

SEX RATIO AT BIRTH—PROSPECTS FOR CONTROL

A Symposium

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PREFACE

THE symposium "Sex Ratio at Birth—Prospects for Control" was held July 31 and August 1, 1970 at the Pennsylvania State University, University Park. The symposium was conceived in an informal meeting of the two editors of these proceedings at the Annual Meeting of the American Society of Animal Science in 1969 at Purdue University. Man's desire to control the sex of offspring from domestic animals is as old as animal husbandry. Although a great deal has been written on the subject, most has been in the popular press and, unfortunately, the optimism often expressed has not been warranted. Consequently, a symposium of scientists engaged in this kind of research was held to summarize the experimental approaches which have been tested and to stimulate discussions and ideas which might hasten the accomplishment of sex control. This volume records the papers and discussions of the symposium.

The symposium was organized under the auspices of the American Society of Animal Science and its Physiology Program Committee. Extremely valuable aid in the organization and conduct of the symposium was provided by Dr. Ruppert Amann of Pennsylvania

State University. Special thanks are extended to the invited speakers without whose contributions the symposium would not have been possible. It was unfortunate Sir Alan Parkes could not attend, but his contribution was appreciated nevertheless. Recognition is also due Drs. R. G. Saacke, R. J. Gerrits and N. L. VanDemark for acting as chairmen of symposium sessions.

It would not have been possible to hold the symposium had it not been for the generous financial support of American Breeder's Service, Inc., Curtiss Breeding Service, Linde Division—Union Carbide Corporation, National Association of Animal Breeders, Ralston Purina Company, Syntex Research and The Upjohn Company.

The papers presented and the discussions following them serve to focus on some important aspects of current knowledge and attitudes about the ratio of sexes at birth and prospects for its control. We hope that this volume will serve to stimulate further thought and action on the subject.

CHARLES A. KIDDY
HAROLD D. HAFS

LIST OF INVITED SPEAKERS

- G. F. BAHR, M.D. Armed Forces Institute of Pathology, Washington, D.C.
R. A. BEATTY, Ph.D., University of Edinburgh, Scotland
L. E. CASIDA, Ph.D., University of Wisconsin, Madison
R. H. FOOTE, Ph.D., Cornell University, Ithaca, New York
W. D. FOOTE, Ph.D., University of Nevada, Reno
H. D. HAFS, Ph.D., Michigan State University, East Lansing
U. LAVON, Ph.D., The Volcani Institute of Agricultural Research, Rehovot, Israel
P. E. LINDAHL, Ph.D., University of Uppsala, Sweden
A. S. PARKES, Ph.D. The Galton Foundation, Lond
(Prepared a paper read by C. A. Kiddy)
E. SCHILLING, Ph.D., Max Planck Institute, Marier
R. STAMBAUGH, Ph.D., University of Pennsylvania, Philadelphia
J. A. Weir, Ph.D., University of Kansas, Lawrence

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Alhusen, H. D., Springdale, Ark.
 Allan, M. and W., Westtown, Pa.
 Alliston, C. W., West Lafayette, Ind.
 Almquist, J. O., University Park, Pa.
 Alverson, R., Columbus, Ohio
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 Arora, K. K., East Brunswick, N. J.
 Barnhill, L. L., St. Louis, Mo.
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 Benedict, R. C., Wyndmoor, Pa.
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 Boese, R. F., Cary, Ill.
 Brown, W. F., Palo Alto, Ca.
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 Brubaker, G. L., Doylestown, Pa.
 Buraimo, O. O., Quebec, Can.
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 Buss, E. G., University Park, Pa.
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 Dickey, J. F., Clemson, S. C.
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WHAT MIGHT SEX RATIO CONTROL MEAN IN THE ANIMAL WORLD?

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IN examining what sex ratio control might mean in the animal world from a positive viewpoint, one may ask "What are the advantages of sex control?" The answer most frequently given is that it permits the breeder to have what he wants. However, in practice, what the breeder and commercial producer of domestic animals, including poultry, want is the most efficient and profitable program. It is, perhaps, *not* surprising that little appears to have been published suggesting specifically what impact sex control might have on the production of milk, meat and eggs, considering the myriad of possibilities as well as the hazards of prediction. This paper will discuss several factors likely to be important in applying sex control, particularly to farm animals, and will give selected examples of its possible contribution to the production of food and other animal products.

Throughout, we will assume that the sex ratio at birth (secondary sex ratio) is 50 ♂ : 50 ♀, although it is known to deviate slightly from this for most species (Lawrence, 1941; Altman and Dittmer, 1962). Furthermore a variety of natural conditions has been reported to be associated with minor changes in the sex ratio (Lawrence, 1941), and some investigators have reported spurious deviations in sex ratio as a result of unfortunate classification of data.

General Advantages and Limitations of Sex Ratio Control. Effective sex ratio control could permit producing the optimum proportion of males and females to take advantage of phenotypic differences in sex-limited traits, such as milk and egg production, in sex-influenced traits such as rate of gain and body composition and in sex-linked traits, associated primarily with undesirable recessive genes. Simultaneously, regulation of sex of offspring to increase selection pressure and optimize genetic gain should be considered. The vagaries of chance deviation, often troublesome in small subclasses, as in certain breeding experiments, might be eliminated.

