# Population Reports 

## PERIODIC ABSTINENCE

Department of Medical and Public Affairs, The George Washington University Medical Center, 2001 S Street, N.W. Washington, D.C. 20009

# Sex Preselection Not Yet Practical 

## SUMMARY

For centuries prospective parents have sought ways to influence the sex of their children before birth, but a reliable method acceptable for general use has yet to be found. Many methods have been studied in the last 50 years, and, while most have proved disappointing, research continues. Three types of sex preselection methods are being tried:

- Timing of coitus, douching, and other changes in human behavior or environment intended to influence the sex of the child conceived;
- Manipulation of sperm in vitro;
- Selective abortion.

Although pre-coital douches and timing of coitus have been widely popularized, neither has been proved effective as a sex preselection method. Recent epidemiological evidence suggests that timing of coitus does affect sex of offspring, with intercourse close to the time of ovulation favoring conception of a female, but the effect is slight. Thus, even if a workable sex preselection method can be based on coital timing, it would have little appeal to most people.

In vitro techniques attempt to separate human or animal sperm into male-engendering and female-engendering fractions. Centrifugation, sedimentation, electrophoresis, sperm motility, and immunologic phenomena have all been tried as means of separating sperm. Results have varied, and successes have been difficult to repeat. Nevertheless, research will continue because an effective method would be valuable to cattle breeders. While it might be highly reliable, a separation method is likely to require special skills and sophisticated facilities. Its technical com-plexity-and the necessity of artificial inseminationwould limit human use of a sperm separation method, especially in developing countries where sex of child preferences are strongest.

The only effective preselection method now available is selective abortion after identifying the sex of the fetus. The method can be used only relatively late in pregnancy because fetal sex cannot be determined earlier. Since late


#### Abstract

This Population Report on sex determination was prepared by Ward Rinehart on the basis of published reports and articles, unpublished papers, personal interviews, and correspondence.

The assistance of the following reviewers is appreciated: Joan Abbott, Rodrigo Guerrero, Louis Keith, Charles A. Kiddy, Richard Lincoln, Malcolm Potts, and J. Joseph Speidel. Frances G. Conn is Executive Editor. Comments and additional updated material are welcome.


abortion is expensive and somewhat risky, its use for sex preselection seems unlikely to become popular, and may remain limited to cases of sex-linked hereditary diseases like hemophilia.

In summary, medical science is still exploring and may be close to finding methods of determining sex at conception, Probably, however, simple methods will have only marginal effect, while methods offering greater effectiveness will be technically complex and so not widely used.

## Impact Uncertain

There have been predictions that the use of sex determination would slow population growth. If couples could choose, it is argued, many would have one or several sons and fewer daughters, and families would be smaller. Then in the following generation the shortage of marriageable females would reduce the population's total reproductive capacity, further slowing population growth. Some also contend that an imbalance in the sex ratio, resulting from the use of sex preselection, would cause radical social changes. Such predictions are highly speculative: the demographic and social effects of a sex preselection method cannot be foreseen.

At the moment no generally acceptable and effective method of sex determination is available. Therefore,

## CONTENTS

Past Theories ..... 1-22
Present Knowledge ..... 1-22
Current Research ..... 1-23
Potential Effects ..... 1-27
Bibliography ..... 1-28

Population Reports are published bi-monthly at 2001 S Street, N.W., Washington, D.C. 20009, USA, by the Population Information Program, Science Communication Division, Department of Medical and Public Affairs of the George Washington University Medical Center and are supported by the United States Agency for International Development. P. T. Piotrow, Ph.D., Director.

Second class postage paid Washington, D.C.
family planning programs can best respond to sex of child preferences by helping couples to value children of both sexes equally and to emphasize the quality of life for daughters and sons alike.

## PAST THEORIES

Throughout history, folk methods, most "scientific" methods, and chance alone have been equally successful at determining sex-they produce a child of the desired sex approximately half the time $(30,129)$. But the desire for an effective sex preselection method has helped to keep some techniques popular in both lay and scientific circles for years, even centuries, often despite evidence of their ineffectiveness or physiological improbability.

The only failure-proof folk method for controlling the sex of offspring was selective infanticide (72). It was employed, usually against female infants, by various cultures ranging from the Eskimo to the Maori of New Zealand and the Toda of India (9). During the Tokugawa period (16001868 A.D.) in Japan, some districts reportedly registered nine male births for every female birth, implying that seven or eight out of every nine female infants were destroyed (176).

Innumerable other folk methods attempted to select a child's sex at or before conception. Examples include reciting chants during intercourse; timing coitus in relation to wind direction, rainfall, temperature, or phases of the moon or tides. One folk prescription advised eating sweet foods to produce girls or bitter or sour foods to produce boys, Another recommended that a man have intercourse with his boots on to have a son. In parts of Austria, midwives buried the placenta under a nut tree to ensure that the next child would be male. In the Palau Islands of the Pacific, a woman wanting to bear a son dressed in man's clothing before coitus. And in some regions of the USA, a man hung his pants on the right side of the bed if he wanted a son; on the left side if he wanted a daughter $(101,146)$. In West Bengal, the belief persists that coitus on even numbered days of the menstrual cycle produces a boy, while coitus on the odd numbered days produces a girl (139).

Early, ostensibly scientific methods of sex preselection arose largely from faulty assumptions about reproductive physiology. The Greek philosopher Anaxagoras (500?428 B.C.) contended that sperm from the right testicle produced male offspring, while sperm from the left testicle produced females. Therefore, tying off one testicle before coitus would determine sex $(39,204)$. This notion per-
sisted at least until the 18 th century, when French noblemen were advised that surgical removal of the left testicle would guarantee them an heir (62).

Other theories asserted that the female determined sex of offspring. Parmenides of Elea (c. 5th century B.C.) and Hippocrates (460?-377? B.C.), assuming by analogy with animals that women had two-horned uteri, concluded that males developed in the right horn; females, in the left $(101,146)$. Based in part on this theory, Aristotle (384322 B.C.) offered a complex prescription for choosing a child's sex, which Lawrence summarizes:

> The woman wanting a male child should lie on her right side after intercourse, in order that this side might be the place of conception, "for therein is the greatest generative heat, which is the chief procuring cause of male children." The method was said to fail only rarely, especially if the woman kept warm and with little motion, also drinking hissop and saffron in a glass of malaga. In order to have a female child the woman should lie on the left side and think strongly of a female, for Aristotle believed that imagination of the mother might often determine the sex (101)

Similar theories persisted into this century. In 1917 Dawson contended that the child's sex depended upon which ovary had ovulated and, furthermore, that the ovaries produced alternately. A couple, by calculating from the birthdate and sex of the previous child, could control their child's sex by choosing the correct month for procreative intercourse (34).

## Timing of Intercourse Theories

The theory that sex of offspring depends on the timing of intercourse in the menstrual cycle may have been first put forth by Empedocles (494-434 B.C.) in ancient Greece (39). The theory has persisted to the present day. A 19th century version contended that an unripe ovum produces females; a ripe ovum, males. Therefore, conception soon after menstruation, when ovulation was thought to take place, was likely to result in a female. In 1898 Schenk, director of the Embryologic Institute in Vienna, refined this hypothesis into a practical sex control technique. The ripeness of the ovum depended on nutrition, Schenk contended. Because a high protein diet supposedly promoted maturation of the ovum, a woman wanting a son should eat more meat (129). The Empress of Russia reportedly used this method, but, like many other devotees of sex preselection before and since, without success (34).

## PRESENT KNOWLEDGE

Since early in this century the chromosomal mechanism has been recognized as the primary determinant of sex (39). Theoretically, if chromosomes alone controlled sex at birth, an exactly equal number of males and females would be born (84). The fact that the sex ratio at birth varies somewhat in association with certain variables has prompted a search for other factors which might also be involved.

## The Chromosomal Mechanism

Whether an individual begins development as a male or a female depends upon chromosomes (the gene-carrying material in cell nuclei) in the gametes which join at fertilization. The gametes (sperm and ovum) form through the divisions of a parent cell (gametocyte), each gamete re-
ceiving half the gametocyte's chromosomes. In female mammals all body cells, including the gametocytes, contain two identical sex chromosomes, known as X -chromosomes. Therefore, every female gamete contains one $X$ chromosome. All male body cells contain one X -chromosome and one $Y$-chromosome. When a male's gametocyte divides, it forms an equal number of $X$-bearing and $Y$ bearing sperm. At fertilization, when ovum and sperm join, the full complement of chromosomes is restored. If the X -bearing ovum combines with an X -bearing sperm, the result will be a female. If the X -bearing ovum combines with a $Y$-bearing sperm, the result will be a male, who will carry in all his cells the XY combination, thereby preserving into the next generation the sex determination mechanism (see Fig. 1). Thus, it is the man, not the woman, whose gamete determines the sex of the child, a fact which should be made clear to men in areas where a wife can be divorced or forced to accept a second wife in the home if she "fails" to produce a son.

