formed. The first part contains a large number of embryonic outer cells which is called the trophectoderm. This develops predominantly into protective and nutritive tissue including the placenta which enables an exchange of substance between the mother and the embryo. The second part of the embryo contains a small group of inner cells (called the Inner Cell Mass) which produces the structures of the postnatal body. Cells in the Inner Cell Mass are now pluripotent.

During this time, the embryo moves from the fallopian tubes into the uterus. The embryo then begins to discard its zona pellucida after 5-7 days of development, in order to implant itself into the uterus of the mother.

Implantation which begins at about 5-7 days after the generation of a one-cell embryo is usually complete after 14 days. In addition, this 14-day stage is the point in time when identical twins can no longer be obtained through the division of the inner cell mass of the embryo. In other words, before this stage, pluripotent cells can divide inside the outer membrane of an embryo to form two or more embryos. In addition, this 14-day stage is about when the primitive streak begins to appear from which the first rudiments of the nervous system are developed.

Until the 15-16 day stage conjoined twins can develop.

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[10] There is no evidence for totipotency persisting to the 8-cell stage in humans, and only one report in one animal species (which could not be replicated), that totipotency can persist this late in development. The overwhelming weight of the data suggests that totipotency does not persist beyond the 4-cell stage in most cases in most mammals, and therefore (by extension) in humans. Mammalian embryos are 'regulative' in that they are able to repair injuries and restore normal function even in the face of significant loss of cells. This occurs by cell-cell interaction and does not require the presence of any individual totipotent cell.

At about the 16-day stage, the Inner Cell Mass divides into the following three different embryonic parts:

- The Endoderm: the innermost of the three primitive germ layers of the embryo. It later gives rise to the lungs, liver, and digestive organs.

- The Mesoderm: the middle layer, which consists of cells which later become the bones, muscles and connective tissue.

- The Ectoderm: the outermost layer, which gives rise to skin, nerves and brain.

In normal circumstances this embryo then becomes a foetus after eight weeks of development and is born after about 36 weeks.

2. Principles and Purpose

It is important for society to determine when a human being has died in addition to when an organism has stopped developing as a functional whole. This is because ambiguity around death can be traumatic, especially with respect to medical uncertainties and what death means to people.

However, determining when a human being has died is scientifically challenging. In part, this may reflect the great variety of ways in which death occurs. But even when death follows a relatively common event, such as heart failure, the transition from a living human being to a collection of human cells and tissues in a corpse cannot be directly observed. The simplest criterion for death is when a living organism becomes a collection of non-living organic matter when all the living cells are also dead. But some living cells persist for hours or even days after an individual has died.[11] Thus, the physical criteria used to determine death cannot usually pinpoint the moment of death but identify, instead, a point at which it is possible to state with confidence that death has already occurred.[12]

In defining the death of an organism, it is important to determine when the activity observed in a biological system is self-regulated in the service of the 'whole' and when it merely reflects the intrinsic properties of cellular parts. In other words, the organism has died when it has completely lost its capacity for global and autonomous self-regulation and integration. But this is different from when a living organism is simply 'blocked' from exercising its self-integrating capabilities.[13]

3. History

The Danish/French anatomist Jacob Winsløw (1669 – 1760) wrote: 'Death is certain, since it is inevitable', adding 'but also uncertain, since its diagnosis is sometimes fallible'.[14] His contention that traditional signs of death are not conclusive, backed up by a catalogue of supposed cases of live burial given by French physician Jean-Jacques Bruhier d'Ablaincourt (1685-1756), sparked public questioning concerning the criteria for the diagnosis of death. Winsløw argued that resuscitation should be attempted, which could include the use of whips and shrieks. This is because, if an individual is not breathing, it does not mean that he or she is necessarily dead. In other words, that this apparent death is not necessarily permanent.[15]

Death, in the past, was usually defined as the cessation of (1) heartbeat (cardiac arrest) and of (2) breathing, which was then defined as clinical death. But developments in resuscitation and artificial respiration raise new challenges, rendering the previous definition inadequate since breathing and heartbeat may now be restarted in some cases. Events which were causally linked to death in the past are now prevented from having an effect; even without a functioning heart and lungs, a person can be sustained with life-support devices.

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[11] Condic ML. Determination of Death: A Scientific Perspective on Biological Integration. *J Med Philos*. 2016;41(3):257-278.

[12] Condic ML. Determination of Death: A Scientific Perspective on Biological Integration. *J Med Philos*. 2016;41(3):257-278.

