On the Embryological Foresight of the Talmud

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A well-known passage in the Talmud states that parents can pray for the gender of their unborn child only during the first forty days of pregnancy. Another passage states that the female identity of an embryo takes eighty days to be formed.

At first blush, this appears to be contradictory to the basic facts of reproductive biology. Isn't the gender of the embryo determined at the moment of conception? A more careful analysis reveals that the chromosomal makeup of the fertilized egg, XX or XY, is not the only factor determining the embryo's gender. The successful expression of the SRY gene located on the short arm of the Y chromosome is another crucial factor.

In fact, it takes approximately forty days from the time of conception for male gender to become irreversibly determined and about eighty days for female gender to be determined.

One can only wonder at the prophetic insight of the Talmud Sages, who pinpointed the precise time frame for the formation of gender—long before the science of genetics was developed.

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Western versus Talmudic Perspectives

Embryological development has until recently been cloaked in mystery. With no definitive knowledge of what occurred between conception and birth, pre-scientific thinkers alternated between different theories of fetal development.

Early civilizations worshipped the female as the source of life. In more recent times, this attitude changed and the male was considered the originator of life, with the female no more than a nurturing vessel.

Pre-formationists, starting with Pythagoras, suggested that all organisms developed from fully formed beings. The idea that the male seed contained a complete but miniature person survived well into the seventeenth century CE.

Epigenesists held that the development of the embryo is caused by

an external vital force. The most distinguished epigenesist was the seventeenth-century British physician William Harvey, who was the first scientist to describe the structure and function of the circulatory system.

In 1677 the Dutch scientist Antonie van Leeuwenhoek, using the newly invented microscope, discovered spermatozoa. Van Leeuwenhoek himself, and many after him, claimed to see a complete pre-formed human being (called a homunculus) in the sperm. These views helped the pre-formationists hold on to their ideas for almost two more centuries.

The only disagreement left among the pre-formationists was the location of the homunculus. The "spermist" camp thought it was stored in the spermatozoa, while the "ovists" argued that it was situated in the ovum, the female egg. Only in 1827 did the German scientist Karl Ernst van Baer describe how all mammals develop from the ovum. Martin Barry observed the moment of fertilization in a mammal and saw that male spermatozoa penetrated the female egg. This evidence laid the foundation for understanding that both the mother and the father contribute to the formation of the child.

The views of the Talmud Sages differ from those of early Western civilization described above. In several instances, the Talmud, compiled by the Sages of Israel and Babylon from the second to the fifth centuries CE, addresses the topic of fetal development. As it is primarily a legal work, the references in the Talmud to our subject are laconic. Most of these references are made in relation to the laws of postpartum female impurity. Other talmudic discussions on the topic provide interesting perspectives.

Talmud *Niddah* 31a records a discussion of the respective contributions of both mother and father to the formation of the child:

> There are three associates in the creation of a person: G-d, the father, and the mother. The father provides the white seed, from which are formed bones and nerves, the nails, the brain, and the white of the eye. The mother provides the red seed, from which are formed the skin and the flesh, the hair and black of the eyes…[1]

The Talmud in *Brakhot* 60a touches upon the gender determination

of a child in a most intriguing manner, presenting divergent views. Interpreting Leviticus 12:1, "When a woman conceives and gives birth to a male," Rav Yitshak, son of Rav Ami, deduces that the gender of the fetus is determined by certain circumstances at the time of conception. However, the continuing discussion on this page contains a *baraita* (mishnaic material not included in Rabbi Yehudah Ha'Nasi's *Mishnah*) that seems to contradict Rav Yitshak. The baraita lists a sequence of requests to G-d that a husband should pray for during his wife's pregnancy:

> For the first three days he should pray that the seed should not be lost and conception should occur.
>
> From the third to the fortieth day he should pray that the child should be a male.
>
> From the fortieth day to the third month, he should pray that the fetus develop healthily.
>
> From the third to the sixth month he should pray that no miscarriage should occur.
>
> From the sixth month he should pray that the birth should be successful.

The timeline of this baraita suggests that gender is not sealed permanently until the fortieth day of fetal development. However, Talmud in *Niddah* 30b cites an opinion by Rabbi Ishmael (albeit challenged by other Sages) that it takes eighty days for an embryo to become completely formed as a female.

This apparent disagreement regarding on exactly which day gender is determined in an embryo presents a challenge. If the sex of a fetus is determined at conception (as Rav Yitshak claimed), how can the baraita advise a husband to pray for a male child until the fortieth day? Furthermore, considering the binary nature of gender determination, how can there be two different time periods for male or female formation—forty days for a male and eighty days for a female? If forty days pass and the fetus does not develop as a male, isn't it automatically deemed a female?

The Current Genetic Description of Gender Development

To answer these questions, let us look at the biological process of sexual differentiation—the development of the differences between a male and a female from an undifferentiated fertilized egg. The process of the development is a very complex series of genetically programmed events at critical periods of fetal life.