## Variations in the Sex Ratio at Birth

In theory, the testes form an equal number of $X$ - and $Y$ bearing sperm $(84,86)$. If no other factors intervened between sperm formation and birth, an exactly equal number of boys and girls would be born. In fact, however, in most regions of the world slightly more boys are born than girls (172). For example, in Europe and the USA the ratio for white births is between 105 and 106 males to 100 fe males (150). Ratios as high as 116.2 males per $100 \mathrm{fe}-$ males in Gambia and as low as 90.2 males per 100 females in Montserrat have been reported (191). Furthermore, the sex ratio appears to vary slightly in relation to certain characteristics of the parents and their environment. Researchers have suggested more than 30 variables associated with variations in the sex ratio $(179,181)$. It has been noted that:

- The percentage of male births rises during and after wars (112.151).
- The percentage of female births increases with increase in age of the mother (104,150), father (128), or both $(101,177)$.
- The percentage of female births increases with birth order (101,111,125,150,151,172,180,183). First births are more likely to be male than subsequent births $(101,151)$.
- A higher percentage of sons is born to couples of higher socio-economic status $(101,151,180,181$, 182,200,201).
- The ratio of sons to daughters is slightly lower among Negroes than among Caucasians (150.172, 180,181,182,190).
- The ratio of sons to daughters is higher for couples with higher coital rates $(75,76,78)$.
- The sex ratio varies with the season $(109,130,151)$. In the USA, the ratio of male to female births is highest in June (108).
- The ratio of male to female births has been lower after certain disasters such as flood, smog (106). and hepatitis outbreak (143).

Many of these findings have been contested $(173,181)$, and such disputes are difficult to resolve. Many births must be studied in order to determine whether slight variations-and most are very slight-are significant or chance. Methods of ascertaining relationships between variables differ, and so do their results. Essential variables may escape identification or may be left unstudied due to lack of data $(180,181)$.


Fig. 1. Simplified schematic representation of the chromosomal mechanism of sex determination.

Variations in the sex ratio at birth imply that one or both of two factors may be influencing the sex ratio. First, conditions of the male and/or female reproductive tracts may favor survival of and fertilization by sperm carrying a particular sex chromosome $(73,109,130,144,163,164$. 165). Second, after fertilization conditions in the uterus may favor the implantation or fetal survival of one sex over the other $(88,101,107,113,151,172,200,201)$. Presumably, a sex determination technique would have to affect one of these two factors. But the complexity of statistical analysis of sex ratio variations makes it difficult for such studies to reveal the biological factors involved, and, at this point, the discovery of any mechanism which might be manipulated to preselect sex seems more likely to come from laboratory and clinical investigations,

## CURAENT RESEARCH

Research on sex preselection has concentrated on five areas:

- timing of coitus in relation to ovulation
- altering conditions in the female reproductive tract
- separating $X$ - from $Y$-bearing sperm in vitro
- immunizing females against $Y$-bearing sperm
- determining the sex of the fetus in utero.

The first four approaches depend on the existence of consistent differences in the morphology or behavior of $X$ and $Y$-bearing sperm. Much sex determination research has been a search for such differences. Some have been found, but utilizing them to affect sex of offspring has proved to be another matter (15). Success has been achieved in the fourth area of research; reliable methods of ascertaining the sex of a fetus are available, but they are limited to use when pregnancy is relatively advanced.

## Timing of Insemination

The most popular of modern sex preselection techniques rests on the hypothesis that timing of coitus in relation to ovulation affects the sex of offspring. Since almost a cen-
tury ago, when data to support this theory were first presented, researchers have disputed over whether such an effect exists and, if it does, whether insemination close to intercourse favors the conception of males or females.

Most studies with rodents, rabbits, and cattle have found that the timing of insemination in estrus did not affect the sex ratio of offspring ( $6,11,33,69,131,189$ ), although some report otherwise $(31,70)$. Human births are much more difficult to study because records of coital timing may be unreliable and because many births must be recorded if small changes are to be detected.

Regarding the effect of timing of insemination on the sex of human offspring, two opposing claims exist. The older theory contends that a male child is more likely when insemination takes place early in the menstrual cycle. Statistical evidence to this effect was reported by German researchers in the late 19th and early 20th centuries, before it was known that ovulation occurs not during menstruation, but in mid-cycle $(56,138,168)$. Recently James has presented indirect evidence (76) to back up the early data, including, for example, his observation that in Israel a lower ratio of male to female births occurs among Jews than among non-Jews. James attributes this to the practice by Orthodox Jews of niddah-abstinence from coitus for a week after menstruation (80). No biological explanation for this effect has been offered.

The opposite hypothesis, and a basis for the sex determination method popularized by Shettles $(146,147)$, is that a male child is more likely when coitus takes place close to ovulation. Shettles derives his theory from reports by Kleegman $(89,90,91)$ and others $(70,153)$ on the outcomes of artificial inseminations. To explain the effect of timing of insemination, Shettles hypothesizes that Y -bearing sperm, having slightly less nuclear material than X-bearing sperm, move more rapidly but lose fertilizing capacity more quickly. Therefore, he argues, if insemination occurs at the time of ovulation, when cervical mucus is most easily penetrated by sperm, a Y-bearing sperm is more likely to reach the ovum first, producing a male child. If insemination takes place several days before ovulation, most $Y$-bearing sperm will have died before the ovum becomes available, making fertilization by an X-bearing sperm-and the conception of a female-more likely (146,147,163,164,165,167).

Shettles claims that when the last insemination takes place two or three days before ovulation, the children conceived will be female in 80 percent of the cases, while insemination within a few hours of ovulation will produce 80 percent males. As evidence of the effectiveness of his sex determination method, which also includes recommendations about coital position, pre-coital douching, and desirability of female orgasm, Shettles cites 19 successes in 22 attempts to conceive boys and 16 successes in 19 attempts to conceive girls (164). Seguy reports 77 successes in 100 cases with a similar method (160).

## Coitus or Artificial Insemination

Guerrero claims to have resolved the conflict between the opposing versions of the timing theory by finding opposing trends for coitus and artificial insemination. In a study of 875 pregnancies among users of the rhythm method of contraception and 443 pregnancies following artificial insemination, he relates the sex of offspring to the time


Fig. 2. Sex ratio of children born, by day of coitus or of artificial insemination relative to basal body temperature (BBT) shift, as reported by Guerrero (66). Reprinted with permission from the New England Journal of Medicine (291: 1057, 1974).
interval between insemination and the slight rise in basal body temperature (BBT) which usually accompanies ovulation (see Population Report 1-1). Guerrero finds that, among the offspring of rhythm users, the percentage of males was highest when the interval between insemination and BBT shift was longest. For example, when coitus took place six to nine days before ovulation, 68.3 percent of all births were male. When coitus took place the day of ovulation, 43.5 percent were male. Among infants born after artificial insemination, the opposite trend appeared (66) (see Fig. 2). Both trends were statistically significant for the period before the BBT shift. Biological mechanisms responsible for the difference in the trends have yet to be found (118).
While Guerrero's study finds a significant relationship between sex of offspring and interval between insemination and BBT shift, it also illustrates the difficulty of using coital timing as a sex preselection technique. The day of BBT shift is not predictable (149), so a couple can never know exactly how soon ovulation will occur. Because the chances for conceiving a girl apparently rise as high as 2 out of 3 only when intercourse occurs on the day of the BBT shift, a couple wanting a girl might be able to use coital timing effectively for sex preselection-provided they could correctly guess that an observed rise in BBT signaled ovulation. The chances of conceiving a boy apparently rise as high as 2 out of 3 only when the coitus responsible for fertilization occurs four or more days before the BBT shift. But, since usually sperm live no more than two days in a woman's reproductive tract (17), coitus four days before ovulation seldom results in fertilization. According to Marshall's calculations, the chance of pregnancy due to insemination on the fourth day before ovulation is only 13 percent and on earlier days is far less (117). Couples desiring a boy might have to wait several years for a live birth and then would face a 1 in 3 chance that the child would be female (141). Using coital timing in the hope of conceiving a boy might prove moderately effective as a contraceptive technique, but disappointing as a sex determination method.

## Douches

Pre-coital douches have been recommended as a sex determination method, but they have not been proved effective. Such douches are intended to alter the acidity ( pH )
of the vagina in order to create an environment favorable to sperm bearing one sex chromosome and hostile to the others.

Altering vaginal pH by douching was first recommended as a sex preselection method in the 1930s $(30,159)$, after Unterberger's report that an alkaline vaginal environment inactivated X -bearing sperm (186). The report had no factual basis (159). Recently one researcher claimed to have demonstrated the effect of altered vaginal pH on sex ratios in rabbits (193), but in vitro tests show no difference in the rates at which $X$ - and $Y$-bearing human sperm move through fluids of various pHs (37). Despite lack of conclusive evidence, recommendations for douching have persisted. Shettles suggests douching with diluted white vinegar to create a more acid environment, favoring conception of a girl, or with a baking soda solution, which is slightly alkaline, to favor boys (164). Any effect of these mild douches, however, is probably obscured by the alkalinity of the ejaculate (119).

