

SCIENTIFIC REFERENCES FOR THE COLORADO PERSONHOOD CONSTITUTIONAL AMENDMENT

Dianne N. Irving, M.A., PhD
May 1, 2009

2010 PERSONHOOD COLORADO AMENDMENT

Purpose:

To establish that legal personhood is granted to all human beings from the beginning of their biological development.

Text:

SECTION 1. Article II of the constitution of the state of Colorado is amended
BY THE ADDITION OF A NEW SECTION to read:

Section 32. Person defined. AS USED IN SECTIONS 3, 6, AND 25 OF ARTICLE II OF THE
STATE CONSTITUTION, THE TERM "PERSON" SHALL APPLY TO EVERY HUMAN BEING FROM THE
BEGINNING OF THE BIOLOGICAL DEVELOPMENT OF THAT HUMAN BEING.

Scientific Definitions

Human Being: Any organism, including the single-cell human embryo, irrespective of the method of reproduction, who possesses a genome specific for and consistent with an individual member of the human species.

Personhood: The legal recognition of a human being's full status as a human person that applies to all human beings, irrespective of age, health, function, physical or mental dependency or method of reproduction, from the beginning of their biological development.

Human fetus: The term is used to define all human beings from the beginning of the fetal period of their biological development (the beginning of nine weeks) through birth; irrespective of age, health, function, physical or mental dependency or method of reproduction, whether in vivo or in vitro.

Human embryo: The term is used to define all human beings from the beginning of the embryonic period of their biological development through eight weeks; irrespective of age, health, function, physical or mental dependency or method of reproduction, whether in vivo or in vitro.

Human Genome: The total amount of nuclear and extra-nuclear DNA genetic material that constitutes an organism as an individual member of the human species—including the single-cell human embryo.

I. THE SINGLE-CELL HUMAN EMBRYO SEXUALLY REPRODUCED IS A HUMAN BEING FROM THE BEGINNING OF THE PROCESS OF FERTILIZATION..... pg. 2-6

II. THE SINGLE-CELL HUMAN EMBRYO ASEXUALLY REPRODUCED IS A HUMAN BEING WHEN THE CELL'S DNA IS IN THE STATE OF DIFFERENTIATION AS THAT OF A SINGLE-CELL SEXUALLY REPRODUCED HUMAN EMBRYO..... pg. 6-11

III. THE SINGLE-CELL HUMAN EMBRYO POSSESSES A GENOME SPECIFIC FOR AND CONSISTENT WITH AN INDIVIDUAL MEMBER OF THE HUMAN SPECIES..... pg. 11-18

I. THE SINGLE-CELL HUMAN EMBRYO SEXUALLY REPRODUCED IS A HUMAN BEING FROM THE BEGINNING OF THE PROCESS OF FERTILIZATION.

The following were taken from embryology textbooks, full citation listed along with pertinent material.

Carlson, Bruce M. *Human Embryology and Developmental Biology* (St. Louis, MO: Mosby, 1994)

After the eighth week of pregnancy the period of organogenesis (**embryonic period**) is largely completed and **the fetal period begins** (p. 407).

Carlson, Bruce M. *Human Embryology and Developmental Biology*, 2nd ed. (St. Louis, MO: Mosby, 1999)

“Human pregnancy begins with the fusion of an egg and a sperm, but a great deal of preparation precedes this event. First both male and female sex cells must pass through a long series of changes(gametogenesis) that convert them genetically and phenotypically into mature gametes, which are capable of participating in the process of fertilization. Next, the gametes must be released from the gonads and make their way to the **upper part of the uterine tube, where fertilization normally takes place**. ...Finally, the **fertilized egg**, now properly called an **embryo**, must make its way into the uterus ...” (p. 2).

...Fertilization age: dates **the age of the embryo from the time of fertilization** (p. 23).

...In the female, sperm transport begins in the upper vagina and ends in the **ampulla of the uterine tube [fallopian tube] where the spermatozoa make contact with the ovulated egg** (p. 27).

The **sex of the future embryo is determined by the chromosomal complement of the spermatozoon**. (If the sperm contains 22 autosomes and an X chromosome, the embryo will be a genetic female, and if it contains 22 autosomes and a Y chromosome, the embryo will be a male.) ... Through the mingling of maternal and paternal chromosomes, **the zygote is a genetically unique product of chromosomal reassortment**, which is important for the viability of any species (p. 32).

Larsen, William. *Human Embryology*, 2nd ed. (New York: Churchill Livingstone, 1997)

... [W]e begin our description of the developing human with the formation and differentiation of the male and female sex cells or gametes, which will unite at fertilization to initiate the **embryonic** development of **a new individual** (p. 1).

... **Fertilization takes place in the oviduct** [not the uterus]... resulting in the formation of a **zygote** containing a single diploid nucleus (p. 1).