[13] Condic ML. Determination of Death: A Scientific Perspective on Biological Integration. *J Med Philos*. 2016;41(3):257-278.

[14] Winslow, Jacob, *Morte Incertae Signa*, 1740

[15] In 2004, two brothers aged seven and nine who were clinically dead, with a cardiac arrest, for more than an hour and a half after falling through ice into a frozen lake in Austria were brought back to life. After nearly a month in a coma, both brothers were well on their way to full recovery. The freezing water cooled their body temperature down so much that they went into a state of almost suspended animation. The cold considerably reduces the need for oxygen, therefore slowing their metabolism. http://news.scotsman.com/archive.cfm?id=238102004

4. Present Situation

Not a lot of legislation generally exists, in the world, regarding the definition of death, which may betray different attitudes to death. Moreover, it is only until relatively recently that death was defined in different ways.

The current position in UK law is that there is no statutory definition of death. Subsequent to the proposal of the 'brain death criteria' by the Conference of Royal Colleges in 1976 and 1979,[16,17] the courts in England adopted these criteria, as part of the law, for the diagnosis of death.[18,19] And there is no reason to believe that courts in other parts of the UK would not follow this approach. Moreover, in Scotland, the independent judgement of one registered health care professionals[20] is required before someone can be declared dead in normal circumstances and only a medical doctor can issue a death certificate.[21]

In 1995, a paper entitled *Criteria for the diagnosis of brain stem death* was published by the Royal College of Physicians, giving a definition of death as the 'irreversible loss of the capacity for consciousness, combined with the irreversible loss of capacity to breathe'.[22] This provided the first definition of death for the UK. It was argued that when the brain is completely dead, the body has no centre and cannot be thought of as an integrated living organism. The organs may still be alive but the system, as an integrated whole, is defunct and only the continual support of artificial ventilation gives the temporary appearance of continued life. In reality the integrated body is dead.[23]

In considering the death of an early embryo, the cardio-respiratory arrest criteria are of no use, as no heart or lungs are present. And brain death criteria are not an option since the nervous system is not developed. Thus, it is possible to ask whether an early embryo is something that dies at all, and if so, how can its death be the same sort of concept as adult death, when none of the same changes seem to be taking place? The consequences of such questioning are obvious. If an embryo is not the sort of entity that dies, then it is not alive in the first place, and so many of the ethical objections to using human embryos for research have no foundation. However, if the death of an embryo can be considered, and if that same research causes embryos to die, then the same ethical objections to those that oppose any destruction of human life may apply.

5. Why Determining Embryonic Death is Important

In 2005, the US President's Council on Bioethics produced a white paper on various proposals for alternative sources of embryonic stem cells, which hold great promise in regenerative medicine. One of these was offered by the researchers Landry and Zucker entitled *'Embryonic Death and the Creation of Human*

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[16] Conference of Medical Royal Colleges and their Faculties in the United Kingdom. Diagnosis of brain death. *BMJ* 1976 ii:1187-1188.

[17] Conference of Medical Royal Colleges and their Faculties in the United Kingdom. Diagnosis of brain stem death. *Lancet* 1976 ii:1069-1070.

[18] Re A (A Minor) [1992] 3 Medical Law Reports 303.

[19] Re TC (A Minor) [1994] 2 Medical Law Reviews 376.

[20] The certification of death remains the sole domain of a registered medical practitioner (Certification of Death (Scotland) Act). However, there is no restriction in law as to who can confirm death. Suitably trained and competent Registered Healthcare Professionals are able to confirm death, recognising their accountability and autonomy, and there is no requirement for permission to be given for a specified period of time by a registered medical practitioner.
Police and Ambulance technicians in certain situations such as decapitation, decomposition and fire deaths, can confirm that death has occurred.
See: https://www.gov.scot/publications/confirmation-of-death-by-registered-healthcare-professionals-framework/

[21] Every death in Scotland must be certified by a doctor who completes a form called a Medical Certificate of Cause of Death which confirms that the death has occurred and records key information about the death (including the cause of death). Only one doctor needs to judge and certify death in normal circumstances. However, in the past, and before cremation could occur, two signatures were needed for the cremation form, but this was probably to indicated that no suspicious circumstances existed surrounding the death, before the evidence is destroyed. This requirement stopped with electronic certification of death a few years ago in the UK. In addition, special requirements exist in certain circumstances, such as for persons with brain damage and who are on ventilators.

