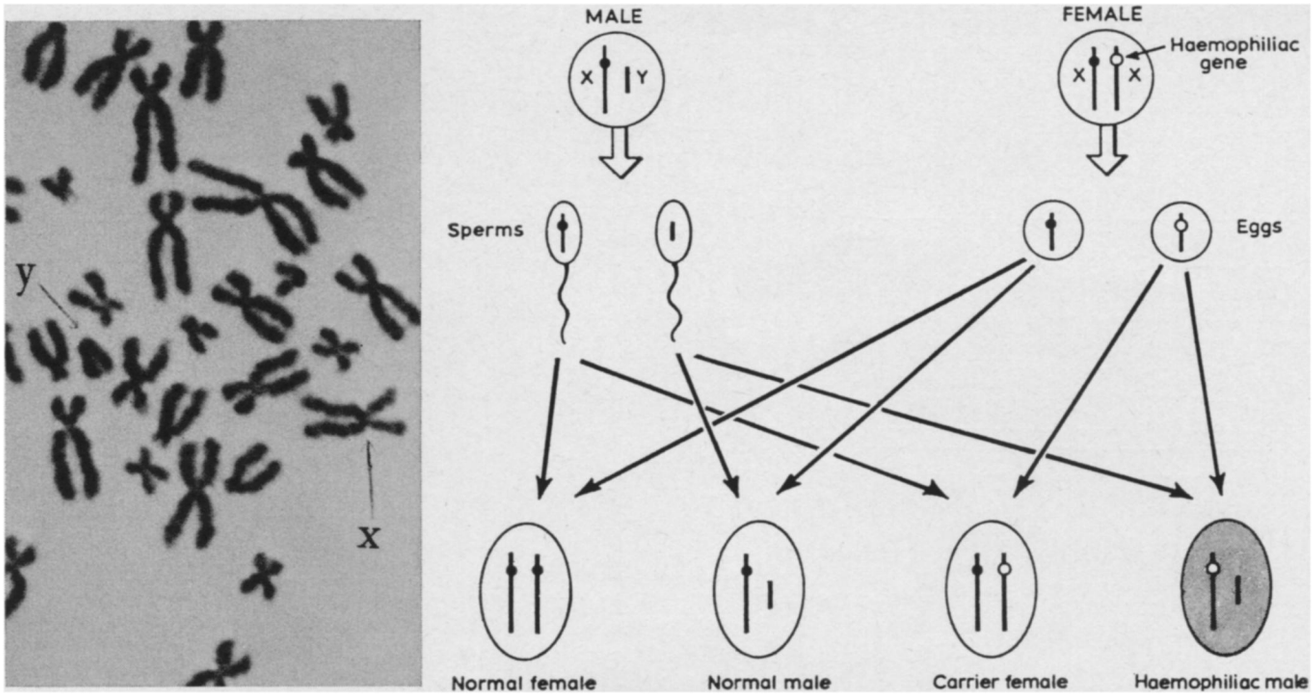


Human X and Y chromosomes (left). Diagram (right) shows hemophilia gene passed on by carrier female.

MICROBIOLOGY

Toward preselected sex

Scientists take the first step toward controlling or eradicating some sex-linked hereditary diseases

by Christopher Weathersbee

Galen, personal physician to the Roman Emperor Marcus Aurelius, told pregnant women to fill two small holes in the ground with urine. In one hole they were to plant wheat, in the other barley. If the wheat sprouted first they would bear a boy, if the barley, a girl.

It is probable that Galen got this recipe (for which, incidentally, an empirical basis has not been ruled out) from an Egyptian papyrus written 3,000 or 4,000 years earlier. This may be an indication of how long man has been gnawed by the urge to know, and even control, the sex of his unborn offspring.

Superstitions in this regard have persisted up until the present day, presumably filling the gap left by an almost total lack of scientific knowledge on the matter. Mothers bearing children this year are in the same state of ignorance as were ancient Egyptians.

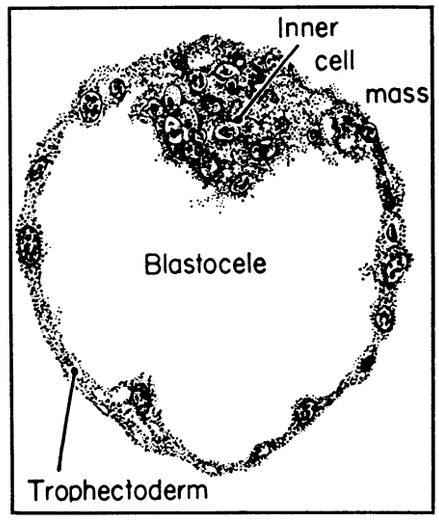
Some light on the subject is beginning to dawn. Not only is the possibility of accurate prediction raised, but also the possibility of controlling the sex of the child. It has already been done, in fact, with rabbits.

The researchers involved, however, are careful to point out that there is a big, perhaps unbridgeable gap between rabbits and men.