Gender at the fetal stage is first established by the nature of the chromosomal composition of the fertilized egg: XY composition is a male karyotype, and the XX composition is a female karyotype. By default, every embryo would develop as a female, and it only becomes male upon the successful expression of the SRY gene located on the short arm of the Y chromosome.

But chromosomal distribution alone is not in itself enough to determine the gender of a child. To understand this requires a detailed understanding of the role of SRY in gender determination.

The SRY gene was discovered in 1990 by Andrew H. Sinclair.[2] It contains one exon and codes for a protein composed of 204 amino acids. This protein binds in specific places to the DNA molecule itself, causing it to bend at about 70 degrees, in turn affecting the action of a number of genes on both X and Y chromosomes. The activation of SRY thus causes the repression of these genes on the X chromosome that would otherwise affect the development to the female phenotype. If, however, the expression of SRY is disrupted, the embryo remains female, even if it has an XY karyotype. Such a scenario can develop as a result of a mutation on the correlating DNA sequence on the Y chromosome or as a result of the recombination of parental X and Y chromosomes. Depending on the site of such crossing-over, the SRY gene could be switched from the Y chromosome to the X chromosome, creating a Y chromosome lacking the SRY gene and an X chromosome containing it. Fertilization of an egg by sperm containing the X chromosome with SRY creates an XX embryo, which develops as a male (called the de la Chapelle syndrome, occurrence 1:25,000). Fertilization of an egg by sperm containing a Y chromosome

without SRY creates an XY embryo, which develops as a female (called the Swyer syndrome, occurrence 1:100,000).

In the early stage of development, a small group of cells, called the "indifferent gonads," begin to form. These cells will eventually become ovaries or testes. The gonad contains cells that will produce hormones, androgens, or estrogens, depending on the direction of the development. This complex sequence of hormonal changes, which encourages the action of the genes in developing some characteristics and inhibiting others, is set off by activation of the SRY gene.

The activation of SRY expression occurs during the sixth week of gestation, approximately the fortieth day, as the Talmud remarkably predicts. If this decisive event, bringing about the male type development, does not occur on time, a male fetus cannot be properly formed. This may be why, according to the Talmud, a husband should still pray for a male child until the fortieth day of his wife's pregnancy. If the SRY does not activate at that pivotal time, even though the fetus has the XY chromosomal composition, it cannot develop as a healthy male.

Interestingly, Rabbi Ishmael did not think that if an embryo has not been formed as a male by the fortieth day that on the forty-first day it is a female. In other words, he did not equate femaleness with the absence of maleness. This counterintuitive idea could be illuminated by examining pathological cases. As was briefly mentioned earlier, in the case of SRY slippage during the pairing of the parental chromosomes, if the resulting embryo had the XX composition, it would produce a male, though infertile. If the embryo had the XY chromosomal composition, without the SRY gene on the Y chromosome, the male development would not take place. Though such a child would look like a female, it would not have the ability to perform the essential female function of bearing offspring.

Even if the parental chromosomes are intact, some chromosomal mistakes could interfere with the normal gender development of the embryo. The following table illustrates a few such instances.

Disorder	Genotype	Phenotype	Sexual development
Kleinfelter syndrome	XXY	Tall male	Infertile 1:1,000 live births
Trisomy X	47XXX	Female, usually tall	Usually normal 1:1,000 live births
XYY syndrome	XYY	Tall male	Usually normal 1:1,000 live male births
Turner syndrome	45X	Short female, distinctive features	Infertile 1:2,000 live female births

Some authors[3] claim that up to 2 percent of live births may show deviation from the ideal male or female, though others insist that the prevalence of the conditions in which chromosomal sex is inconsistent with phenotypic sex is about 0.018 percent.[4]

For a fetus to develop as a fully developed fertile female there must be two X chromosomes and no Y chromosome. If two X chromosomes are present, under the influence of rising estrogen in the female embryo from about six weeks—paralleling the rise of androgens in the male—the morphological changes take place.

In a normally developing embryo, the indifferent gonad begins to develop into recognizable female structures by the twelfth week. Only at that period is it possible to judge the success of female development. This coincides with Rabbi Ishmael's eighty days.

We can only marvel at the foresight of the Talmud Sages, who, almost a millennium and a half before the Age of Science, not only understood that both parents contribute to the biological development of their child, but were able to accurately determine the time line of embryonic gender development.

Notes

[1] For an excellent discussion on this statement in Talmud *Niddah* 31a on the paternal and maternal contributions through the prism of modern genetics, see Marvin Gold, "Gene Imprinting and Gene Silencing" *B'Or Ha'Torah*, vol. 16 (2006) pp. 19-31.

[2] Andrew H. Sinclair et al., "A Gene from the Human Sex-Determining Region Encodes a Protein with Homology to a Conserved DNA-Binding Motif" *Nature*, vol. 346 (1990) pp. 240-244.

[3] Melanie Blackless et al., "How Sexually Dimorphic Are We?" *American Journal of Human Biology*, vol. 12, no. 2 (2000) pp.151-166.

[4] L. Sax, "How Common Is Intersex?" *Journal of Sex Research*, vol. 39, no. 3 (Aug 2002) pp. 174-178.