## Sperm Separation

Sedimentation, centrifugation, natural sperm motility, and electrophoresis have been used in attempts to separate X - from Y -bearing sperm in vitro. Some experiments have been successful, but they have been difficult to repeat because many uncontrolled variables exist in most procedures (170). Sperm separation techniques are still at a primitive stage of development, but, if a practical method is developed, it could be highly effective.

Until recently, the study of sperm separation has proceeded slowly because no X - and Y -bearing sperm could be distinguished in vitro. Animal sperm fractions must be tested by inseminating females, then determining the sex of offspring. The process requires time and money, and, due to the limited number of animals which can be conveniently studied, it cannot clearly reveal small shifts in the sex ratio (159).

A major advance came several years ago, when researchers discovered an in vitro technique for distinguishing $X$ from $Y$-bearing human sperm. When human sperm are stained with quinacrine, quinacrine mustard, or quinacrine hydrochloride, the Y -chromosome fluoresces more brilliantly under a mercury vapor light source than does other cell material $(13,175,203)$ (see Fig. 3). This technique should speed research into separation methods because it can be used to screen human sperm fractions before trying insemination. Quinacrine staining does not identify the Y -chromosome in nonprimate species, however, so experimentation is still limited.

## Separation by Sedimentation or Centrifugation

Because X -bearing sperm contain 3 or 4 percent more chromosomal material (175) and therefore may have a higher specific gravity and/or volume than $Y$-bearing sperm (102), attempts have been made to separate sperm by sedimentation or by centrifugation. In some experiments, rabbit and bull sperm fractions have produced significantly altered sex ratios $\{23,24,92,97,102,103$, $154,155,169,170$ ), but other experiments have failed $(14,18,19,25,32,100,102,105)$. The successful techniques have proved difficult to standardize, and other researchers have been unable to duplicate them (10). Rohde et al., using quinacrine staining to check results, recently reported separating humari sperm according to sex chromosomes by centrifuging (145).

Some researchers conclude that no sedimentation or centrifugation method can consistently separate $X$ - and $Y$ bearing sperm. They point out that any differences in volume or specific gravity of sperm resulting from weight and size differences between the sex chromosomes are obscured by much greater variation among individual sperm, in different ejaculates from the same donor, and among sperm from different donors $(10,142)$. On the other hand, some researchers attribute the success of their experiments not directly to volume or specific gravity differences, but to greater damage to $X$-bearing sperm due to centrifugal force (103) or to greater agglomeration of Xbearing sperm during sedimentation (97).

## Separation by Sperm Motility

Several attempts to separate $X$ - from $Y$-bearing sperm have been based on the hypothesis of differential sperm motility-that is, that Y -bearing sperm swim faster than $X$-bearing sperm. This has been demonstrated in vitro in human cervical mucus $(82,144)$, but not enough $Y$-bearing sperm could be obtained by the techniques involved to make them practical as sperm separation methods (144). Ericcson et al. recently reported separating $X$ - from $Y$ bearing human sperm by placing a solution of sperm on a column of bovine serum albumin. Apparently, Y-bearing sperm moved more quickly into the albumin. The researchers hypothesize that $Y$-bearing sperm swim faster and are better able to penetrate the boundary between solution and albumin than are X-bearing sperm (43). Although others have been unable to duplicate the experiment $(46,148)$. Ericcson has recently established a com-pany-named "Gametrics"-in California which will specialize in separating both human and animal sperm.

## Separation by Electrophoresis

Electrophoresis of sperm is based on the hypothesis that X - and Y -bearing sperm carry opposite electrical charges (93). Sperm in solution are placed in a chamber, direct current is run through the solution, and sperm which may collect at the electrodes are drawn off to be tested by insemination or quinacrine staining (see Fig. 4).

Schröder, who performed the first electrophoresis experiment in the 1930s in Moscow, claimed that under certain conditions 80 percent females were conceived from rabbit sperm drawn off at the negative electrode $(157,158)$ Gordon, in the 1950s, also claimed some success with rabbit sperm $(60,61)$, but other studies have failed to demonstrate conclusively that electrophoresis separates $X$ - from $Y$-bearing sperm $(67,68,96,110,162)$ or, more fundamentally, that $X$-bearing and $Y$-bearing sperm possess different surface charges $(12,126,132,188)$, Despite the apparent lack of agreement, researchers now studying electrophoresis still believe the technique will work if proper in vitro conditions can be discovered (184).

Passing sperm through an ion-exchange resin to separate $X$ - from $Y$-bearing sperm on the basis of electrical charges has not succeeded. A large European trial with bull sperm treated in this way failed to produce the desired sex ratio shift (86). Black reports that he could not consistently separate human sperm in ion exchange resins, partly because sperm from different donors reacted differently and because many other variables, some difficult to control, affected the experimental process (26).


Fig. 3. Y-chromosomes are identified by bright spots (see arrows) in human sperm stained with quinacrine hydrochloride and observed through a fluorescence microscope, at approximately $2,500 \times$ magnification. (Courtesy of Dr. Peter W. Barlow) Photograph has been retouched to make the spots more visible.

Other attempts at separating X - from Y -bearing sperm include froth flotation, which was unsuccessful (123). and subjection of sperm to reduced atmospheric pressure, which appeared to have some effect in one study (49) but could not be confirmed (87). Schilling and Petac report altering sex ratios by treating rabbit and swine sperm with various enzymes and chemicals. Significant shifts toward a higher proportion of males-up to 65 percentwere produced by treating rabbit sperm with the hormone estradiol, with the enzyme esterase, and with ammonium sulfate; and by treating swine sperm with sodium hydroxide and with ammonium sulfate. A lower proportion of males-as low as 33 percent-resulted from rabbit sperm treated with hypotonic extender (a sodium chloride solution) and with the enzymes asparaginase and hyaluronidase; and from swine sperm treated with ascorbic acid. The researchers found that the sex ratio of offspring depended not only on the substance used to treat sperm, but also on the proportion of sperm remaining motile in the treated sample (156).

## Immunologic Means

The possibility of altering sex ratios by immunologic means has been recognized since the 1950s (47.152), when the Y -linked histocompatibility ( $\mathrm{H}-\mathrm{Y}$ ) antigen was discovered (42). This antigen causes female mice to produce antibodies and reject skin transplants from male mice of the same inbred strain. Its presence on mouse sperm $(58,95)$ and on cells from other male mammals, including men, (192) has recently been demonstrated. Since more of the antigen resides on $Y$-bearing than on X -bearing sperm $(58,95)$, theoretically a serum from females immunized with male cells would inactivate mostly Y -bearing sperm.

So far, most attempts to immunize female mice or rabbits by injecting them with sperm or other sources of male antigens have failed to alter the sex ratio of offspring (16,

76,120,121,122). Immunization against $Y$-sperm may be unsuccessful not because anti-Y antibodies do not develop, but because sperm in the female reproductive tract are inaccessible to the antibodies (20). Furthermore, male fetuses are unaffected by immunization of the mother (121). Since a maternal immune response to paternal antigens occurs in normal pregnancies, maternal recognition of and immunologic tolerance to male cells may also be a normal part of pregnancy (88). Lappé and Schalk hypothesize that, at least in some mouse strains, normal immunologic responses act to maintain a balanced sex ratio at birth. By removing the spleen, which is essential for the production of certain antibodies, they were able to increase significantly the percentage of males in mouse litters (98).

The attempt to use immunologic means to affect mouse sperm in vitro has been moderately successful. Researchers at the Memorial Sloan-Kettering Cancer Center in New York City, after treating mouse sperm with H-Y antiserum and inseminating females, found that offspring showed a slightly altered sex ratio-approximately 45 percent were male (20).

Immunologic sperm treatment is far from having practical application. The alternation of the sex ratio is slight Also, because almost all mouse sperm carry $H-Y$ antigens in varying amounts, treatment with H-Y antiserum apparently inactivates 70 to 80 percent of the sperm $(58,95)$. creating a sample rich in X-bearing sperm but low in fertility. In order to make the method practical, ways must be found not only to increase the alteration in the sex ratio, but also to concentrate surviving sperm in a more fertile sample (5). The method allows only selection for females.

## Fetal Sex Identification and Induced Abortion

The sex of the fetus in utero can be identified and selective induced abortion used to assure that only a child of the desired sex is born alive. Methods of ascertaining fetal sex have been available since the mid-1950s. They are used on a limited scale to identify the possible victims of sex-linked hereditary diseases (such as hemophilia), which in most cases strike only males, but their use for sex preselection probably will not be widely adopted.

Fetal sex can be identified by examining fetal cells found in amniotic fluid. The cells, obtained by amniocentesis (the withdrawal of amniotic fluid by a needle inserted through the abdominal wall) can be checked for the presence of sex chromatin, a mass of stainable nuclear material seen in some body cells from females (36,55, $74,83,113,166)$, or of fluorescent $Y$-bodies $(85,187)$, or analyzed by karyotyping, an examination of individual chromosomes to determine which sex chromosomes are present. Amniocentesis can only be safely performed after 16 weeks' gestation (114), past the period when relatively safe and simple early abortion methods can be employed. It seems unlikely, therefore, that fetal sex determination and induced abortion will be widely adopted as a sex preselection technique. Only five percent of US doctors recently surveyed would perform amniocentesis for sex preselection (44).