Larsen, William. *Essentials of Human Embryology* (New York: Churchill Livingstone, 1998)

Moore, Keith, and T.V.N. Persaud, *The Developing Human: Clinically Oriented Embryology*, 6th ed. Only. (Philadelphia: W.B. Saunders Company, 1998)

The usual site of fertilization is the ampulla of the uterine tube [fallopian tube], its longest and widest part. If the oocyte is not fertilized here, it slowly passes along the tube to the uterus, where it degenerates and is reabsorbed. Although fertilization may occur in other parts of the tube, **it does not occur in the uterus**. ... **Human development begins when an oocyte is fertilized** (p. 34).

The embryo's chromosomes sex is determined at fertilization by the kind of sperm (X or Y) that fertilizes the ovum; hence it is the father rather than the mother whose gamete determines the sex of the embryo (p. 37).

Moore, Keith, and T.V.N. Persaud, *The Developing Human: Clinically Oriented Embryology*, 7th ed. (Philadelphia: W.B. Saunders Company, 2003)

Muller, Fabiola, and Ronan O'Rahilly. *Human Embryology & Teratology*, 3rd ed. (New York: Wiley-Liss, 1994)

The **embryonic period** proper ...**occupies the first 8 postovulatory weeks** (i.e., timed from the last ovulation) ... The **fetal period extends from 8 weeks to birth** (p. 55).

Muller, Fabiola, and Ronan O'Rahilly. *ibid.* (New York: Wiley-Liss, 2001)

Recapitulation, the So-Called Biogenetic Law. The theory that successive stages of individual development (ontogeny) correspond with ("recapitulate") successive adult ancestors in the line of *evolutionary descent* (phylogeny) became popular in the nineteenth century as the so-called biogenetic law. **This theory of recapitulation, however, has had a "regrettable influence on the progress of embryology"** (G. de

Beer). ... According to the “laws” of von Baer, general characters (e.g., brain, notochord) appear in development earlier than special characters (e.g., limbs, hair). Furthermore, during its development an animal departs more and more from the form of other animals. Indeed, the early stages in the development of an animal are not like the adult stages of other forms but resemble only the early stages of those animals. The pharyngeal clefts of vertebrate embryos, for example, **are neither gills nor slits**. Although a fish elaborates this region into gill slits, in reptiles, birds, and mammals it is converted into such structures as the tonsils and the thymus (p. 16).

... (Fertilization is) the procession of events that begins when a spermatozoon **makes contact** with a secondary oocyte or its investments, and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote. The zygote is characteristic of the **last phase** of fertilization and is identified by the first cleavage spindle. It is a unicellular embryo (p. 19).

Although life is a continuous process, **fertilization** ... is a critical landmark because, under ordinary circumstances, **a new, genetically distinct human organism** is formed... (p. 31).

... **Fertilization takes place normally in the ampulla (lateral end) of the uterine tube** (p. 31).

“The term ‘**pre-embryo**’ is not used here for the following reasons: (1) **it is ill-defined** because it is said to end with the appearance of the primitive streak or to include neurulation; (2) **it is inaccurate** because purely embryonic cells can already be distinguished after a few days, as can also the embryonic (not pre-embryonic!) disc; (3) **it is unjustified** because the accepted meaning of the word embryo includes all of the first 8 weeks; (4) **it is equivocal** because it may convey the erroneous idea that a new human organism is formed at only some considerable time after fertilization; and (5) it was introduced in 1986 ‘largely **for public policy reasons**’ (Biggers).” ... Just as postnatal age begins at birth, **prenatal age begins at fertilization,**” (p. 88).

“Undesirable terms in Human Embryology”: “**Pre-embryo**”; **ill defined and inaccurate;** Use “**embryo**” (p. 12).

[Note: O’Rahilly is one of the originators of *The Carnegie Stages of Early Human Embryological Development*, and has sat on the international *Nomina Embryologica Committee* for decades]

The following were taken from web sites, full citation listed along with pertinent material.

“Carnegie Stages of Early Human Embryonic Development,” http://nmhm.washingtondc.museum/collections/hdac/Select_Stage_and_Lab_Manual.htm

Carnegie Stages of Early Human Embryonic Development, Stage 1: Embryonic life commences with fertilization, and hence **the beginning of that process may be taken as the point de depart of stage 1**. Despite the small size (ca. 0.1 mm) and weight (ca. 0.004 mg) of the organism at fertilization, the embryo is “*schon ein individual-spezifischer Mensch*” (Blechs Schmidt, 1972).

... Fertilization is the procession of events that begins when a spermatozoon **makes contact** with an oocyte or its investments and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote (Brackett *et al.*, 1972).

... Fertilization, which takes place normally in the ampulla of the uterine tube, includes **(a) contact of spermatozoa with the zona pellucida of an oocyte, penetration of one or more spermatozoa through the zona pellucida and the ooplasm, swelling of the spermatozoal head and extrusion of the second polar body**, (b) the formation of the **male and female pronuclei**, and (c) the beginning of the first mitotic division, or cleavage, of the **zygote**.

