{Part II of IV contains the entirety of Section II on our Earliest Days and on Embryonic Engineering}

Part II: Earliest Days and Embryonic Engineering

Section II: Homo sum

"The deeper you go into biology, the more it shades into something that appears to be religious"

Jordan Peterson, March 2021, before he received the grace to accept that it's quite alright to be terrified that the mythological narrative world and the real historic objective world do touch, and it is those who surrender to that terror and strive to live up to the Ideal despite their weakness, who are the saints.

Embryo

The embryo stage refers to the early development period in multicellular organisms and the term is derived from the Greek *embruon* meaning "the young one". In many multicellular organisms, "embryo" can be used more broadly to refer to any early developmental or life cycle stage prior to birth or hatching. Human embryology is the study of human ontogeny in the first 8 weeks of our lives beginning with our origination usually within the process of fertilisation and ending when more than 90 percent of the 4500 identifiable structures of the adult body have appeared and we assume the name of foetus, which also means "the young one" but originates from Latin. The division of human development into an embryonic or embryo and foetal or foetus periods is historical and arbitrary, based on an observation of the replacement of cartilage in the humerus with bone marrow. The first eight weeks constitute the embryonic period of human development and embryonic development begins when the embryo begins and that is at the earliest stages in the process of fertilisation, and continuous growth and development proceed thenceforth through recognisable stages. When we are born, we will be called infant, even if we are born prematurely.

First Journey

Consequent to syngamy, and the formation of the first mitotic spindle, we undergo our first cleavage within a day or a little longer and each new cell is called a blastomere. Two become three and we become multi-cellular as we move towards the uterine cavity. When we have 8 cells or more on day 3, there is a tightening and realignment between adjacent cells and a polarisation between inner and outer blastomeres become visible. We may be called a morula towards the end of our third day because we look like a mulberry consisting initially of 16-32 blastomeres. From around the fourth day a fluid-filled cavity begins to form within, and we are named blastula or blastocyst and a distinction between our outer layer of trophoblasts and an inner cell mass of pluripotent blastomeres referred to misleadingly as embryoblasts becomes apparent. During our fifth day, our blastocystic cavity the blastocoele continues to enlarge, our cells continue to multiply and the inner cell mass begins to differentiate.

Implantation

Each of us move and develop at our own pace, and usually by our fifth day, having completed the journey along the Fallopian tube, we enter the lumen of the uterus and hatch out herniating through an opening on the zona or now *capsula pellucida* and expanding so that we may embed in mother's endometrium.

The inner cell mass begins to specialise into epiblast that in turn gives rise to the hypoblast which together form a double-layer disc. Our trophoblasts further differentiate into the cytotrophoblast and the outer synctiotrophoblast which derives from it, and which initiates the process of placentation. By the day 6 while we begin settling into mother's uterine wall that is already prepared *via* decidualisation and made hospitable for receiving us, having rotated to align our inner cell mass to be adjacent to the endometrium and benefitting from integrin-mediated adhesion. This first attachment is called adplantation and indicates the onset of implantation. During this time and into the following day our didermic disc separates the blastocoele from the emerging amniotic cavity. Our synctyotrophoblast forms the syncytium which causes apoptosis of the endometrial epithelium enabling penetration into the stroma beneath and into maternal blood capillary walls by the seventh day.

While our amniotic cavity is expanding, a layer of amnioblast cells is formed from differentiating epiblasts, that separate it from the cytotrophoblast on day 8. Early in our second week extracellular vacuoles appear in the syncytium which join to form lacunae that get filled with uterine secretions and further to rupturing of maternal capillaries are filled with maternal blood. By the ninth day the hypoblasts have also multiplied and grow ventrally along the inner side of the blastocystic cavity. We are now entirely embedded within the endometrium, and the syncytium has grown to surround the cytotrophoblast. By the tenth or eleventh day while the lacunae network expands, the hypoblasts extend completely to form the wall of what is called the primary umbilical vesicle, exocoelomic cavity or yolk sac which replaces the blastocystic cavity and that facilitates preplacental nutrition and gas exchange - and which in turn becomes surrounded by a fine exocoelomic membrane, that by day 11 develops into a short-lived reticulum of acellular material.

It is yet to be confirmed whether it is hypoblast cells from the extracoelomic membrane or epiblasts and cytotrophoblasts, that differentiate into cells referred to as "extra-embryonic" mesoblasts - and it appears likely that they both do, but in varying degrees at different stages of our development, that give rise to a new chorionic cavity in place of the reticulum, that lies between the umbilical vesicle and the cytotrophoblast. By day 12, implantation is complete and the invasive growth of the syncytium ceases. By day 13 the umbilical vesicle has transitioned into the secondary umbilical vesicle, the localised thickening of hypoblast that is the prechordal plate is formed and an arterial inflow and venous outflow system is established for obtaining mothers blood to continue to nourish us and take away waste products and the primitive utero-placental circulatory system has arisen. By day 13 the chorionic cavity is surrounded by a layer of mesoblast cells forming its walls that cover the inner side of the cytotrophoblasts layer and the outer sides of the umbilical vesicle and amniotic cavity, the chorion itself being a double-layered membrane formed by the trophoblast and the "extra-embryonic" mesoderm.