Searching for a simpler way to determine fetal sex, researchers have examined maternal blood for fetal lymphocytes (a type of white blood corpuscle) which may pass
through the placenta. The presence of Y -chromosomes in the lymphocytes indicates a male fetus. Preliminary work looks promising, but the method cannot be used before the 12 th week of pregnancy $(35,64,65)$. Another technique, which attempts to determine fetal sex by examining cells in cervical mucus taken from pregnant women in the first (59) or second trimesters (114), has not succeeded.

Edwards and Gardner have developed an alternate method of postfertilization sex selection $(41,57)$. They have been able to determine the sex of rabbits at the blastocyst stage-after fertilization but before implantation-by recovering the blastocyst, removing a few cells, checking them for the presence of sex chromatin, then, if the blastocyst is of the desired sex, transferring it to a recipient female. Removing a few cells apparently does not damage the blastocyst $(57,194)$. Edwards and Gardner have not yet conducted detailed work involving human embryos (40). The technical difficulties of recovering the blastocyst, removing a few cells, and returning it to the uterus will probably keep the technique from ever becoming a practical sex preselection method.

## POTENTIAL EFFECTS

Some social scientists and demographers predict that sex determination would result in smaller families, a surplus of males, slowed population growth, and dramatic social change. Others claim the effects would be slight or shortlived. The debate cannot be resolved; the effects of sex determination remain a subject for intriguing but largely unverifiable speculation.

## Possible Demographic Effects

Two arguments support the contention that the use of sex determination would reduce population growth. First, at present, it is argued, some couples will continue having children until their desires for offspring of a certain sexusually for one or more sons or for at least one child of each sex-are satisfied. Sex preselection would make such "gambling" unnecessary and thus would allow smaller families. Second, many couples want more boys than girls, while few want the reverse. If sex preselection allowed these desires to be translated into fact, and a great preponderance of boys were born, there would be a shortage of females when those children grew up. The total reproductive capacity of the population would then be less than if an equal number of both sexes had been born (133). If a preference for a majority of male offspring persisted for several generations, the effect could eventually be substantial (161).

Evidence about couples' sex of child preferences comes mainly from three sources:

- Attitude surveys, in which couples were asked about family sex composition and size ideals or child-bearing expectations.
- Analyses of fertility behavior, which study, for example, whether those with few sons at low parities went on to have more children than other couples did.
- Studies which examine whether current contraceptive practice is related to the sex of the acceptor's children.

Attitude surveys reveal the widespread desire for at least one child of each sex $(51,53,137,174)$ or for at least one son $(53,94)$. Perhaps the strongest desire for sons is reported from Korea, where 53 percent of the women polled in a 1971 survey said they would continue having children until they bore a son and 25 percent in Seoul would permit their husbands to take concubines if they themselves produced no sons (28). Attitude surveys show that couples with few or no sons $(21,52,53,94,124)$ or whose children are all of the same sex $(7,51,137,195$ 196) intend or expect to have more additional children than do other couples. Polls also report that many people prefer a majority of boys among their offspring $(7,28,38$, $48,52,94,99,115,116,174,198)$.

Some evidence suggests that sex of child preferences affect fertility behavior. Some studies report that couples whose first several children were of the same sex $(51,63,185,195)$ or predominantly female $(53,199,202)$ tended to have another child sooner or to have larger completed families than did other couples. Reports from several developing countries show that contraception acceptance rates or particularly sterilization and IUD acceptance rates were low among those with few or no sons $(4,27,53,54,94$, 133).

Not all studies find evidence that the lack of sons leads to larger families. Data from north India, Morocco, and East Pakistan (now Bangladesh) show that couples with a high percentage of sons tended to have more children than did others (140). Repetto concludes that, because sons brought in more income or burdened family resources less than did daughters, couples with sons may have felt able to afford more children.


Fig. 4. Electrophoresis device used in attempt to separate bull sperm. (Courtesy of Dr. H. D. Hafs)

SOURCE: Reprinted from Hafs \& Boyd (67) with the permission of H. D. Hafs and the American Society of Animal Science.

Although methodological problems make drawing conclusions from these data risky (199), in general the evidence seems to indicate a strong preference for sons in some developing areas, no apparent strong preference in other developing areas, and some desire for at least one child of each sex in developed countries (53). Such desires probably affect fertility behavior, but, because so many factors interact to influence childbearing, it is difficult to assess the role that sex of child preferences actually play. A consistent relationship between son preference and fertility behavior cannot be assumed (199).

It is even more difficult to predict how couples might behave if sex determination were available (197). Much would depend upon the method and its effectiveness $(80,81,197)$. For example, if a sperm separation technique is developed, its use would be limited by the acceptance of artificial insemination. In a small sample of US college students, 17 percent of those who in general approved of sex determination would not use a method that required artificial insemination; an additional 33 were "not sure" (116). Furthermore, techniques affecting sex at conception could be used only with planned pregnancies, and many pregnancies are unplanned ( 44 percent in the USA between 1966 and 1970, for example) (197).

Whether sex control would have long-term demographic effects due to an unbalanced sex ratio also cannot be assessed because many interrelated factors influence fertility decisions. If boy preference in one generation resulted in a shortage of women in the next, would the "value" of girls then rise, encouraging couples to have more girls and in the long run returning the sex ratio to approximately 50:50 ( 136,197 )? Or would long-standing cultural attitudes perpetuate boy preference for many generations, whatever the social consequences (45)?

## Possible Social Effects

Despite the fact that no sex preselection method is likely to be completely effective or universally used, both proponents and opponents of sex determination have predicted extreme social consequences if an effective method became available $(45,127,134,135)$. Etzioni foresees that in the USA a sex ratio shift as small as seven percent (or a ratio of 54.75 males to 45.35 females) would bring later marriage, more prostitution and male homosexuality, an increased number of men who never marry, less cultural activity, and more crime (45). Postgate, considering the effect of sex control on the developing countries especially, speculates that:

> All sorts of taboos would be expected and it is probable that a form of purdah [the Hindu practice of secluding women] would become necessary. Women's right to work, even to travel alone freely, would probably be forgotten transiently. Polyandry might well become accepted in some societies; some might treat women as queen ants, others as rewards for the most outstanding (or most determined) males. Masculine homosexuality would almost certainly become accepted. . Substitutes for normal sex, mechanical and pictorial, would be widely used. . . (127).

Even if the use of sex preselection did not unbalance the sex ratio, it might have some social consequences. Where the desire for a male first child prevails, academic and economic success, susceptibility to social pressure, and other characteristics more common to firstborn than to subsequent children would fall increasingly to males (3, 197).

Since no effective and generally acceptable sex determination method exists, speculations about demographic and social effects are hypothetical. If, at present, boy preference does lead to larger families, family planning programs which seek to encourage parents to plan and space their offspring can best respond by encouraging an equal appreciation of children of both sexes. This has already begun in some countries. In Korea the Planned Parenthood Federation has started an education campaign to change the strong preference for sons. Its slogans now appear on posters, hand fans, and bus window stickers: "Daughter or son, without distinction": "Daughter or son, stop at two and bring them up well" $(1,2)$. For the foreseeable future this approach can make a more practical and positive contribution to family welfare than claims that modern science can help parents preselect the sex of their children.