... **The three phases (a, b, and c) referred to above will be included here under stage 1, the characteristic feature of which is unicellularity.**

Irving, Dianne, M. “The Carnegie Stages of Early Human Embryonic Development: Chart of all 23 Stages, and Detailed Descriptions of Carnegie Stages 1 – 6,” April 22, 2006. http://www.lifeissues.net/writers/irv/irv_123carnegiestages2.html

Irving, Dianne, M. “Playing God by manipulating man: Facts and frauds of human cloning,” October 4, 2003. http://www.lifeissues.net/writers/irv/irv_22manipulatingman1.html.

“This new single-cell human being **immediately produces specifically human proteins and enzymes** (1) (not carrot or frog enzymes and proteins), and genetically directs his/her own growth and development. (In fact, this genetic growth and development has been proven *not* to be directed by the mother, but rather by the *embryo*.) (2) The human embryo begins to divide and *grows bigger and bigger*, developing through several stages as an embryo over an 8-week period. Several of these developmental stages of the growing embryo are given special names, e.g., a morula (about 4 days), a free blastocyst (about 4-5 days), an implanting blastocyst (about 5-7 days), a bilaminar (two layer) embryo (during the second week), and a trilaminar (3 layer) embryo (during the third week). But it is the very *same* human embryo who is progressing throughout all of these various stages of growth and development.”

References:

Kollias, et al. “The human beta-gobulin gene contains downstream developmental specific enhancer *Nucleic Acids Research* 15 (14) (July 1987), pp. 5739-47.

Also similar work by R. K. Humphries, A. Schnieke.

E.g., as determined in extensive numbers of transgenic mice experiments, “The human beta-gobulin gene contains downstream developmental specific enhancer.”

Moore, Keith, and T.V.N. Persuad, “*The Developing Human: Clinically Oriented Embryology*, 6th ed. (Philadelphia: W.B. Saunders Company, 1998)

“Sutton and Boveri declared independently in 1902 that the behavior of chromosomes during germ cell formation and fertilization agreed with Mendel’s principles of inheritance. In the same year, Garrod reported alcaptonuria as the first example of Mendelian inheritance in human beings.

Many consider Garrod to be the Father of Medical Genetics. It was soon realized that **the (single-cell embryo) contains all the genetic information necessary for directing the development of a new human being** (p. 12).

Holtzer *et al.*, “Induction-dependent and lineage-dependent models for cell-diversification are mutually exclusive,” *Progress in Clinical Biological Research* 175:3-11 (1985).

Also similar work by, e.g., F. Mavilio, C. Hart.

(3) Larsen, pp. 19, 33, 49.

II. THE SINGLE-CELL HUMAN EMBRYO ASEXUALLY REPRODUCED IS A HUMAN BEING WHEN THE CELL’S DNA IS IN THE STATE OF DIFFERENTIATION AS THAT OF A SINGLE-CELL SEXUALLY REPRODUCED HUMAN EMBRYO:

The following were taken from embryology books, full citation listed along with pertinent material.

Campbell, Keith, and Ian Wilmut. *Cambridge Quarterly of Healthcare Ethics* 139 (Spring 1988).

“One potential use for this technique would be to take cells – skin cells, for example – from a human patient who had a genetic disease... **You take these and get them back to the beginning of their life by nuclear transfer into an oocyte to produce a new embryo. From that new embryo, you would be able to obtain relatively simple, undifferentiated cells**, which would retain the ability to colonize the tissues of the patient.”

On being asked in an interview: “Do you think that society should allow cloning of human embryos because of the great promise of medical benefit?”: “Yes. Cloning **at the embryo stage** – to achieve cell dedifferentiation – could provide benefits that are wide ranging...” – Keith Campbell, head of embryology at PPL Therapeutics

Carlson, Bruce M. *Human Embryology and Developmental Biology*, 2nd ed. (St. Louis, MO: Mosby, 1999)

“Early mammalian embryogenesis is considered to be a highly regulative process. **Regulation** is the ability of an embryo or an organ primordium to produce a normal structure if parts have been removed or added. At the cellular level, it means that the fates of cells in a regulative system are not irretrievably fixed and that the cells can still respond to environmental cues.” (p. 44).

“Of the experimental techniques used **to demonstrate regulative properties of early embryos, the simplest is to separate the blastomeres of early cleavage-stage embryos and determine whether each one can give rise to an entire embryo.** This method has been used to demonstrate that **single blastomeres, from two- and sometimes four-cell embryos can form normal embryos, ...**” (p. 44).