As the generation of the embryo occurred during a moment in the process of fertilisation, likewise the development of the embryo continues during the movement into the uterine cavity and during the process of implanting into the uterus, extending from the onset through the embedment to the completion of implantation. Development and change continue thereafter during the remaining pre-natal period whether pre- or post-gastrulation and during foetogenesis, and thereafter after birth, through childhood, youth and adulthood. Even though obvious, it needs to be stated that the pre-implantation period of embryonic development ends with the completion of implantation on day 12, but our growth and development continue unabated. By day 14 we are constituted of a bi-layer disc surrounded by the amniotic cavity, the umbilical vesicle and the chorionic cavity that is attached by a thick stalk to the chorion, within the syncytium, which itself is surrounded by maternal decidual cells.

Gastrulation and Beyond

Prior to gastrulation a subpopulation in the proximal posterior region of the epiblast initiates the expression of the transcription factor protein T/Brachyury thus defining the site of gastrulation. Migrating epiblasts which initially appear as a linear grooved band of cells called the primitive streak by around day 14 which marks the onset of gastrulation, ingress early in our third week into the primitive groove and at the primitive pit within the primitive node at its cranial end to begin forming a third germinal layer called the "intra-embryonic" mesoderm between the two existing layers that constituted the bi-laminar disc. During this time, these mesenchymal cells migrating through the primitive knot begin forming the notochord that establishes a central body axis, and the buccopharyngeal and cloacal membranes which will be our future mouth and anal cavities appear. Consequently, epiblast and hypoblast are replaced with epiblast-derived ectoderm and endoderm, the now trilaminar embryonic disc thickens and we could be called a gastrula by day 19.

Induced by the notochord, neurulation also begins in our third week with the formation of the neural tube out of neural tissue differentiated from the ectoderm and a transient neurenteric canal appears connecting the amniotic cavity to the primitive gut that is the umbilical vesicle, and organogenesis begins - and proceeds and continues after birth as well, while a finger-like outpocketing of the posterior wall of the umbilical vesicle develops into the allantoic diverticulum, a primitive excretory duct of the embryo that will become part of the urinary bladder. Beginning in the third week and continuing into the fourth, somitomeres that will form transitional organs called somites appear from paraxial mesoderm, our umbilical vesicle folds to close off the body cavity and form the gut by day 22 and the disc takes on a cylindrical shape in transverse view or head on, and a convex shape from a rostral-caudal view, or when seen sideways. Our heart is the first functional organ with cardiac pulsation in the primitive heart tube beginning on day 21 or 22, the maturation of the heart having begun in the early stages of gastrulation on day 15 with migration into regions known as heart fields of mesodermal cells that specialise into myocytes.

As the placenta, formed by the chorion on the embryonic side, takes over our nourishment beginning week 4, the umbilical vesicle reduces in size having begun to vascularise on day 17 giving rise to erythroid precursors and remaining to serve in haematopoesis - and harbouring in its wall our primordial germ cells which will give rise to our gametes, at the base of the allantois. During all this time, our continuous and multi-faceted growth in size, complexity and capability continue marvelously as it has done from our beginning, and continues to do likewise at the end of our eighth week when we are kicking and capable of jumping when startled as we graduate from embryohood, into a time when we become able to respond to music that mother is listening to, and even later when we change environment and emerge to breath the air, and at all other milestones we pass after that as well.

Unusual natural means of embryo origination

While the total self-giving union of paternal and maternal gametes in the process of fertilisation of sexual reproduction is the usual means though which a human being begins, there are other natural means through which some of us have originated. Monozygotic twinning occurs when an embryo conceived though a normal fertilisation process, splits during cleavage or morula stages, when the inner cell mass splits entirely or partially at the blastocyst stage before or after we squeeze out of the pelludic capsule, or when duplicate primitive streaks may form at the onset of gastrulation and perhaps even after the formation of a single primitive node where partial splitting of the streak may produce twins whose major embryonic structure remains conjoined - while noting that errors in gastrulation also lead to expressions

of teratogenesis that does not constitute twinning. Asymmetry in conjoined twins may lead to the situation of *fetus-in-fetu* where one twin is completely encapsulated within the torso of the otherwise normally developed host twin.

These are abnormal phenomena where from one embryo generated in sexual reproduction, another is generated subsequently *via* an asexual means of reproduction. In these unusual instances by which a twin may originate asexually, the mechanisms of origination are different, even though once the new human being has come into existence, it is indeed a new human being.

