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Current Theories on the Human Sex Ratio

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ABSTRACT

The human sex ratio is skewed toward males, and this is the subject of much research. A review of some of the theories currently available was conducted, searching and analyzing the current scientific literature. Suggestions to explain the ratio include unequal proportions of X and Y sperm, the effect of maternal diet, maternal testosterone levels, and the natural fluctuations in the consistency of the cervical mucus. Although the difference in X/Y sperm proportions does not adequately explain all the data, the other theories do seem to explain the greater percentage of male births. However, there is still not enough information available to verify which theory is the most plausible.

INTRODUCTION

When asked what percentage of births is male and what percentage is female, most people will answer that it is 50-50%. However, the human sex ratio, or ratio of males to females, is not even; rather more males are born than females. The actual ratio of males to females is approximately 1.05:1 (Mathews and Hamilton 2005). This is against convention, and possible causes have been suggested. Understanding the causes may be of practical use to couples seeking to select the gender of their children. There is great interest among many couples to have a child of a specific gender, often for family balancing among couples who already have a few children of one gender (Belkin 1999). Understanding the natural causes for selection of gender would be of great benefit to such couples. If a cause for the higher ratio of males can be determined, it can be used to select for males, or avoided to select for females. However, the current theories do not offer a practical and guaranteed method for selecting gender.

DOCUMENTATION OF RATIO

The sex ratio has been well documented, initially using census data (Table 1). In the United States, the ratio for male births from 1943 to 2002 is reported as 105 (convention in reporting ratio gives the figure for males in respect to 100 females). There are variations based on race, ethnicity, and maternal age (Tables 2 and 3). Whites seem to have a male birth ratio around 105, and among African Americans, the ratio is around 103 (Mathews and Hamilton 2005). Among Americans of Asian descent, the ratio is around 107. Variation in the ratio is also seen in different countries. In fact, in some countries, a ratio as high as 107 has been observed, while other countries have reported lower ratios (Grech et al. 2002). It is important to note that in some countries, such as China and India, the sex ratio is extremely high (113 and 109, respectively). However, these high numbers are mainly a result of artificial factors, not natural ones. These countries have a culture that favors males, resulting in sex-selective abortion and infanticide. This paper will focus on possible causes for the natural sex ratio observed in countries that do not have a culture of sex-selection practices.

Year	2002	2001	2000	1999	1998	1997	1996	1995	1994
Males	2,057,979	2,057,922	2,076,969	2,026,854	2,016,205	1,985,596	1,990,480	1,996,355	2,022,589
Females	1,963,747	1,968,011	1,981,845	1,932,563	1,925,348	1,895,298	1,901,014	1,903,234	1,930,178
Ratio	104.8	104.6	104.8	104.9	104.7	104.8	104.7	104.9	104.8

Table 1: Number of male and female births and sex ratio at birth, in the United States, 1994-2002. Source: Mathews and Hamilton 2005

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White	Black	Japanese	Hawaiian	Chinese	Filipino	Mexican	Non-Hispanic white	Non-Hispanic black
105	103.2	108.9	107.5	107	107	103.8	105.4	103.2

Table 2: Sex ratio at birth by race and origin of mother, in the United States, 2002. Source: Mathews and Hamilton 2005

under 15	15-19	20-24	25-29	30-34	35-39	40-44	Over 45
105.1	105.2	104.7	105	104.9	104.2	103.7	109.7

Table 3: Sex ratio at birth by age of mother, in the United States, 2002. Source: Mathews and Hamilton 2005