Dr. Robert Edwards and Richard Gardner of Cambridge University's department of physiology say they have been able to remove rabbit embryos while still in the blastocyst stage, surgically remove some blastocyst cells for a test to determine sex, then reimplant only the blastocysts destined to develop into the chosen sex.

Apart from the interest of ranchers and dairy farmers, the implications are obvious and enormous. If this procedure could be extended easily to man there might, for instance, be imbalances, even fads, in the selection by parents of one sex of child over another. Large imbalances in the ratio of men to women could strain society's seams, to put it mildly.

"The application of similar techniques to man is still remote," the researchers wrote in the May 2 NEW SCIENTIST, "and depends upon solutions being found to the many problems still



Pig blastocyst: too small to operate.

bedevilling attempts at the *in vitro* fertilization of human ova and the *in vitro* culture of human embryos." (A few workers report doing this, but others have not been able to duplicate their results.)

"But once such problems have been solved, these techniques could be used to eradicate sex-linked diseases. When it becomes possible to determine the sex of human blastocysts with certainty, and also to identify quite certainly women who are (carriers of) a sex-linked disease, then it will be a simple matter to insure that no such woman bears a male child.

(Male children suffer the preponderance of sex-linked hereditary diseases. Further, for a disease such as hemo-

. . . preselected sex

philia to occur in a female the father must also have it, so that preventing the birth of male hemophiliacs would eliminate the disease.)

"Would not the non-replacement of a blastocyst," the researchers conclude, "be socially and ethically far more acceptable than a full-scale abortion of the implanted, thriving fetus—the only alternative (to birth of diseased offspring) available today?"

Scientists trying this method on humans may be in for a fight despite this plea, however. Dr. Paul Ramsey, professor of religion at Princeton University now visiting Georgetown University Hospital, says there is a moral dividing line drawn in the early stages of the development of a fertilized egg.

Dr. Ramsey says that while the dividing cells still are capable of splitting into twin cell masses, each able to develop into a fetus, the cells cannot be considered to be invested with individuality. Beyond the stage where it can become two or more beings, the cell mass must be considered simply a human in the early stages of development.

He admits that the point appears a fine one, but he says it is strong and will bear a heavy argument. That argument is that destruction of the cell mass while it still is capable of twinning can only be considered contraception. Destruction after the twinning capability is lost is abortion, no matter what the stage of development nor how thriving.

The blastocyst is considered to be much too far along to be capable of twinning; twinning generally occurs during the third or fourth cell division.

Thus the physician applying the technique to a human would be in a dilemma. If he produced artificial twinning, as Dr. Edwards suggests, then the cell mass grown for tests, according to Dr. Ramsey's hypothesis, would be a perfectly legitimate human individual; destroying it in testing or because it is the wrong sex would be abortion.

In addition the physician more than likely would have induced superovulation to be sure of getting a fertilized ovum of the right sex. He might have eight cell masses, far more than the mother could nurture through pregnancy, yet each of the masses would be an individual whose destruction would be abortion.

While the basic idea is simple—throw out those fertilized eggs with the wrong sex—the technique is painstaking and beset with practical difficulties. It is based currently on the detection of bodies called sex chromatin that show up very early in the development of the female rabbit embryo.

Not many cycles of cell division after fertilization the ovum has developed into a tiny sphere filled with fluid, the blastocyst. In the rabbit (though not in man) the 2.4-millimeter diameter blastocyst has still to implant itself in the wall of the uterus. It can be removed from the mother's body and examined.

Holding the blastocyst by suction on the end of a micropipette, Gardner and Dr. Edwards make a slit in it. An even finer pipette is inserted and used to draw off 200 to 300 of the cells that line the blastocyst. The withdrawn cells are examined for sex chromatin. After recuperating from the surgery the blastocyst is either replaced in the womb of the mother or foster mother, or is discarded.

The microsurgical methods used are still not fully developed, and only about 20 percent of the reimplanted blastocysts came to term (some 75 percent would have been expected to survive removal and reimplantation if no operation had been performed). However, all the newborn rabbits were of the predicted sex.

The rabbit blastocyst is relatively far along in development before it buries itself in the wall of the uterus beyond possibility of removal. It can well afford to lose a few cells to testing and the sex chromatin is quite visible. This is not the case with all species. Mouse blastocysts, for instance, contain only about 100 cells, too few for operation.

Human blastocysts may contain 2,000 to 3,000 cells, enough that a few can be spared. But it remains to be seen whether the sex chromatin is visible before implantation. If it is not, other sexing techniques must be developed.

One such technique, Dr. Edwards suggests, might be to divide the ovum after it has gone through only three or four cycles of cell division; this happens spontaneously in the formation of identical twins. One part of the cell mass might somehow be stored while the other is allowed to develop outside the uterus to the point where its sex can be determined. If it is the right sex, the stored cells can be reimplanted.

The first application of the technique is likely to be found in animal breeding. Farmers building dairy herds don't want more than one or two male calves. The best beef, on the other hand, comes from males, so meat ranchers want only enough cows for breeding. purposes.

Other immediate benefits of the work may be felt in the laboratory. Using the microsurgical techniques, embryologists might perform operations on blastocysts to determine the effect of removing or adding various tissues.