Engineered natural embryo generation

In artificial insemination, gamete intra-fallopian transfer, and *in vitro* fertilisation procedures with or without intracytoplasmic sperm injection, the embryo is generated *via* a fertilisation process albeit under extraordinary and unnatural circumstances. In IVF fertility processes, apart from circumjacent sins prerequisite to the objective, cells are removed from embryos generated to conduct eugenic quality control to discard those with genetic anomaly, and for sex determination so that the boys can be destroyed if girls are wanted, and the surplus may be frozen. Cryopreserved and subsequently thawed embryos who continue development make real the visions of cryonic time travel articulated over a century ago, but the traveler here has no opportunity to consent. In intentional embryo splitting, artificial means are employed to achieve what naturally occurs in the case of early natural monozygotic twinning.

Engineered Unnatural Embryo Generation

Somatic or germ-line cell nuclear transfer or what is popularly known as cloning involves enucleation or removal of the haploid chromosomes comprised of the meiotic spindle complex from a metaphase II stage oocyte, which thereafter is called a cytoblast, followed by the transfer into it and fusion of a diploid cell, the karyocyte, from a suitable donor. This manipulated oocyte is then artificially activated by means of either electric pulses or chemical stimulation, thus inducing subsequent development of the newly generated embryo, generated at a stage that would be post-syngamic when compared with a naturally sexually generated embryo. In pronuclei transplantation, one or both pronuclei of a pronuclear embryo is removed and transferred either to another embryo at a similar development stage or an enucleated oocyte, and while the pronuclei donors may be discarded killing them in the process, a new embryo originates at this engineered pronuclear stage, and begins development. Blastomere aggregation can generate an embryo out of viable blastomeres taken from several non-viable embryos.

At the cutting edge today are what are referred to as SHEEFs, an acronym for “synthetic human entities with embryo-like features”. Among these are gastruloids classified ironically juxtaposed as “embryonic organoids”. These are formed by three-dimensional aggregation of embryonic so-called “stem” cells – the harvesting of which kill the embryos they belonged to, or of human induced pluripotent cells which are mature somatic cells such as skin or blood cells that have been re-programmed to embryonic stem cell-like state, to form relatively larger but morula-like structures that can grow subject to chemical manipulation like early embryos and undergo gastrulation and form the three germ cell types. Other related techniques aggregate a greater number of trophoblasts and embryonic stem cells to form what resembles a natural human blastocyst at 3-4 days and are called blastoids. ETX embryos composed of stem cells derived from embryonic epiblast, trophoblast and extraembryonic endoderm that mimic the

endoblast and does not have an evident corresponding stage in the naturally developing embryo have also been produced, in addition to post-implantation amniotic sac embryoids.

Embryoid means non-embryo but having embryo-like form or characteristics, and likewise with blastoid. There is evidence of epiblast expansion, cell lineage segregation, bi-laminar disc formation, amniotic and umbilical vesicle cavitation, trophoblast diversification and even gastrulation in these creations, and they demonstrate autonomy in the sense of self-organising or morphogenetic capability with minimal signaling from without. While not all SHEEFs are integrated in the sense of organismic wholeness, some certainly are, but one could argue that if we are cultured *ex utero* we could develop without the need of cell lineages that specialise for *in utero* logistics. There is also the case of harvested embryonic "stem" cells and induced pluripotent stem cells that in controlled culture usually remain as they are, but spontaneous formation of embryoid structures have been observed. If there is a question regarding the ontological and thereby moral status of these aggregated and engineered living entities that are complete developmental systems - whether they are actually embryo or embryoid, blastula rather than blastuloid, it is best to err towards safety than otherwise, since such errors may in many instances turn out to be correct.

In unnatural reproductive techniques, the means of generating an embryo whether for reproductive, academic or therapeutic purposes, are different, but not what an embryo is once he is generated and commences development at a point of development which could be a single-cell pronuclear or zygotic stage, a morula or blastocyst-like stage or perhaps even another stage that does not have a corresponding stage in natural embryological development such as in the case of some of the engineered embryo/oids. The state of origin will not always be at the point of a primordial embryo as in the case of normal sexual reproduction - but there will be a human being alive and in morphogenetic development.

In retrospect, it is astonishing how inadvertently prophetic Mary Shelley was when, glavanised by the intellectual temper of her time regarding reanimation of cadavers using electricity consequent to the discoveries of Galvani and Volta, and the stirring public demonstrations in England by Galvani's nephew Giovanni Aldini, she composed the benchmark for an English horror novel and became a pioneer of science-fiction. While Aldini's experiments originated the pattern in which nuclear transfer cloning was initially conducted, there is another parallel in that Frankenstein aggregated parts of different persons and made one body, a larger body, and induced the composite whole to begin living as a human being precisely as in the case of pronuclei combination, blastomere and stem cell aggregations forming morula and blastocysts or even later stage embryos that are *via* genetic or chemical signaling in inverted culture dishes - sometimes in an environment called matri-gel, brought to life possibly as a human being. One might remark also that at least Shelley's Frankenstein experienced subsequent remorse, and his creature at least was able to ask him "how dare you sport thus with life?"

{End of Part II of IV. In Part III, the concepts utilised to dehumanise are described, dissected and dissolved}

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