SECONDARY AND PRIMARY RATIOS

The observed ratio, known as the secondary sex ratio, reflects the ratio of males to females at birth. Initially, it was suggested that the primary sex ratio, or ratio at conception, is equal, and only the secondary ratio is skewed due to a higher rate of miscarriages among female fetuses. The female was believed to be weaker, resulting in a higher ratio of live male births. However, when studying fetuses from miscarriages, researchers found the opposite to be true. They found that a greater percentage of males than females were spontaneously aborted (Klug et al. 2009). These findings suggested that the primary ratio was even higher than the observed secondary ratio. The data suggested that the primary ratio at conception was at least 120, and some researchers even suggest 160. These numbers demonstrate a great selectivity for males at conception, although the subsequent reduction in the ratio from 120 at conception to 105 at birth reflects a weakness among male embryos. This weakness may be partially explained as an immune reaction against the male fetus. Research on pregnant mothers diagnosed with toxemia, a condition among pregnant women that causes severe hypertension and risk of stroke, shows a greater proportion of toxemia among women carrying male fetuses (Toivanen and Hirvonen 1970). This suggests that toxemia, suspected to be an autoimmune reaction, is more sensitive to triggers in the male embryo than in the female embryo, resulting in more male embryos being spontaneously aborted than female embryos. This may be a possible explanation for the sharp decrease from the primary sex ratio to the secondary ratio.

However, the initial ratio, with greater rates of conception of males, is somewhat of a biological mystery. In humans, like all mammals, sex is determined by the sex chromosomes, the X and Y chromosomes. Females carry an XX chromosome, and males carry an XY chromosome. Since all females have XX, the haploid ovum will only contain an X chromosome, and the sex of an embryo will be decided by the sex chromosome contained in the sperm that fertilizes the ovum. If the sperm cell contains a Y chromosome, the resulting embryo will be male (XY), and if it contains an X chromosome, the embryo will be female (XX). Spermatogenesis, the formation and maturation of sperm, is a result of meiosis. Through meiosis,

one germ cell divides into four haploid gametes. This should result in an equal number of X-bearing and Y-bearing sperm, as the germ cell containing one X and one Y chromosome should be divided equally. If X and Y sperm rates are equal, no noticeable difference in the sex ratio should be observed, as the odds of fertilization by an X-bearing sperm should be the same as that of a Y-bearing sperm.

UNEQUAL SPERM RATIOS

There are those who argue that sperm are not equally divided into X and Y sperm. This would have to be a result of some factor in spermatogenesis resulting in higher rates of maturation for Y-bearing spermatozoa than X-bearing spermatozoa. Selective elimination of X-bearing sperm would result in an increase in the ratio of Y sperm, explaining the higher ratio of male births. However, there does not seem to be any clear mechanism explaining the selective elimination or failure of X-sperm maturation.

Some studies suggest that environmental factors may influence the ratio of X and Y bearing sperm, selectively eliminating X-bearing sperm. One study has linked the exposure of POPs (persistent organohalogen pollutants) to an increase in the ratio of Y-sperm to X-sperm in males. POPs include pollutants such as DDT (dichlorodiphenyltrichloroethane) and PCBs (polychlorinated biphenyls). Studies by Tiido et al. (2006) seem to show a positive association between the ratio of Y-bearing sperm and serum concentration of PCB-153. Swedish and Greenlandic men had high levels of PCB, and their sperm had a higher proportion (51.2%) of Y-sperm than expected. On the other hand, Polish men, who did not have elevated serum levels of PCB-153, had almost equal sperm distribution (50.3% Y and 49.7% X). These numbers suggest that environmental factors may play a role in the maturation of X and Y sperm, and may, in fact, be responsible for the observed sex ratio.

However, this theory does not adequately explain the sex ratio. If uneven X and Y sperm distribution is behind the greater proportion of live male births, then countries with low POP exposure (and, thus, even sperm distribution) would be expected to correlate with an even ratio of live births. This is clearly not the case. For example, in Poland, where males have been found to produce sperm with an even distribution of X and Y sperm, the sex ratio is still skewed towards males, with a reported ratio of 106 (Grech et al. 2002). Furthermore, equal proportions of X and Y sperm were found in males who had fathered three or more children of the same gender (Irving et al. 1999). The study, trying to explain the apparent altered sex ratio observed in these families, fails to find a correlation between X/Y sperm proportion and gender of the offspring. Men bearing only sons were found to have an almost equal amount of Y-sperm (49.7%) as X-sperm, and the same results were found among those who fathered only females. These findings, as well as the lack of correlation between observed sperm distribution and the actual sex ratio in counties like Poland, suggest that the factors causing the sex ratio are of maternal origin, not paternal origin. Maternal influences would likely play a role in increasing the odds of fertilization by Y-sperm, resulting in a higher ratio of males.