Also, populations of wild animals might be regulated by limiting the production of females.

The potential disadvantages of sex control seem to be possible cost, possible damage to genetic material during processing, and possible increased inbreeding. Also, it would seem essential to carefully analyze the consequences of alteration of sex ratios, since miscalculations in practice could prove to be as harmful as proper application could be beneficial.

Factors Affecting Application. Factors which clearly would influence the degree of sex control practiced include (1) the degree to which the sex ratio is altered, (2) the fertility or number of progeny/female/year in a sex control program, (3) the number of progeny per top sire possible if sperm processing is involved, (4) direct cost of the sex control technology and (5) the opportunity to combine sex control with other procedures of potential economic benefit. These factors all concern the economic aspect of decision making. In addition, (6) convenience and (7) tradition, ethical and moral considerations could influence decisions, particularly in humans.

The method(s) of sex control available can markedly affect these factors. Separation or selective inhibition of the sperm cells in mammals to achieve sex control in conjunction with artificial insemination could be convenient. Marked, consistent and predictable alteration of the sex ratio, a high yield of usable sperm and good fertility would be desired. Recognition of the two types of sperm (Barlow and Vasa, 1970; Beatty, 1970; Rorvik and Shettles, 1970) to monitor batch separation would be extremely useful. Treatment of the male or female could be more convenient or acceptable under conditions of natural mating. Cloning would achieve absolute sex control, as well as propagation of established genotypes. Thus, it has distinct advantages over several other methods. Parthenogenesis and sex reversal offer other potential avenues of sex control (Lerner and Donald, 1966). Post-fertilization alteration of sex ratio through examination of amniotic fluid and selective abortion currently is possible, but

¹ The authors acknowledge with thanks helpful suggestions by many researchers too numerous to mention individually.

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this would decrease the progeny possible per unit of time and would offer no control of the sex at the next pregnancy. Sexing and transfer of selected blastocysts also could have practical benefits. We will not describe methods used in attempting to control sex ratio (see Gordon, 1958; Yamamoto, 1965; Etzioni, 1968; Hafs, 1968; Beatty, 1970; Turner, 1969; Rorvik and Shettles, 1970) since other speakers will treat this in detail.

Livestock and Poultry in the U.S. The size of the animal industry in the U.S. at the beginning of 1970 is shown in table 1. The number of dairy cows and sheep has been declining gradually. The number of beef animals and chickens increased 3% over the previous year. Swine decreased 6%, but the number tends to fluctuate. Corresponding statistics could be obtained for several other countries, but these for the U.S. will serve as an example.

The estimated value of the animal industry is shown in table 2. With the value of livestock and poultry on farms estimated to total \$25.4 billion, it is obvious that sex control potentially involves a large economic enterprise. The economic value per animal or progeny produced is an important consideration.

TABLE 1. INVENTORY OF LIVESTOCK AND POULTRY ON FARMS IN THE U.S.^a

Class of livestock	No. of head (millions)
Dairy cattle	
Females≥2 years	13.9
Females<2 years	7.3
Total	21.2
Beef cattle	
Cows 2 years or older	37.4
Heifers 1 to 2 years	9.7
Calves under 1 year	29.1
Steers 1 year and older	13.0
Bulls 1 year and older	2.0
Total	91.1
Sheep	
Ewe lambs	2.4
Wether and ram lambs	0.5
Ewes≥1 year	14.0
Rams≥1 year	0.5
Wethers≥1 year	0.1
Others on feed	2.8
Total	20.3
Swine, total	90.0 ^b
Chickens for eggs	431.5 ^b
Broilers	3000.- ^b
Turkey breeders	6.7
Turkeys for meat	100.- ^b

^a Adapted from U.S.D.A. Statistical Reporting Service, 1970.
^b Represents the number produced for market annually.

TABLE 2. VALUE OF LIVESTOCK AND POULTRY ON FARMS IN THE U.S.^a

Class of livestock	Value (dollars)	
	Per head	Total (millions)
Dairy cows≥2 years old	300.00	4,170.00
All other cattle	162.00	15,950.00
Sheep	25.00	508.00
Swine	39.00	2,211.00
Chickens for egg	1.35	583.00
Broilers	0.50	1,500.00
Turkey breeders	5.50	37.00
Turkeys for meat	4.00	400.00
Total	25,359.00

^a See footnote table 1.

Clearly, the cost of sex control per progeny would have to be lower in sheep, swine and poultry than in cattle to be as acceptable economically.

Potential Benefits by Species

Several ways that regulating sex might be beneficial are summarized in table 3. Since males are preferred in some schemes and females of the same species in others, it is certain that the overall desired ratio in a species will be a summation of vastly different ratios optimum for certain conditions. In addition, if sex control is achieved for one of the species shown in table 3, it is likely that the method will be successfully adapted to other species. Applications may range from the control of sex ratios in drosophila experiments in the genetics classroom to human endeavors to choose the sex of the progeny of their own species.