“...The relationship between the position of the blastomeres and their ultimate developmental fate was incorporated into **the inside-outside hypothesis.** The outer blastomeres ultimately differentiate into the trophoblast, whereas the inner blastomeres form the inner cell mass, from which the body of the embryo arises. Although this hypothesis has been supported by a variety of experiments, the mechanisms by which the **blastomeres recognize their positions and then differentiate accordingly** have remained elusive and are still little understood. **If marked blastomeres from disaggregated embryos are placed on the outside of another early embryo, they typically contribute to the formation of the trophoblast. Conversely, if the same marked cells are introduced into the interior of the host embryo, they participate in formation of the inner cell mass.** Outer cells in the early mammalian embryo are linked by tight and gap junctions ... Experiments of this type demonstrate **that the developmental potential or potency (the types of cells that a precursor cell can form) of many cells is greater than their normal developmental fate (the types of cells that a precursor cell normally forms)**” (p. 45).

“Another means of demonstrating **the regulative properties of early mammalian embryos** is to dissociate mouse embryos into **separate blastomeres** and then to **combine the blastomeres** of two or three embryos. The combined blastomeres soon aggregate and **reorganize to become a single large embryo**, which then goes on to become a normal-appearing tetraparental or hexaparental mouse. By various techniques of making chimeric embryos, it is even **possible to combine blastomeres to produce interspecies chimeras** (e.g., a sheep-goat)” (p. 45).

“... Blastomere removal and addition experiments have convincingly demonstrated **the regulative nature (i.e., the strong tendency for the system to be restored to wholeness)** of early mammalian embryos. Such knowledge is important in understanding the reason exposure of early human embryos to unfavorable environmental influences typically results in either death or a normal embryo.” (p. 46).

“... Classic strategies for investigating developmental properties of embryos are (1) removing a part and determining **the way the remainder of the embryo compensates for the loss** (such experiments are called deletion experiments) and (2) adding a part and determining **the way the embryo integrates the added material into its overall body plan** (such experiments are called addition experiments). Although some deletion experiments have been done, the strategy of addition experiments has proved to be most fruitful in elucidating mechanisms controlling mammalian embryogenesis.” (p. 46).

“...**Some types of twinning represent a natural experiment that demonstrates the highly regulative nature of early human embryos,**” (p. 48).

“...**Monozygotic twins and some triplets**, on the other hand, are the product of one fertilized egg. They **arise by the subdivision and splitting of a single embryo**. Although monozygotic twins could ... arise by the splitting of a two-cell embryo, it is commonly accepted that most arise by the subdivision of the inner cell mass in a blastocyst. **Because the majority of monozygotic twins are perfectly normal, the early human embryo can obviously be subdivided and each component regulated to form a normal embryo.**” (p. 49)

Elder, Kay T. “Laboratory techniques: Oocyte collection and embryo culture,” ed. Peter Brinsden, *A Textbook of In Vitro Fertilization and Assisted Reproduction*, 2nd ed. (New York: The Parthenon Publishing Group, 1999)

“**Surprisingly, fragmented embryos, repaired or not, do implant and often come to term. This demonstrates the highly robust nature of the human embryo, as it can apparently lose over half of its cellular mass and still recover.**” (p. 197)

Irving, Dianne N.

Even proponents of human cloning research admit that the immediate product of cloning is a new living human embryo, a human being. See, for example: Ian Wilmut: “The majority of reconstructed embryos were cultured in ligated oviducts of sheep... **Most embryos that developed to morula or blastocyst after 6 days of culture were transferred to recipients and allowed to develop to term,**” etc.

Larsen, William. *Essentials of Human Embryology* (New York: Churchill Livingstone, 1998)

“**If the splitting occurred during cleavage** – for example, if the two blastomeres produced by the first cleavage division become separated – the monozygotic twin blastomeres will implant separately, *like dizygotic twin blastomeres*, and will not share fetal membranes. Alternatively, if the twins are formed by splitting of the inner cell mass within the blastocyst, they will occupy the same chorion but will be enclosed by separate amnions and will use separate placentae, each placenta developing around the connecting

stalk of its respective embryo. Finally, **if the twins are formed by splitting of a bilaminar germ disc**, they will occupy the same amnion.” (p. 325)

Muller, Fabiola, and Ronan O’Rahilly. *Human Embryology & Teratology*. (New York: Wiley-Liss, 2001)

“**Biopsy of an embryo** can be performed by removing one cell from a 4-cell, or two cells from an 8-cell, embryo. **This does not seem to decrease the developmental capacity of the remaining cells.**” (p. 37).

“The **embryo** enters the uterine cavity after about half a week ... **Each cell (blastomere) is considered to be still totipotent (capable, on isolation, of forming a complete embryo), and separation of these early cells is believed to account for one-third of cases of monozygotic twinning,**” (p. 37).

National Bioethics Advisory Commission. *Cloning Human Beings: Report and Recommendations*. (Rockville, MD: June 1997)

“The Commission began its discussions fully recognizing that any effort in humans to transfer a somatic cell nucleus into an enucleated egg **involves the creation of an embryo, with the apparent potential to be implanted** in utero and developed to term” (p. 3).

National Institutes of Health. *Background Paper: Cloning: Present uses and Promises*, Jan. 29, 1998.

“This experiment [producing Dolly] demonstrated that, when appropriately manipulated and placed in the correct environment, **the genetic material of somatic cells can regain its full potential** to direct embryonic, fetal, and subsequent development” (p. 3).