NUTRITION AS A POSSIBLE CAUSE

Some studies link the skewed ratio to maternal nutrition. Noorlander et al. (2010), studying Danish women, compared blood sodium (Na^+) and calcium (Ca^{2+}) levels with the ratio of males and females at birth. Noorlander et al. hypothesized that higher blood mineral levels result in a higher ratio of females, and that the observed sex ratio, with higher male ratios, is a result of low Na^+ and Ca^{2+} levels. To test the hypothesis, women who were planning on becoming pregnant were placed on a high calcium diet, and their serum Na^+ and Ca^{2+} levels were monitored for at least nine weeks prior to planned conception. The researchers used a

prediction rule to satisfy their requirements: women with Na^+ values of at least 140 mmol/L and an increase in Ca^{2+} levels by at least 0.1 mmol/L were predicted to conceive a female. The results showed that 73% of those who had satisfied the prediction rule had females, much higher than the expected 50%, suggesting a positive association between mineral levels and female conception. This would suggest that the overall sex ratio, with higher proportion of males, is an effect of low mineral intake. The role of Ca^{2+} in fertilization has been studied and found to play a crucial role in both capacitation of sperm and activation of metabolism in a fertilized ovum. However, it is not clear if it would affect X and Y sperm differently, and no mechanism for the link between Ca^{2+} levels and sex selection has been proposed.

MATERNAL DOMINANCE HYPOTHESIS

The maternal dominance hypothesis is the result of studies suggesting that women with more dominant personalities are more likely to conceive males. According to Valerie J. Grant (1996), a dominant personality is defined as authoritative or influential and is measured by personality tests. Although a theory based on difficult to measure personality traits may be considered suspect, this claim is based on a biological theory. It is postulated that the dominant personality is a result of higher testosterone levels, and this has an influence on the gender that is conceived. Grant suggests this to be responsible for the skewed sex ratio, as the maternal influence results in more male conceptions.

The elevated testosterone level that is the subject of this theory is not serum level; rather it is the level in the follicular fluid. Follicular fluid is secreted by granulosa cells in the secondary follicle surrounding a developing oocyte, and it contains steroids—both estradiol and testosterone—in concentrations that may be 40,000 times that of serum concentrations. The theory proposes that these higher testosterone levels influence the selection of sperm, causing greater rates of capacitance among Y-bearing sperm. However, studies on the effects of follicular fluid on sperm counts show that it does not result in a higher proportion of Y-sperm than in samples incubated in standard growth media (Bahmanpour et al. 2009). It is, therefore, difficult to claim an effect on the sperm itself by follicular testosterone. It is possible, however, that the effect is not on the incoming sperm; rather the effect is on the receptiveness of ova to X or Y sperm. It is thought that during the development of the zona pellucida, the glycoprotein layer that surrounds the ovum, its molecular composition may be somewhat influenced by the high testosterone levels. As a result of these subtle changes, the zona pellucida would be more receptive to a Y-bearing sperm, resulting in a higher ratio of male conceptions (Grant and Chamley 2010). It is important to note, though, that a difference in receptiveness to X or Y sperm would involve a biochemical difference between the two. To date, the only difference that has been found is morphological, not chemical, and it is not known if such a difference is sufficient to play a role in zona pellucida selectivity.