## BIBLIOGRAPHY

1. ANONYMOUS Hand-fans, posters push stop at two, WPY. PPFK Activity Report (Planned Parenthood Federation of Korea) No. 26, July-August 1974. [p. 3]
2. ANONYMOUS. Production of educational materials. PPFK Activity Report (Family Planning Federation of Korea) No. 22. October-December 1973. [p. 3]
3. ANONYMOUS. Selecting the sex of one's children. [Editorial] Lancet 1(7850): 203-204. February 9, 1974.
4. ANONYMOUS. Survey shows men accepting vasectomy at earlier age. PPFK Activity Report (Planned Parenthood Federation of Korea) No. 28, November-December 1974. [p. 2]
5. ABBOTT, J. Personal communication, March 26, 1975.
6. ADLER, H. C. and AUTRUP, E. H. Inseminationstidspunkt, befrugtningseffektivitet of konsfordeling hos kvaeg. In: Annual Report, Royal Veterinary and Agricultural College, Sterility Research Institute. Copenhagen, A/S Carl Fr. Mortensen, 1966. p. 155-160.
7. AGARWALA, S. N. A family planning survey in four Delhi villages. Population Studies 15: 110-120. 1961
8. ANDERSEN, H. and ROTTENSTEN, K. Forsøg med kønskontrol pä kaniner In: Annual Report, Royal Veterinary and Agricultural College, Sterility Research Institute. Copenhagen, A/S Carl Fr. Mortensen, 1962. p. 125-135.
9. APTEKAR, H. Anjea: infanticide, abortion and contraception in savage society. New York, William Goodwin, Inc., 1931. 192 p.
10. BAHR, G. F. Separation of $X$ - and $Y$-bearing spermatozoa by gravity: a reconsideration. In: Kiddy, C. A. and Hafs, H. D., eds. Sex ratio at birth-prospects for control. [Champaign, IIlinois ] American Society of Animal Science, 1971. p. 28-37.
11. BALLINGER, $H$. J. The effect of inseminations carried out early or late in oestrus on the sex ratio of calves born. Veterinary Record 86. 631. May 23, 1970.
12. BANGHAM, A. D. Electrophoretic characteristics of ram and rabbit spermatozoa. Proceedings of the Royal Sociely of London B: Biological Sciences 155: 292-305. 1961.
13. BARLOW, P. and VOSA, C, G. The Y chromosome in human spermatozoa. Nature 226: 961-962. June 6, 1970.
14. BEATTY, R. A. Genetic content and buoyant density of rabbit spermatozoa. Journal of Reproduction and Fertility 19: 379-384. 1969.
15. BEATIY. R. A. Phenotype of spermatozoa in relation to genetic content. In. Kiddy, C, A. and Hafs, H. D., eds. Sex ratio at birth-prospects for control. [Champaign, Illinois] American Society of Animal Science. 1971. p. 10-18.
16. BEATTY, R. A. The possibility of controlling sex ratio at conception. II. The phenotype of X - and Y -bearing spermatozoa. Memoirs of the Society for Endocrinology 7: 93-97. 1960.
17. BEDFORD, J. M. Sperm transport, capacitation and fertilization. In: Balin, H. and Glasser, S., eds. Reproductive biology. Amsterdam, Excerpta Medica, 1972. p. 338-392.
18. BEDFORD, J. M. and BIBEAU, A. M. Failure of sperm sedimentation to influence the sex ratio of rabbits. Journal of Reproduction and Fertility 14: 167-170. 1967.
19. BENEDICT, H. C., SHUMAKER, V. N., and DAVIES, R. E. The bouyant density of bovine and rabbit spermatozoa Journal of Reproduction and Fertility 13: 237-249. 1967.
20. BENNETT, D. and BOYSE, E. A. Sex ratio in progeny of mice inseminated with sperm treated with H-Y antiserum. Nature 246(431): 308-309. November 30, 1973.
21. BERELSON, B. Turkey: national survey on population. Studies in Family Planning No. 5. December 1964. p. 1-5.
22. BERGUES, H. La prévention des naissances dans la famille: ses origines dans les temps modernes. IThe prevention of birth in the family: its origins in modern times] Paris, Presses Universitaires de France, 1960. 400 p .
23. BHATTACHARYA, B. C. Die verschiedene Sedimentationsgeschwindigkeit der $X$ - und $Y$-Spermien und die Frage der willkurlichen Geschlechtsbestimmung IThe different sedimentation speeds of $X$ - and $Y$-sperm and the question of optional sex determination) Zeitschrift für Wissenschaftliche Zoologie 166: 203250. 1962.
24. BHATTACHARYA, B C. Sex control in mammals. Zeitschrift für Tierzuchtung und Zuchtungsbiologie 72: 250-254, 1958.
25. BHATTACHARYA, B. C., BANGHAM, A. D., CRO, R. J., KEYNES, R. D, and ROWSON, L. E A. An attempt to predetermine the sex of calves by artificial insemination with spermatozoa separated by sedimentation. Nature 211(5051): 863. August 20, 1966.
26. BLACK, D. Personal communication, May 6, 1975
27. CHITRE, K. T., SAXENA, R. N., and RANGANATHAN, H. N. Motivation for vasectomy. Journal of Family Welfare 11(1): 36-49. September 1964.
28. CHUNG, B. M., PALMORE, J. A., LEE, S. J., and LEE, S. J. Psychological perspectives: family planning in Korea. Psychological Studies in Population/Family Planning 1(7): 1-43. November 1973
29. COHEN, M. R. Differentiation of sex as determined by ovulation timing International Journal of Fertility 12(1): 32-38 January-March 1967.
30. COOK, R. Sex control again in the "News," Journal of Heredity 31: 265-271. 1941.
31. COOLEY, C L. and SLONAKER, J. R. The effects of early and late breeding on the mother and the sex ratio of the albino rat. American Journal of Physiology 72: 595-613. 1925.
32. COUROT, M. and ESNAULT, C. Sédimentation du sperme et sex-ratio chez les bovines. [Sedimentation of sperm and sex ratio of cattle] Annales de Biologie Animale, Biochimie, Biophysique 13(3): 329-334. 1973.
33. CREW, F. A. E, The relation of the sex of offspring to the time of coitus during the oestrus cycle. British Medical Journal 2(3489): 917-919. November 19, 1927.
34. DAWSON, E. R. The causation of sex in man. 2nd ed. London, H. K. Lewis \& Company, 1917. 226 p.
35. De GROUCHY, J. and TREBUCHET, C. Transfusion foetomaternelle de lymphocytes sanguins et detection du sexe du foetus. [Feto-maternal transfusion of blood lymphocytes and detection of sex of letus] Annales de Genetique 14(2): 133-137. 1971.
36. DEWHURST, C. J. Diagnosis of sex before birth Lancet 1(6921) 471-472. Aprit 21, 1956.
37. DIASIO, R. B. and GLASS, R. H. Effects of pH on the migration of $X$ and $Y$ sperm. Fertility and Sterility 22(5) 303-305. May 1971
38. DINITZ, S., DYNES, R., and CLARKE, A. Preference for male or female children: traditional or affectional? Marriage and Family Living 16(2): 128-130. 1964.
39. EDWARDS, A. W. F. Genetics and the human sex ratio Advances in Genetics 11: 239-272. 1962.
40. EDWARDS, R. G. Personal communication, April 14, 1975.
41. EDWARDS, R. G. and GARDNER, R. L. Sexing of live rabbit blastocysts. Nature 214: 576-577. May 6, 1967.
42. EICHWALD, E. J. and SILMSER, C. R. [Discussion of skingraft datal Transplantation Bulletin 2: 148-149. 1955.
43. ERICCSON, R. J., LANGEVIN, C. N., and NISHINO, M. Isolation of fractions rich in human $Y$ sperm. Nature 246: 421424. December 14, 1973.
44. ETZIONI, A. Selecting the sex of one's children. [ Letter to the Editor] Lancet 1(863): 932-933. May 11, 1974.
45. ETZIONI, A. Sex control, science, and society Science 161: 1107-1112. September 13, 1968.
46. EVANS, J. M. DOUGLAS, T. A. and RENTON, J. P. An attempt to separate fractions rich in human $Y$ sperm. Nature 253 (5490): 352-354. January 31, 1975.
47. FELDMAN. M. The antigen determined by a $Y$-linked histocompatibility gene. Transplantation Bulletin 5: 15-16. 1958.
48. FLANAGAN, J. C. A study of factors determining family size in a selected professional group. Genetic Psychology Monographs 25: 3-99. 1942
49. FOOTE, W. D. and QUEVEDO, M. M. Sex ratio following subjection of semen to reduced atmospheric pressure, In: Kiddy, C. A. and Hafs, H. D., eds Sex ratio at birth-prospects for control. [Champaign, illinois] American Society of Animal Science, 1971. p. 55-58
50. FRANKEL, M, S Sex preselection, [Letter to the Editor] Science 185(4157): 1109. September 27, 1974.
51. FREEDMAN, D. S., FREEDMAN, R., and WHELPTON, P. K. Size of family and preferences for children of each sex. American Journal of Sociology 66: 141-146, 1960.
52. FREEDMAN, R. Changing fertility in Taiwan. In: Greep, R. O., ed. Human fertility and population problems. Cambridge. Massachusetts, Schenkman, 1963. p. 106-149.
53. FREEDMAN, R. and COOMBS, L. C. Cross-cultural comparisons: data on two factors in fertility behavior. New York, Population Council. 1974. 94 p.
54. FREEDMAN, R. and TAKESHITA, J, Family planning in Taiwan Princeton, New Jersey, Princeton University Press, 1969. 501 p.
55. FUCHS, F, and RIIS, P. Antenatal sex determination, Nature 177: 330. February 18, 1956.
56. FURST, C. Knabenuberschuss nach Conception zur Zeit der postmenstruelien Anamie. IPredominance of the male sex in conceptions at the time of postmenstrual anemial Archiv fuer Gynakologie 28: 14-38. 1886.
57. GARDNER, R. L. and EDWARDS, R. G. Control of the sex ratio at full term in the rabbit by transferring sexed blastocysts. Nature 218; 346-349. April 27, 1968.
58. GOLDBERG, E. H., BOYSE, E. A., BENNETT, D., SCHEID, M and CARSWELL, E. Serological demonstration of H-Y (male) antigen on mouse sperm. Nature 232: 478-480. August 13, 1971.
59. GOLDSTEIN, A. L., LUKESH. R. B., and KETCHUM, M Prenatal sex determination by fluorescent staining of the cervical smear for the presence of a Y chromosome: an evaluation. American Journal of Obstetrics and Gynecology 115(6); 866. March 15, 1973.
60. GORDON. M. J. The control of sex, Scientific American 199 87-94. 1958.
61. GORDON, M. J. Control of sex ratio in rabbits by electrophoresis of spermatozoa. Proceedings of the National Academy of Sciences 43: 913-918. 1957.
62. GRAHAM, $H$. Eternal Eve: the history of gynaecology and obstetrics. Garden City, New Jersey, Doubleday. 1951. 691 p.
63. GRAY, E. and MORRISON, N. M. Influences of combinations of sexes of children on family size. Journal of Heredity 65(3): 169-174. May June 1974.
64. GROSSET, L. Personal communication, March 27, 1975.
65. GROSSET, L., BARRELET, V., and ODARTCHENKO, N. Antenatal fetal sex determination from maternal blood during early pregnancy. American Journal of Obstetrics and Gynecology 120(1): 60-63. September 1. 1974.
66. GUERRERO, R. Association of the type and time of insemination within the menstrual cycle with the human sex ratio at birth.