Read, Andrew P., and Tom Strachan. *Human Molecular Genetics 2*, 2nd ed. (New York: John Wiley & Sons, Inc., 1999)

Nuclear transfer technology was first employed in embryo cloning, in which the donor cell is derived from an early embryo, and has been long established in the case of amphibians. ... Wilmut *et al* (1997) reported successful cloning of an adult sheep [“Dolly”].

For the first time, **an adult nucleus had been reprogrammed to become totipotent once more, just like the genetic material in the fertilized oocyte** from which the donor cell had ultimately developed. ... Successful cloning of adult animals has forced us to accept that **genome modifications once considered irreversible can be reversed and that the genomes of adult cells can be reprogrammed by factors in the oocyte to make them totipotent once again.**

... Animal clones occur naturally.... For example, **genetically identical twins are clones who happened to have received exactly the same set of genetic instructions from two donor individuals**, a mother and a father. A **form of animal cloning can also occur as a result of artificial manipulation** to bring about a type of asexual reproduction. The genetic manipulation in this case **uses nuclear transfer technology: a nucleus is removed from a donor cell then transplanted into an oocyte whose own nucleus has previously been removed.**

The resulting ‘renucleated’ oocyte can give rise to an individual who will carry the nuclear genome of only one donor individual, unlike genetically identical twins. The individual providing the donor nucleus and the individual that develops from the ‘renucleated’ oocyte are usually described as “clones”, but it should be noted that they share only the same nuclear DNA; they do not share the same mitochondrial DNA, unlike genetically identical twins.

Silver, Lee M. *Remaking Eden: Cloning and Beyond in a Brave New World* (Avon Books 1997)

“Yet there is nothing synthetic about the cells used in cloning... **The newly created embryo** can only develop inside the womb of a woman **in the same way that all embryos and fetuses develop**. Cloned children will be full-fledged human beings, indistinguishable in biological terms from all other members of the species. Thus, the notion of a soulless clone has no basis in reality,” (p. 107).

Van Blerkom, Jonathan. *American Medical News*, Feb. 23, 1998.

[Expressing disbelief that some deny that human cloning produces an embryo]: **“If it’s not an embryo, what is it?”**

Dr. Van Blerkom said **researchers’ efforts to avoid the word “embryo” in this context are “self-serving.”**

Wilmut, Ian, et al. “Viable offspring derived from fetal and adult mammalian cells,” 385 *Nature* 810-813 (Feb. 27, 1997)

The following were taken from web sites, full citation listed along with pertinent material.

National Institutes of Health, Office of Science Planning and Policy, “CLONING: Present Uses and Promises”, April 27, 1998. <http://www1.od.nih.gov/osp/ospp/scipol/cloning.htm>.

“Cloning and somatic cell nuclear transfer are not synonymous. Cloning is the production of a precise genetic copy of DNA, a cell, or an individual plant or animal. Cloning can be successfully accomplished by using a number of different technologies. Somatic cell nuclear transfer is one specific technology that can be used for cloning.”

“The Cloning of Humans (Prevention) Bill 2001,” http://www.parliament.qld.gov.au/Parlib/Publications_pdfs/books/2001036.pdf.

“Cloning can occur naturally in the asexual reproduction of plants, the formation of **identical twins** and the multiplication of cells in the natural process of repair. The cloning of DNA, cells, tissues, organs and whole **individuals is also achievable with artificial technologies**. ... **The cloning of a cell or an individual may be achieved through a number of techniques**, including: molecular cloning ..., **blastomere separation (sometimes called “twinning”** after the naturally occurring process that **creates identical twins): splitting a developing embryo soon after fertilization of the egg by a sperm (sexual reproduction) to give rise to two or more embryos. The resulting organisms are identical twins (clones)** containing DNA from both the mother and the father. ... **somatic cell nuclear transfer: the transfer of the nucleus of a somatic cell into an unfertilized egg whose nucleus, and thus its genetic material, has been removed.**

A number of scientific review bodies have noted that the term “cloning” is applicable in various contexts, as a result of the development of a range of cloning techniques with varying applications.”

III. THE SINGLE-CELL HUMAN EMBRYO POSSESSES A GENOME SPECIFIC FOR AND CONSISTENT WITH AN INDIVIDUAL MEMBER OF THE HUMAN SPECIES.

The human genome is not defined in terms of the nuclear genes alone, but in terms of **the total DNA in the cell**, including DNA found outside of the nucleus in the cytoplasm:

The following were taken from embryology books, full citation listed along with pertinent material.