TIMING OF OVULATION

Another theory that suggests maternal cause of the skewed sex ratio is the effect of the timing of ovulation on the gender that is conceived. An often-cited study by Susan Harlap (1979) shows that the timing of coitus in respect to ovulation seems to influence the sex ratio. Other studies agree, their data showing a U-shaped curve, with coitus closer to ovulation reflecting an equalization of the sex ratio, and coitus farther away (both before and after ovulation) skewing the ratio (Gray et al. 1998). Coitus more than two days before or after ovulation resulted in males in more than 60% of conceptions, and inseminations closer to ovulation had a more even ratio of males to females, with some studies showing only 49.3% male for coitus within one day of ovulation. The overall result would be a higher ratio of male conceptions, as the even ratio at

time of ovulation is skewed towards males when the total number of conceptions, including those farther away from ovulation, is included.

It is tempting to explain this with the adage that Y sperm swim faster than X sperm, a result of the smaller mass of the Y-sperm. If ovulation would precede coitus, then the ovum is already in the oviduct, and the faster swimming Y sperm would be expected to fertilize the egg, resulting in a greater ratio of males. This is clearly not satisfactory, as the sex ratio of conceptions arising from coitus within one day of ovulation should display the same effect, as the faster swimming Y-sperm should have greater fertilization rates. Furthermore, coitus performed before ovulation should not result in a greater proportion of males, and this is not the case. In addition, it is now believed that faster swimming sperm do not have greater odds at fertilizing the ovum. The current hypothesis is that sperm have a window of competence for a brief time, and the timing and length of this capacitance depends on many factors, including location in the reproductive tract. In addition, sperm do not have the ability to undergo the acrosome reaction necessary for fertilization until they have spent some time in the environment provided by the female reproductive tract (Gilbert 2006). If the sperm that first arrive at the ampulla of the oviduct are not in the narrow time frame of capacitance, they will not be able to fertilize the ovum.

EFFECT OF CERVICAL MUCUS

A more plausible explanation for the correlation between timing of ovulation and the gender of the conceived embryo is the effect of the cervical mucus on sperm penetration. The cervical mucus, produced by secretory cells in the cervix, consists of glycoproteins and lipids, mixed with water. It acts as a plug that physically impedes the entry of foreign material (including sperm) into the cervix. The consistency and pH of the cervical mucus change during the ovulatory cycle, and these change appear to be affected by hormones, with estrogen and progesterone have opposing effects on the mucus. Prior to ovulation, the cervical mucus is viscous, and sperm penetration is poor. Close to ovulation, the mucus changes. The mucus becomes more alkaline (pH 8.5) and less viscous, resulting in the formation of channels through the mucus. This appears to be a result of rising estrogen levels. At ovulation, the mucus is very porous and watery, and sperm penetration is high. After ovulation, in response to the secretion of progesterone, the viscosity of the mucus increases, and the channels begin to close up (Linford 1974).

Y-bearing sperm have different morphology than X-bearing sperm. As the Y chromosome contains less genetic material, the Y-sperm contains less chromatin than the X chromosome (about 3% by mass), resulting in less dense sperm. This affects the shape of the sperm head of the Y-sperm compared with that of the X-sperm. The difference in shape has been observed to be a more streamlined Y-sperm, with a smaller width-to-length ratio than the X-sperm (McCoshen et al. 1994).

It has been postulated that the streamlined Y-sperm, with narrower heads, would pass through the channels in cervical mucus more easily than X-sperm. This difference in penetration would be more pronounced farther away from ovulation as the viscosity of the mucus begins to decrease. At that point, there would be channels in the mucus wide enough to allow passage of Y-sperm but not X-sperm, and Y-sperm penetration would be expected to occur at a greater rate than X-sperm penetration. More Y-sperm would enter the oviduct, making fertilization of a male more probable, effectively skewing the ratio in favor of males. However, this difference in morphology between X and Y sperm would play less of a role closer to ovulation, as the channels would be open wide enough to allow penetration of X and Y sperm at equal rates. At

that point, both X and Y-sperm would be present in the oviduct in equal numbers, and fertilization of a male would have the same probability as fertilization of a female. Consequently, an equal ratio of male to female conceptions would be expected for conceptions resulting from coitus on the day of ovulation (Martin 1997). (It is worth noting that when coitus is the same day as ovulation, conception rates for a male is slightly lower than the expected 50%. The observed 49.3% ratio might be explained by the greater preponderance of male fetuses to spontaneously abort, raising the possibility that when odds of fertilization are equal for both X and Y sperm, less male pregnancies will be detected due to an almost immediate termination of a small percentage of male pregnancies.)