[22] Criteria for the diagnosis of brain stem death. Review by a working group convened by the Royal College of Physicians and endorsed by the Conference of Medical Royal Colleges and their Faculties in the United Kingdom. *J R Coll Physicians Lond.* 1995; 29(5):381-2.

[23] David Albert Jones, The UK Definition of Death, 1999, The Linacre Centre, http://www.linacre.org/death.html

Embryonic Stem Cells'.[24] They argued that the irreversible arrest of cell division in the whole human embryo can be considered as the organismic death of the embryo. Cells (which are still alive) in this dead embryo could then be removed (in a similar way to organs being removed from the deceased for transplantation) and used for the creation of stem cell lines. This is because many irreversibly arrested embryos contain a substantial number of living cells 6 days after the embryos' development, as a whole, is arrested (72% have >1 viable cell, 47% have >5 viable cells).[25]

In 2006 Landry and Zucker published another paper detailing their natural history study of human embryos left over from IVF treatment. In this, they suggested that '*arrested development at the multicellular stage on embryonic day-5 indicates an irreversible loss of integrated function, and hence, the condition of death for the organism*.'[26] Thus, any whole embryo displaying no cellular division after five days at normal conditions could be considered dead. Living cells could then be taken from the embryo, without killing it (since it is suggested to be already dead from natural causes), thus providing possible embryonic stem cell lines while avoiding ethical controversy.

However, in the experiments performed by Landry and Zucker, the embryos (as a whole) naturally arrested at the 5-day and 6-day stage, meaning that the cells inside the embryo were no longer totipotent. But this does not mean that they do not (theoretically) have a capacity to develop into new individuals inside the outer membrane if the living pluripotent cells were separate from the dead ones. Indeed, the possibility of obtaining two or more individuals through division of the embryonic cells can happen until the 15-16 days stage. Moreover, embryos with grave morphological impairments and only a few surviving cells have sometimes gone on to normal development. Thus, it is unclear how it is possible to declare an early embryo to be dead.

To determine the natural history of embryo failure, Landry and Zucker proposed a 'death watch' study of embryos that have been set aside by IVF clinicians because they are believed to be unsuitable for transfer. Nevertheless, this research requires a willingness to (1) create supernumerary embryos and (2) stand by as multiple embryos are frozen, thawed, and allowed to die, meaning that the whole procedure could be seen as ethically contentious.[27]

But if the irreversible arrest of cell division in a whole human embryo older than 15-16 days of development (at which stage no cells are even able to form conjoined twins inside the out-membrane) is noticed, the embryo will then gradually deteriorate. If living cells can then be extracted and made to continue dividing, this process could be seen as an extraction similar to the use of organs in transplantation from a person who died naturally.

Another natural form of embryonic death takes place when two early embryos combine, naturally, to form a chimeric embryo. In this case, both embryos die in order to form a new embryo, or one dies by combining with the second, which continues to exist. Similarly, an early embryo may divide to become two or more embryos which will go on to develop into separate individual lives as 'identical' (or monozygotic) twins, triplets, etc. In this case, some commentators[28] suggest that the process of twinning may be considered as either (1) the continuation of the original individual in its development from which a number of cells separated giving rise to a new individual[29] or (2) the ending of existence of one embryonic individual (a form of death) to give rise to two new individuals. In this latter case, there would be a form of embryonic death without the existence of any material corpse.

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[24] Landry, Donald W. and Zucker, Howard A., 'Embryonic Death and the Creation of Human Embryonic Stem Cells', *Journal of Clinical Investigation* 114:1184-1186 (2004).

[25] S Gavrilov et al., Non-viable human embryos as a source of viable cells for embryonic stem cell derivation, *Reprod Biomed Online*. 2009; 18(2): 301-8.

[26] Landry DW, Zucker HA, Sauer MV, Reznik M, Wiebe L. 'Hypocellularity and absence of compaction as criteria for embryonic death', *Regen Med.* 2006; 1(3):367-71.

[27] *Ronald M. Green,* Can we develop ethically universal embryonic stem-cell lines?, NATURE REVIEWS – GENETICS, Vol. 8, June 2007, p.480-485

[28] David Albert Jones, The Soul of the Embryo, *Continuum*, 2004, p.226-227.

[29] An embryo's potential for spontaneous twinning seems to be established at an early stage by factors determining the thickness of the Zona Pellucida. *Kennedy Institute of Ethics Journal*, June 1999, John Hopkins University Press, Maryland, pg. 138.