Lewin, Benjamin. *Genes VII* (New York: Oxford University Press, 2000)

“A genome consists of the entire set of chromosomes for any particular organism, and therefore comprises a series of DNA molecules, each of which contains a series of many genes. The ultimate definition of a genome is to determine the sequence of the DNA of each chromosome. (p. 4)

...Genes not residing within the nucleus are generally described as extranuclear; they are transcribed and translated in the same organelle compartment (mitochondrion or chloroplast) in which they reside. By contrast, nuclear genes are expressed by means of cytoplasmic protein synthesis.” (p. 81)

Read, Andrew P., and Tom Strachan. *Human Molecular Genetics 2*, 2nd ed. (New York: John Wiley & Sons, Inc., 1999)

In animal cells, **DNA is found in both the nucleus and the mitochondria.** (p. 10)

The mitochondria also have ribosomes and a limited capacity for protein synthesis.” (p. 18)

“The **human genome** is the term used to describe the **total genetic information (DNA content) in human cells. It really comprises two genomes:** a complex **nuclear** genome..., and a simple **mitochondrial** genome...Mitochondria possess their own ribosomes and the few polypeptide-encoding genes in the mitochondrial genome produce mRNAs, which are translated on the mitochondrial ribosomes. (p. 139)

The following were taken from embryology books, full citation listed along with pertinent material.

Carlson, Bruce M. *Human Embryology and Developmental Biology* (St. Louis, MO: Mosby, 1994)

After the eighth week of pregnancy the period of organogenesis (**embryonic period**) is largely completed and **the fetal period begins.** (p. 407)

Carlson, Bruce M. *Human Embryology and Developmental Biology*, 2nd ed. (St. Louis, MO: Mosby, 1999)

“**Human pregnancy begins with the fusion of an egg and a sperm,** but a great deal of preparation precedes this event. First both male and female sex cells must pass through a long series of changes (gametogenesis) that convert them genetically and phenotypically into mature gametes, which are capable of participating in the process of fertilization. Next, the gametes must be released from the gonads and make their way to the **upper part of the uterine tube, where fertilization normally takes place.** ... Finally, the **fertilized egg**, now properly called an **embryo**, must make its way into the uterus” (p. 2)

... Fertilization age: dates **the age of the embryo from the time of fertilization.** (p. 23)

... In the female, sperm transport begins in the upper vagina and ends in the **ampulla of the uterine tube [fallopian tube] where the spermatozoa make contact with the ovulated egg.** (p. 27)

The **sex of the future embryo is determined by the chromosomal complement of the spermatozoon.** (If the sperm contains 22 autosomes and an X chromosome, the embryo will be a genetic female, and if it contains 22 autosomes and a Y chromosome, the embryo will be a male.) ... Through the mingling of maternal and paternal chromosomes, **the zygote is a genetically unique product of chromosomal re-assortment,** which is important for the viability of any species. (p. 32)

“Early mammalian embryogenesis is considered to be a highly regulative process. **Regulation** is the ability of an embryo or an organ primordium to produce a normal structure if parts have been removed or added. At the cellular level, it means that the fates of cells in a regulative system are not irretrievably fixed and that the cells can still respond to environmental cues.” (p. 44).

“... Blastomere removal and addition experiments have convincingly demonstrated **the regulative nature (i.e., the strong tendency for the system to be restored to wholeness)** of early mammalian embryos. Such knowledge is important in understanding the reason exposure of early human embryos to unfavorable environmental influences typically results in either death or a normal embryo.” (p. 46)

“...**Some types of twinning represent a natural experiment that demonstrates the highly regulative nature of early human embryos ...**” (p. 48)

“...The relationship between the position of the blastomeres and their ultimate developmental fate was incorporated into **the inside-outside hypothesis**. The outer blastomeres ultimately differentiate into the trophoblast, whereas the inner blastomeres form the inner cell mass, from which the body of the embryo arises. Although this hypothesis has been supported by a variety of experiments, the mechanisms by which the **blastomeres recognize their positions and then differentiate accordingly** have remained elusive and are still little understood.

If marked blastomeres from disaggregated embryos are placed on the outside of another early embryo, they typically contribute to the formation of the trophoblast. Conversely, if the same marked cells are introduced into the interior of the host embryo, they participate in formation of the inner cell mass. Outer cells in the early mammalian embryo are linked by tight and gap junctions...

Experiments of this type demonstrate **that the developmental potential or potency (the types of cells that a precursor cell can form) of many cells is greater than their normal developmental fate (the types of cells that a precursor cell normally forms).**” (p. 45).

Elder, Kay T. “Laboratory techniques: Oocyte collection and embryo culture” ed. Peter Brinsden, *A Textbook of In Vitro Fertilization and Assisted Reproduction*, 2nd edition (New York: The Parthenon Publishing Group, 1999)

“Surprisingly, fragmented embryos, repaired or not, do implant and often come to term. This demonstrates the highly robust nature of the human embryo, as it can apparently lose over half of its cellular mass and still recover.” (p. 197)

Larsen, William. *Human Embryology*, 2nd ed. (New York: Churchill Livingstone, 1997)

... [W]e begin our description of the developing human with the formation and differentiation of the male and female sex cells or gametes, which will unite at fertilization to initiate the **embryonic** development of **a new individual**. (p. 1)

In this text, we begin our description of the developing human with the formation and differentiation of the male and female sex cells or gametes, which will unite at **fertilization** to initiate the embryonic development of **a new individual**. ... **Fertilization takes place in the oviduct** [not the uterus]... resulting in the formation of a **zygote** containing a single diploid nucleus. (p. 1).