This has been supported by studies on X and Y sperm penetration through cervical mucus samples. In one such study, samples of cervical mucus were obtained from women at different points in the ovulatory cycle. The samples were mixed with semen samples, allowing the sperm to swim up through the mucus. The samples were then studied, and a difference was noted in the different samples. In the samples that were taken earlier in the ovulatory cycle, the observed proportion of Y-sperm at the far end of the mucus samples was higher (70%) then the proportion of X-sperm. In mucus samples taken at ovulation, the ratio of X and Y sperm was about equal (Rohde et al. 1973). This is because mucus plays a role in selectively rejecting X-sperm, but only in mucus that is not at the stage of ovulation. This suggests that changes in viscosity and consistency of the cervical mucus play a role in the skewing of the sex ratio.

Further evidence for this theory is seen in the change of the sex ratio in conceptions following administration of clomiphene citrate. The observed sex ratio after clomiphene citrate administration is much lower than normal, with a larger number of females being born (Silverman et al. 2002). Clomiphene is used to treat female infertility through induction of ovulation. It is a selective estrogen receptor modulator which blocks estrogen receptors in the hypothalamus, effectively turning off the estrogen negative feedback loop. This results in rising estrogen levels, which will then cause the LH (luteinizing hormone) surge that triggers ovulation. The ovulation being induced has been ruled out as a possible cause of the lowered sex ratio, for the same effect on the ratio is not observed when ovulation is induced via other agents. The clomiphene citrate itself is, therefore, the most probable cause for the change in ratio. This phenomenon can best be explained with the cervical mucus theory. As estrogen affects the cervical mucus consistency, clomiphene citrate can be expected to cause the mucus to become less viscous, similar to mucus at the time of ovulation. This would have the effect of allowing the larger X-bearing sperm equal penetration of the cervical mucus, resulting in lowering of the ratio.

CONCLUSION

The skewed sex ratio, with a greater proportion of both male conceptions and male births, is the subject of various theories. The theory of uneven distribution of X and Y sperm fails to offer a satisfactory explanation for the observed ratio of live births. The theories of maternal nutrition and follicular testosterone levels fail to offer a mechanism of action. The explanation offered by the cervical mucus theory does seem plausible and also explains the effect that timing of coitus relative to ovulation has on the sex ratio.

The sex ratio is well documented, and data show differences among race, ethnicities, and even maternal age. Perhaps this data may be used as further evidence to any of these theories. If, for example, a difference in the cervical mucus consistency is found among different age groups, this difference can then be correlated with the observed sex ratio for each group and can be used to prove the link between cervical mucus and the sex ratio. Studying serum calcium levels

among different ethnic groups and comparing them to the sex ratios of those groups would provide evidence, either for or against, the maternal nutrition theory. Similar research can be done on follicular testosterone levels among different groups to strengthen or weaken the maternal dominance hypothesis. However, no such studies appear to be available at this time.

Influencing the gender of a child to be conceived has long been a subject of interest and the subject of many scientific and non-scientific theories. For parents looking to conceive a child of a specific gender, the current research does not offer much of a practical solution. Diet may be changed to raise mineral levels, and timing of ovulation may be taken into account. However, these methods, even if responsible for the sex ratio, will only skew the odds of conceiving a specific gender by minute amounts. Although a difference in ratio will be seen when documenting hundreds of thousands of births, the slight difference in ratios will not make a significant difference for any individual couple. For couples having a medical need to conceive a child of a specific gender (as in those who are carriers of an X-linked gene), technologies such as pre-implantation diagnosis in conjunction with in-vitro fertilization are available to guarantee the gender of the child. These technologies are usually not offered to those without a medical need, due to ethical concerns, so couples looking to balance their families will often have to rely on these less reliable methods (Grady 2007).

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