New England Journal of Medicine 291(20): 1056-1059. November 14, 1974.
67. HAFS, H. D. and BOYD, L. J. Galvanic separation of X- and Y-chromosome-bearing sperm. In: Kiddy, C. A. and Hafs, H. D., eds. Sex ratio at birth-prospects for control. (Champaign, IIlinois|American Society of Animal Science, 1971. p. 85-97.
68. HAFS, H. D. and BOYD, L. J. Sex ratios of calves from inseminations after electrophoresis of sperm. Journal of Animal Science 38(3): 603-604. 1974.
69. HAMMOND, J. The fertilization of rabbit ova in relation to time. Journal of Experimental Biology 11: 140-163. 1934.
70. HART, D, and MOODY, J, D. Sex ratio: experimental studies demonstrating controlled variations-preliminary report. Annals of Surgery 129: 550-571. May 1949.
71. HAUSCHKA, T, S, GRINNELL, S. T., MEAGHER, M, and AMOS, B. Sex-linked incompatibility of male skin and primary tumors transplanted to isologous female mice. In: Genetics and cancer: a collection of papers presented at the thirteenth annual symposium on fundamental cancer research, 1959. Austin, University of Texas, 1959. p. 271-294.
72. HIMES, N. E. Medical history of contraception. Baltimore, Willams and Wilkins Company, 1963. 521 p.
73. JALAVISTO, E. Geneological approach to factors influencing the sex ratio at birth. Annales Chirurgiae et Gynaecologiae Fennaie 41: 182-196. 1952.
74. JAMES, F. Sexing foetuses by examination of amniotic fluid. Lancet 1(6909): 202. 1956.
75. JAMES, W. H. Coital rate, sex ratio and parental age. [Letter to the Editor] Lancet 1(7712): 1294. June 19, 1971.
76. JAMES, W. H. Cycle day of insemination, coital rate, and sex ratio. Lancet 1(7690): 112-114. January 16, 1971.
77. JAMES, W. H. Cycle day of ovalation. Journal of Biosocial Science 4: 371-378. 1972.
78. JAMES, W. H. Factors affecting sex ratio I Letter to the Editor] New England Journal of Medicine 292(12): 650. March 20, 1975.
79. JAMES, W. H. Marital coital rates, spouses ages, family size and social class. Journal of Sex Research 10(3): 205-218. August 1974.
80. JAMES, W. H. Sex ratios in large sibships, in the presence of twins and in Jewish sibships. Journal of Biosocial Science 7(2): 165-169. April 1975.
81. JONES, R. J Sex predetermination and the sex ratio at birth. Social Biology 20(2); 203-211. June 1973.
82 KAISER, R., BROER, K. H., CITOLER, P., and LEISTER, B. Nachweis $Y$-Chromatin-positiver Spermien im Zervixsekret beim In-vitro-Penetrationstest. | Penetration of spermatozoa with $Y$ chromosomes in cervical mucus by an in vitro test] Geburtshilfe und Frauenheilkunde 34(6): 426-430. June 1974
83. KEYMER, E., SILVA-INZUNZA, E., and COTTS, W. E. Contribution to the antenatal determination of sex. American Journal of Obstetrics and Gynecology 74(5): 1098-1101. November 1957.
84. KEYNES, R. D. The predetermination of sex. Advancement of Science (London) 24: 43-46. 1967.
85. KHUDR, G and BENIRSCHKE, K. Fluorescence of the $Y$ chromosome: a rapid test to determine fetal sex. American Journal of Obstetrics and Gynecology 110(8): 1091-1095. August 15, 1971.
86. KIDDY, C. A. Sex control research. Presented at the Sixth Annual Convention of the American Simmental Association, Louisville, Kentucky, February 1, 1974. 7 p.
87. KIDDY, C. A and BAILEY, L. F. Sex ratio in rabbits from semen subjected to altered atmospheric pressure. Journal of Animal Science 37(3). 758-767. September 1973.
88 KIRBY, D. R. S., McWHIRTER, K. G., TEITELBAUM, M. S., and DARLINGTON, C. D. A possible immunological influence on sex ratio Lancet 2(7507): 139-140. July 15, 1967.
89. KLEEGMAN, S. J. Can sex be planned by the physician? In: Westin, B. and Wiquist, N., eds. Fertility and Sterility (Proceedings of the 5 th World Congress on Fertility and Sterility, Stockholm, June 16-22. 1966). Amsterdam. Excerpta Medica, 1967. (International Congress Series No. 133) p. 1185-1195.
90. KLEEGMAN, S. I Discussion of Tompkins, P. Interpretation of the basal body temperature curves ] In: Engle, E. T., ed. Proceedings, conference on diagnosis in sterility, sponsored by the National Committee on Maternal Health, New York City. January 26-27. 1945. Springfield, Illinois, Charles C Thomas, 1946. p. 152-153.
91. KLEEGMAN, S. J. Therapeutic donor insemination. Fertility and Sterility 5(1): 7-31, 1954.
92. KNAACK, J. Willkürliche Geschlechtsbeeinflussung durch sedimentierte Rinderspermien (Ergebnisse eines Grossversuchs). [Arbitrary influence on sex by sedimented bull sperms (results of a large-scale test)] Fortpflanzung Besamung und Aufzucht der Haustiere 4(4/5): 279-282. 1968.
93. KOLTZOFF, N. K. and SCHRÖDER, V. N. Artificial control of sex in the progeny of animals. Nature 131: 329. 1933.
94. KONG, C.-J. and CHA, J.H. Boy preference in Korea: a review of empirical studies related to boy preference. Psychological Studies in Population/Family Planning 1(8): 1-30. January 1974.
95. KOO, G. C., STACKPOLE, C. W., BOYSE, E. A., HÄMMERLING, U., and LARDIS, M. P. Topographical location of H-Y antigen on mouse spermatozoa by immunoelectronmicroscopy. Proceedings of the National Academy of Sciences 70(5): 1502-1505. May 1973.
96. KORDTS, E. Untersuchungen über die Eignung der männ-chen- und weibchenbestimmenden Spermien beim Kaninchen (zugleich eine Nachprüfung der Befunde von Vera Schröder). I Investigations on the suitability of electrophoresis for the separation of $X$ - and $Y$-bearing spermatozoa in the rabbit, and a re-examination of the findings of Vera Schroder] [Abstract] Animal Breeding Abstracts 21: 178. 1952.
97. KRZANOWSKI, M. Dependence of primaryand secondary sexratio on the rapidity of sedimentation of bull semen. Journal of Reproduction and Fertility 23: 11-20. 1970.
98. LAPPE, M and SCHALK, J. Necessity of the spleen for balanced secondary sex ratios following maternal immunization with male antigen. Transplantation 11(5): 491-495. May 1971,
99. LARGEY, G. P. Sociological aspects of sex pre-selection: a study of the acceptance of a medical innovation. [Ph D., State University of New York at Buffalo, 1972] Ann Arbor, Michigan, University Microfilms, 1975.110 p .
100. LAVON, U., VOLCANI, R., and DANON, D. An attempt to separate ejaculated bull spermatozoa into groups in order to improve fertility, In: Kiddy. C. A and Hafs, H. D., eds. Sex ratio at birth-prospects for control. [Champaign, lllinois] American Society of Animal Science, 1971. p. 19-27.
101. LAWRENCE, P. S. The sex ratio, fertility, and ancestral longevity, Quarterly Review of Biology 16: 35-79, 1941.
102. LINDAHL, $P$. E. Centrifugation as a means of separating $X$ and Y-chromosome-bearing spermatozoa In: Kiddy, C A and Hafs, H. D., eds. Sex ratio at birth-prospects for control. [Champaign, Illinois ] American Society of Animal Science, 1971. p. 69-75.
103. LINDAHL, D. Separation of bull spermatozoa carrying $X$ and $Y$-chromosomes by counterstreaming centrifugation. Nature 181: 784. March 15, 1958
104. LOWE, C. R. and MCKEOWN, T. The sex ratio of human births related to maternal age British Journal of Social Medicine 4: 75-85 1950
105. LUSH, J. L. The possibility of sex control by artificial insemination with centrifuged spermatozoa Journal of Agricultural Research 30(10): 893-913. May 15. 1925.
106. LYSTER, W. R. Altered sex ratio after the London smog of 1952 and the Brisbane flood of 1965. Journal of Obstetrics and Gynaecology of the British Commonwealth 81(8): 626-631. August 1974.
107. LYSTER, W. R. Fecundity and infantile cancer. [Letter to the Editorl Lancet 2(7823): 267.268. August 4, 1973.
108. LYSTER. W. R. Three patterns of seasonality in American births American Journal of Obstetrics and Gynecology 110(7): 1025-1028. August 1, 1971.
109. LYSTER, W. R. and BISHOP, M. W. H. An association between rainfall and sex rato in man. Journal of Reproduction and Fertility 10: 35-47. 1965.
110. MACHOWKA, W, W and SCHEGALOFF, S B. Die Reaktion der Spermatozoen auf konstanten Strom (Galvanotaxis). [The
reaction of spermatozoa to direct current] Wilhelm Roux Archiv für Entwicklungsmuchanik der Organismen 133: 694-700. 1935.
111. MacMAHON, B and PUGH. T. F Influence of birth order and maternal age on the human sex ratio at birth. British Journal of Preventive and Social Medicine 7(2): 83-86. April 1953.
112. MacMAHON, B. and PUGH, T. F. Sex ratio of white births in the United States during the Second World War. American Journal of Human Genetics 6: 284-292. 1954.
113. MAKOWSKI, E. K., PREM, K. A., and KAISER, I. H. Detection of sex of fetuses by the incidence of sex chromatin body in nuclei of cells in amniotic fluid. Science 123: 542-543. March 30 . 1956.
114. MANUEL, M., PARK, I. J., and JONES, H. W.. Jr. Prenatal sex determination by fluorescent staining of cells for the presence of Y chromatin. American Journal of Obstetrics and Gynecology 119(6): 853-854. July 15, 1974.
115. MARKLE, G. E. Sex ratio at birth: values, variance, and some determinants. Demography 11(1): 131-142. February 1974.
116. MARKLE, G. E., and NAM, C. B. Sex predetermination: its impact on fertility. Social Biology 18(1); 73-83. 1971.
117. MARSHALL. J. The risks of conception throughout the menstrual cycle. Medical Counterpoint 3(8): 47-49. August 1971.
118. MASTERS, W. H. Personal communication, March 11,1975, 119. MASTERS, W. H. and JOHNSON, V. E. Human sexual response. Boston. Little, Brown and Company, 1966. 366 p.
120. McLAREN, A. Does maternal immunity to male antigen affect the sex ratio of the young? Nature 195(4848): 1323-1324. September 29, 1962.
121. McLAREN, A. Growth of male young in mothers immunized against $Y$ antigen [Letter to the Editor] Transplantation 3(2): 259-261. March 1965.
122. McLAREN, A. Immunological control of fertility in female mice. Nature 201(4919): 582-585. 1964.
123. MORE O'FERRALL, G. J., MEACHAM, T. M., and FOREMAN, W. E. Attempts to separate rabbit spermatozoa by means of froth flotation and the sex ratio of offspring born. Journal of Reproduction and Fertility 16: 243-252. 1968.
124. MORRISON, W. A. Attitudes of females toward family planning in a Maharashtrian village. Milbank Memorial Quarterly 35: 67-81. 1957
125. MYERS, R. J. The effect of age of mother and birth order on sex ratio at birth. Milbank Memorial Fund Quarterly 32(3): 275281. 1954.
126. NEVO, A. C., MICHAELI, I., and SCHINDLER, H. Electrophoretic properties of bull and of rabbit spermatozoa. Experimental Cell Research 23: 69-83. 1961.
127. NIMKOFF, M. F. Will parents pick the sex of child. Science Digest 30(5): 65-68. November 1951.
128. NOVITSKI, E. and KIMBALL, A. W. Birth order, parental ages, and sex of offspring. American Journal of Human Genetics 10: 268-275. 1958
129. PARKES, A. S. Mythology of the human sex ratio In: Kiddy, C. A and Hafs, H. D., eds. Sex ratio at birth-prospects for control. [Champaign, Illinois] American Society of Animal Science, 1971. p. 38-42.