Moore, Keith, and T.V.N. Persaud, *The Developing Human: Clinically Oriented Embryology*, 6th ed. Only. (Philadelphia: W.B. Saunders Company, 1998)

The usual site of fertilization is the ampulla of the uterine tube [fallopian tube], its longest and widest part. If the oocyte is not fertilized here, it slowly passes along the tube to the uterus, where it degenerates and is reabsorbed. Although fertilization may occur in other parts of the tube, **it does not occur in the uterus**. ... **Human development begins when a oocyte is fertilized**. (p. 34)

... **The embryo's chromosomes sex is determined at fertilization** by the kind of sperm (X or Y) that fertilizes the ovum; hence, it is the father rather than the mother whose gamete determines the sex of the embryo. (p. 37)

Muller, Fabiola, and Ronan O'Rahilly. *Human Embryology & Teratology*, 3rd ed. (New York: Wiley-Liss, 1994)

The **embryonic period** proper ...**occupies the first eight postovulatory weeks** (i.e., timed from the last ovulation) ... The **fetal period extends from eight weeks to birth**. (p. 55)

Muller, Fabiola, and Ronan O'Rahilly. *ibid.* (New York: Wiley-Liss, 2001)

“The term ‘**pre-embryo**’ is not used here for the following reasons: (1) **it is ill-defined** because it is said to end with the appearance of the primitive streak or to include neurulation; (2) **it is inaccurate** because purely embryonic cells can already be distinguished after a few days, as can also the embryonic (not pre-embryonic!) disc; (3) **it is unjustified** because the accepted meaning of the word embryo includes all of the first 8 weeks; (4) **it is equivocal** because it may convey the erroneous idea that a new human organism is formed at only some considerable time after fertilization; and (5) it was introduced in 1986 ‘largely **for public policy reasons**’ (Biggers).” ... Just as postnatal age begins at birth, **prenatal age begins at fertilization**.” (p. 88)

“Undesirable terms in Human Embryology”: “**Pre-embryo**”; **ill defined and inaccurate; use “embryo”** (p. 12).

Recapitulation, the So-Called Biogenetic Law. The theory that successive stages of individual development (ontogeny) correspond with (“recapitulate”) successive adult ancestors in the line of *evolutionary descent* (phylogeny) became popular in the nineteenth century as the so-called biogenetic law. **This theory of recapitulation, however, has had a “regrettable influence on the progress of embryology”** (G. de Beer). ... According to the “laws” of von Baer, general characters (e.g., brain, notochord) appear in development earlier than special characters (e.g., limbs, hair). Furthermore, during its development an animal departs more and more from the form of other animals. Indeed, the early stages in the development of an animal are not like the adult stages of other forms but resemble only the early stages of those animals. The pharyngeal clefts of vertebrate embryos, for example, **are neither gills nor slits**. Although a fish elaborates this region into gill slits, in reptiles, birds, and mammals it is converted into such structures as the tonsils and the thymus. (p. 16)

... (Fertilization is) the procession of events that begins when a spermatozoon **makes contact** with a secondary oocyte or its investments, and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote. The zygote is characteristic of the **last phase** of fertilization and is identified by the first cleavage spindle. It is a unicellular embryo. (p. 19)

Although life is a continuous process, **fertilization** ... is a critical landmark because, under ordinary circumstances, **a new, genetically distinct human organism** is formed.... (p. 31)

... **Fertilization takes place normally in the ampulla (lateral end) of the uterine tube.** (p. 31)

“**Biopsy of an embryo** can be performed by removing one cell from a 4-cell, or two cells from an 8-cell, embryo. **This does not seem to decrease the developmental capacity of the remaining cells.**” (p. 37).

The following were taken from web sites, full citation listed along with pertinent material.

“Carnegie Stages of Early Human Embryonic Development,” http://nmhm.washingtondc.museum/collections/hdac/Select_Stage_and_Lab_Manual.htm

The first 8 weeks of human development are called the embryological period. After eight 8 the embryo becomes a fetus, and after birth a neo-nate. There are various ways to determine the age and development of an embryo. It should be noted that age and stage are not the same thing. An age is a measurement of time where as stage of development is an assessment of the level physical development of the embryo. Like older babies and children, embryos will develop at varying rates, which may depend on a variety of factors in the embryos environment.

Stage One: Embryonic life commences with fertilization, and hence **the beginning of that process may be taken as *the point de depart* of stage 1**. Despite the small size (ca. 0.1 mm) and weight (ca. 0.004 mg) of the organism at fertilization, the embryo is “*schon ein individual-spezifischer Mensch*” (Blechs Schmidt, 1972)

... Fertilization is the procession of events that begins when a spermatozoon **makes contact** with an oocyte or its investments and ends with the intermingling of maternal and paternal chromosomes at metaphase of the first mitotic division of the zygote (Brackett *et al.*, 1972).