130, PARKES, A. S. Sexuality and reproduction. Perspectives in Biology and Medicine 17(3): 399-410. Spring 1974.
131. PEARL, R. Report of progress on animal husbandry investigations in 1916, Bulletin of Maine Agricultural Experiment Station (Orono, Maine) 261:121-144. June 1917.
132. PILZ, A. Das Verhalten der Säugetierspermien im elektrischen Feld. (The behavior of mammalian sperm in an electrical field] Zeitschrift fur Tierzuchtung und Zuchtungs-Biologie 60: 315-330. 1952.
133. POHLMAN, E. Some effects of being able to control sex of offspring. Eugenics Quarterly 14(4): 274-281. 1968.
134. POHLMAN, E. and RAO, K. S Why boy babies are preferred for adoption or procreation. Journal of Family Welfare (India) 15: 45-63. June 1969.
135. POSTGATE, J. Bat's chance in hell. New Scientist 58(840): 12-16. April 5, 1973.
136. POTTS, M. Make the possible available. New Scientist 58 (841): 84-85. April 12, 1973.
137. PRACHUABMOH, V. Factors affecting desire or lack of desire for additional progeny in rural Thailand In: Bogue, D. J., ed. Sociological contributions to family planning research. Chicago, University of Chicago, 1967. p. 364-409.
138. PRYLL, W. Kohabitationstermin und Kindsgeschlecht [Time of cohabitation and sex of the child] Munchener Medizinische Wochenschriff 63: 1579-1582. November 1916.
139. RAO, M. N and MATHEN, K. K. Rural field study of population control, Singur (1957-1969). Calcutta, All-India Institute of Hygiene and Public Health, 1970. 88 p.
140. REPETTO, R. Son preference and fertility behavior in developing countries. Studies in Family Planning 3(4): 70-76. April 1972.
141. REVELLE, R. On rhythm and sex ratio. [Editorial] New England Journal of Medicine 291(20): 1083. November 14, 1974
142. ROBERTS, A. M. Gravitational separatin of $X$ and $Y$ spermatozoa. Nature 238: 223-225. July 28, 1972.
143. ROBERTSON, J. S. and SHEARD, A. V. Altered sex ratio after an outbreak of hepatitis, Lancet 1(7802): 532-534. March 10, 1973.
144. ROHDE, W., PORSTMANN, T.. and DORNER, G. Migration of Y -bearing spermatozoa in cervical mucus. Journal of Reproduction and Fertility 33(1): 157-169. April 1, 1973.
145. ROHDE, W., PORSTMANN, T., PREHN, S., and DÖRNER, G. Gravitational pattern of the Y -bearing human sperm in density gradient centrifugation. Journal of Reproduction and Fertility 42(3): 587-591. March 1975.
146. RORVIK, D. M. and SHETTLES, L. B. You can choose your baby's sex. Look, April 21, 1970. p. 88-98.
147. RORVIK, D. M. and SHETTLES, L. B, Your baby's sex: now you can choose. New York, Dodd, Mead \& Company, 1970.127p.
148. ROSS, A., ROBINSON, J. A., and EVANS, H. J. Failure to confirm separation of $X$ - and $Y$-bearing human sperm using BSA gradients. Nature 253(5490): 354-355. January 31, 1975
149. ROSS, C and PIOTROW, P. T. Periodic abstinence: birth control without contraceptives. Population Report, Series I, No. 1. Washington, D.C., George Washington University Medical Center, Population Information Program, June 1974. 20 p.
150. RUBIN. E. The sex ratio at birth. American Statistician 21(4): 45-48. October 1967.
151. RUSSELL, W. T. Statistical study of the sex ratio at birth. Journal of Hygiene 36: 381-401. 1936.
152. SACHS, L. and HELLER, E. The sex-linked histocompatibility antigens. Journal of the National Cancer Institute 20(3): 555561. March 1958.
153. SCHELLEN, A. Artificial insemination in the human. Amsterdam, Elsevier Publishing Company, 1957. 429 p.
154. SCHILLING, E Experiments in sedimentation and centrifugation of bull spermatozoa and the sex ratio of born calves. Journal of Reproduction and Fertility 11: 469-472, 1966,
155. SCHILLING, E. Sedimentation as an approach to the problem of separating X - and Y -chromosome bearing spermatozoa, In: Kiddy, C. A. and Hafs, H. D., eds. Sex ratio at birth-the prospects for control. [Champaign, Illinois] American Society of Animal Science, 1971. p. 76-84.
156. SCHILLING, E and PETAC. D. Behandlung von Sperma mit chemischen Substanzen und das Geschlechtsverhältnis bei den Nachkommen von Kaninchen und Schwein. [ Treatment of semen with chemicals and sex-ratio in rabbits and swine] In: Proceedings, Seventh International Congress on Animal Reproduction and Artificial Insemination, Munich, June 6-9, 1972. Bonn, Deutschen Gesellschaft für Züchtungskunde, ${ }^{1972}$ ) p. $453-458$
157. SCHRÖDER, V. "Künstliche Geschlechtsregulation der Nachkommenschaft der Säugetiere und itre biologische Kontrolle" und "Ueber die biochemischen und physiologischen Eigentümlichkeiten der X - und Y -Spermien. L"Sex control of mammalian offspring and its biological test" and "The biochemical and physiological properties of X - and Y -bearing sperm"] [Abstract] Animal Breeding Abstracts 10(4): 252. December 1942.
158. SCHRÖDER, V. N. Fiziko-himičeskiil analiz fiziologii spermiev. V. Iskusstvennaja reguljacija pola u mlekopitajuščih. [Physico-chemical analysis of the physiology of spermatozoa. V. Artificial control of sex in mammals] [Abstract] Animal Breeding Abstracts 3: 166-167. 1934.
159. SEGAL. S.J. Status of research on the regulation of fertility. In: Parke, R., Jr, and Westoff, C. F., eds. Aspects of Population Growth Policy (Vol. 6, Research Reports of the Commission on Population Growth and the American Future), Washington, D.C.. U.S. Government Printing Office, 1972. p. 179-204.
160. SÉGUY, B. Les méthodes de sélection naturelle et volontaire des sexes. [Methods of natural and voluntary selection of the sexes] Journal de Gynécologie Obstetrique et Biologie de la Reproduction 4(1): 145-149. 1975.
161. SEROW, W. J. and EVANS, V. C. Demographic effect of prenatal sex selection. [Abstract] Population Index 36: 319. 1970.
162. SEVINC, A. Experiments on sex control by electrophoretic separation of spermatozoa in the rabbit. Journal of Reproduction and Fertility 16: 7-14. 1968.
163. SHETTLES, L. B. Conception and birth sex ratios. Obstetrics and Gynecology 18: 122-130. 1961.
164. SHETTLES, L. B. Factors influencing sex ratios. International Journal of Gynaecology and Obstetrics 8(5): 643-647. September 1970.
165. SHETTLES, L. B. The great preponderance of human males conceived. American Journal of Obstetrics and Gynecology 89(1): 130-133. May 1, 1964.
166. SHETTLES, L. B. Nuclear morphology of cells in human amniotic fluid in relation to sex of infant. American Journal of Obstetrics and Gynecology 71: 834-838. 1956.
167. SHETTLES, L. B. Samenmorphologie, zervikales Milieu, Zeitpunky der Insemination, und Geschlechtsverhältnisse. [Sperm morphology, cervical milieu, time of insemination and sex ratios ] Andrologie 5(3): 227-230, 1973.
168. SIEGEL. P, W. Bedeutung des Kohabitationstermines für die Befruchtungsfahigkeit der Frau und für die Geschlechtsbildung des Kindes. IThe significance of time of cohabitation for the fertility of the woman and for the sex development of the child] Munchener Medizinische Wochenschrift 63(21): 748 750. May 23, 1916.
169. STAMBAUGH, R and BUCKLEY, J. Association of the lactic dehydrogenase $X_{4}$ isozyme with male-producing rabbit spermatozoa. Journal of Reproduction and Fertility 25: 275-278. 1971.

170, STAMBAUGH, R. and BUCKLEY, J. Relationship of the $X$ and $Y$ chromosomes to enzyme variation in fractionated spermatozoa. In: Kiddy, C. A. and Hafs, H. D., eds. Sex ratio at birthprospects for control. [Champaign, Ilinois] American Society of Animal Science, 1971. p. 59-68.
171. STARKWEATHER, G. B. Law of sex London, J\&A Churchill, 1883. 276 p.
172. STERN, C. Principles of human genetics. 3rd ed. San Francisco, W. H. Freeman, 1973. 891 p.
173. STEVENSON, A. C. and BOBROW, M. Determinants of sex proportions in man, with consideration of the evidence concerning a contribution from X-linked mutations to intrauterine death. Journal of Medical Genetics 4. 190-221. 1967.
174. STINNER, W. F. and MADER, P. D. Sons, daughters or both?: an analysis of family sex composition preferences in the Philippines. Demography 12(1): 67-79. February 1975.
175. SUMNER, A. T., ROBINSON, J. A., and EVANS, H. J. Distinguishing between $X, Y$ and $Y Y$-bearing human spermatozoa by fluorescence and DNA content. Nature New Biology 229: 231 233. February 24, 1971.
176. TAEUBER, I. B. The population of Japan. Princeton, New Jersey. Princeton University Press, 1958. 461 p.
177. TAKAHASHI, $E$. The effects of the age of the mother on the sex ratio at birth in Japan. Annals of the New York Academy of Medicine 57: 531-550. 1954.
178. TALWAR, P. P. Effect of desired sex composition in families on the birth rate. Journal of Biosocial Science 7(2): 133-139. April 1975.
179. TEITELBAUM, M. S. Coital frequency and sex ratio. I Letter to the Editor] Lancet 1(7703): 800. April 17, 1971
180. TEITELBAUM, M. S. Factors affecting the sex ratio in large populations. Journal of Biosocial Science Suppl. 2: 61-71. 1970.
181. TEITELBAUM, M. S. Factors associated with the sex ratio in human populations. In: Harrison, G. A. and Boyce, A. J., eds. The structure of human populations, London, Oxford University Press, 1972. p. 90-109.
182. TEITELBAUM, M. S. and MANTEL, N. Socio-economic factors and the sex ratio at birth. Journal of Biosocial Science 3: 23-41. 1971.
183.TEITELBAUM, M. S., MANTEL, N., and STARK, C. R. Limited dependence of the human sex ratio on birth order and parental ages. American Journal of Human Genetics 23: 271-280. 1971.
184. TEJADA, R. Personal communication, March 20.1975.
185. THOMAS, M. H. Sex pattern and size of family. British Medical Journal 1(4709): 733-734. April 7. 1951.
186. UNTERBERGER, F. Geschlechtsbestimmung und Wasserstoffionenkozentration. [Sex determination and hydrogen ion concentration] Deutsche Medizinische Wochenschrift 58: 729 731. May 6, 1932.
187. VALENTI, C., LIN, C. C., BAUM, A., MASSOBRIO, M., and CARBONARA, A. Prenatal sex determination. American Journal of Obstetrics and Gynecology 112(7): 890-895. April 1, 1972.
188. VESSELINOVITCH. S. D. Microelectrophoresis of bovine spermatozoa, Cornell Veterinarian 49: 359-373. 1959.
189. VICKERS, A. D. Delayed fertilization and the prenatal sexratio of the mouse. Journal of Reproduction and Fertifity 20: 63-68. 1969.
190. VILINSKAS, J. Clinical studies in sex pre-determination. Woman Physician 26(8): 419-420. August 1971.
191 VISARIA, P. M. Sex ratio at birth in territories with a relalively complete registration. Eugenics Quarterly 14: 132-142. 1967.
192. WACHTEL, S. S., KOO, G. C., ZUCKERMAN, E. E., HÄMMER LING, U., SCHEID, M. P., and BOYSE, E. A. Serological crossreactivity between $H-Y$ (male) antigens of mouse and man. Proceedings of the National Academy of Sciences 71(4): 1215.1218. April 1974.
193. WAKIM, P. E. Determining the sex of baby rabbits by ascertaining the pH of the vagina of the mother before mating, Journal of the American Osteopathic Association 72(2): 173-174. October 1972.
194. WEATHERSBEE, C. Toward preselected sex. Science News 94: 119-120. August 3, 1968.
195. WESTOFF, C. F., POTTER, R, B., Jr, and SAGI, P, C. The third child: a study in the prediction of fertility. Princeton, New Jersey, Princeton University Press, 1963. 293 p.
196. WESTOFF, C. F, POTTER, R. B,. Jr., SAGI, P, C., and MISHLER, E. G. Family growth in metropolitan America. Princeton, New Jersey, Princeton University Press, 1961. 433 p.
197. WESTOFF, C. F. and RINDFUSS, R. R. Sex preselection in the United States: some implications. Science 184(4127): 633636. May $10,1974$.
198. WHELPTON, P. K., CAMPBELL, A. A., and PATTERSON, J. E. Fertility and family planning in the United States. Princeton, New Jersey, Princeton University Press, 1966, 443 p.
199. WILLIAMSON, N. E. Problems of measuring son preference. [1975] 28 p. (Unpublished)
200. WINSTON, S. The influence of social factors upon the sexratio at birth. American Journal of Sociology 37(1): 1-21. July 1931.
201. WINSTON, S Some factors as related to the different sex ratio at birth. Human Biology 4(2): 272-279. May 1932.
202. WYON, J. B. and GORDON, J. E. The Khanna study, Cambridge, Massachusetts, Harvard University Press, 1971. 437 p.
203. ZECH. L. Investigation of metaphase chromosomes with DNA-binding fluorochromes. Experimental Cell Research 58: 463. 1969.
204. ZIRKLE, C. The knowledge of heredity before 1900. In: Gunn, L., ed. Genetics and the 20th century: essays on the progress of genetics during its first 50 years. New York, Macmillan, 1951. p. 35-37.