... Fertilization, which takes place normally in the ampulla of the uterine tube, includes **(a) contact of spermatozoa with the zona pellucida of an oocyte, penetration of one or more spermatozoa through the zona pellucida and the ooplasm, swelling of the spermatozoal head and extrusion of the second polar body, (b) the formation of the male and female pronuclei, and (c) the beginning of the first mitotic division, or cleavage, of the zygote.... The three phases (a, b, and c) referred to above will be included here under stage 1, the characteristic feature of which is unicellularity.**

Irving, Dianne N., “Playing God by manipulating man: Facts and frauds of human cloning” October 4, 2003. http://www.lifeissues.net/writers/irv/irv_22manipulatingman1.html

“This new single-cell human being **immediately produces specifically *human* proteins and enzymes**

(1) (not carrot or frog enzymes and proteins), and genetically directs his/her own growth and development. (In fact, this genetic growth and development has been proven *not* to be directed by the mother, but rather by the *embryo*.)

(2) The human embryo begins to divide and *grows bigger and bigger*, developing through several stages as an embryo over an 8-week period. Several of these developmental stages of the growing embryo are given special names, e.g., a morula (about 4 days), a free blastocyst (about 4-5 days), an implanting blastocyst (about 5-7 days), a bilaminar (two layer) embryo (during the second week), and a trilaminar (3 layer) embryo (during the third week). But it is the very *same* human embryo who is progressing throughout all of these various stages of growth and development.”

References:

Holtzer *et al.*, “Induction-dependent and lineage-dependent models for cell-diversification are mutually exclusive,” *Progress in Clinical Biological Research* 175:3-11 (1985);

Kollias *et al.*, “The human beta-gobulin gene contains downstream developmental specific enhancer,” *Nucleic Acids Research* 15(14) (July 1987), pp. 5739-47.

Larsen, William. *Human Embryology*, 2nd ed. (New York: Churchill Livingstone, 1997)

pp. 19, 33, 49.

Moore, Keith, and T.V.N. Persaud, *The Developing Human: Clinically Oriented Embryology*, 6th ed. Only. (Philadelphia: W.B. Saunders Company, 1998)

“Sutton and Boveri declared independently in 1902 that the behavior of chromosomes during germ cell formation and fertilization agreed with Mendel’s principles of inheritance. In the same year, Garrod reported alcaptonuria as the first example of Mendelian inheritance in human beings.

Many consider Garrod to be the Father of Medical Genetics. It was soon realized that **the (single-cell embryo) contains all the genetic information necessary for directing the development of a new human being** (p. 12).

Read, Andrew P., and Tom Strachan. *Human Molecular Genetics 2*, 2nd ed. (New York: John Wiley & Sons, Inc., 1999)

Nuclear transfer technology was first employed in embryo cloning, in which the donor cell is derived from an early embryo, and has been long established in the case of amphibians. ... Wilmut *et al* (1997) reported successful cloning of an adult sheep [“Dolly”]. For the first time, **an adult nucleus had been reprogrammed to become totipotent once more, just like the genetic material in the fertilized oocyte** from which the donor cell had ultimately developed. ... Successful cloning of adult animals has forced us to accept that **genome modifications once considered irreversible can be reversed and that the genomes of adult cells can be reprogrammed by factors in the oocyte to make them totipotent once again.** ... Animal clones occur naturally.... For example, **genetically identical twins are clones who happened to have received exactly the same set of genetic instructions from two donor individuals**, a mother and a father. **A form of animal cloning can also occur as a result of artificial manipulation** to bring about a type of asexual reproduction. The genetic manipulation in this case **uses nuclear transfer technology: a nucleus is removed from a donor cell then transplanted into an oocyte whose own nucleus has previously been removed. The resulting ‘renucleated’ oocyte can give rise to an individual who will carry the nuclear genome of only one donor individual, unlike genetically identical twins. The individual providing the donor nucleus and the individual that develops from the ‘renucleated’ oocyte are usually described as “clones”, but it should be noted that they share only the same nuclear DNA; they do not share the same mitochondrial DNA, unlike genetically identical twins** (pp. 508-509).

Also similar work by, e.g., F. Mavilio, C. Hart.

Also similar work by, e.g., R. K. Humphries, A. Schnieke.

The following were taken from embryology books, full citation listed along with pertinent material.

Carlson, Bruce M. *Human Embryology and Developmental Biology* (St. Louis, MO: Mosby, 1994)

After the eighth week of pregnancy the period of organogenesis (**embryonic period**) is largely completed and **the fetal period begins**. (p. 407)

Muller, Fabiola, and Ronan O’Rahilly. *Human Embryology & Teratology*, 3rd ed. (New York: Wiley-Liss, 1994)

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