Dairy Cattle. There seems to be general agreement that female progeny are needed to produce milk! Male calves are more desirable for meat production. The objective is to establish an optimum proportion of male and female progeny to give the most profitable program.

It is usually assumed, and we believe, that a breeding program should maximize milk production. Hence the usefulness of sex control depends upon increased genetic progress and phenotypic gain for milk production, the increased economic value of animals not kept for breeding, and some increases in operational efficiency when sex can be predicted accurately. The genetic advantages of sex control are intimately associated with pedigree evaluation, since, presumably, sex control would be exercised near the time of insemination or mating, and would take the form of

TABLE 3. POSSIBLE USEFULNESS OF SEX RATIO CONTROL

Class	Advantage of one sex
Dairy cattle	<ol style="list-style-type: none"> 1. More ♀ progeny from good cows as herd replacements for milk production, or insuring ♀ from better cows. 2. More ♂ progeny for meat, especially from "cull" cows; dairy x beef crosses. 3. Insuring ♂ progeny as potential sires from top cow x sire crosses. 4. Insuring ♀ progeny when progeny testing young bulls. 5. Avoiding intersexes in multiple births.
Beef cattle	<ol style="list-style-type: none"> 1. More ♂ progeny for meat. 2. Insuring ♂ progeny as potential sires from top cow x sire crosses. 3. Insuring ♀ from next best cows x top sires as future brood cows. 4. In crossbreeding producing all C (AB) ♂ from C ♂ x AB ♀. 5. Avoiding intersexes in multiple births.
Sheep	<ol style="list-style-type: none"> 1. More ♂ progeny for meat. 2. Crossbreeding as for beef cattle.
Swine	<ol style="list-style-type: none"> 1. More ♀ progeny for meat. 2. Crossbreeding as for beef cattle if boar meat were acceptable.
Horses	<ol style="list-style-type: none"> 1. More ♂ progeny for sale. 2. More ♀ progeny when replacing brood mares.
Mink	<ol style="list-style-type: none"> 1. More ♂ progeny for better pelts.
Poultry	<ol style="list-style-type: none"> 1. Egg strains: produce more ♀ progeny; avoid sexing and discarding ♂. 2. Meat strains: produce more ♂ progeny.

deciding which breedings would produce future herd replacements, breeding bulls and meat animals. Since sperm separation seems to be one of the more likely means of controlling sex, artificial insemination probably would be required. Thus, the discussion of potential change in dairy cattle through sex con-

trol is discussed largely in terms of its being linked with artificial insemination.

It is convenient to discuss genetic change in terms of the six avenues (figure 1) in which selection can occur: (1) sires of bull calves for breeding, (2) dams of bull calves for breeding, (3) progeny testing bull calves, (4) sires of herd replacements, (5) dams of herd replacements and (6) selection among heifer calves. Because genetic gain from these six avenues is nearly additive, each will be considered separately, and the parts which any individual deems realistic can be added together.

Avenue 1. The first avenue, sires of bull calves for breeding, has little potential to gain from sex control. Only a few bulls are needed for sampling to obtain progeny tested sires for extensive use. These can be, and often are, highly selected without sex control. Dairy bulls produce an abundance of semen; hence, when superior sires are identified, it is possible to get more than enough sons from each.

Avenue 2. Dams of bull calves for breeding are not evaluated accurately, and intensive selection already is practiced without sex control. It is doubtful that the genetic merit of selected bull dams could be increased by as much as 1% if only half as many bull dams were needed. However, a considerable financial saving might accrue to studs if only half

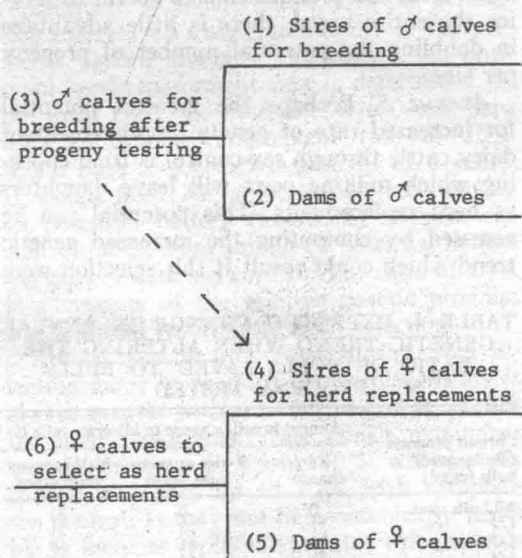


Figure 6. Sperm distribution of first and third progress might be altered by sex control.

as many contract matings were needed to produce the required number of bull calves.

Avenue 3. Young bulls should be progeny tested before heavy use, and the same number of daughters could result from half as many matings, making a few more cows available for other matings. This may have additional advantages which have not occurred to us, but the primary limiting factor in progeny testing is the total number of daughters of unproven bulls which must be milked and tested. Hence, sex control would not affect genetic change because it would neither permit more accurate evaluation nor allow more bulls to be sampled, unless this facilitated developing additional testing programs.

Avenue 4. After top A.B. proven sires (sires proved in artificial breeding) are identified, sex control might allow more effective use of these sires to produce replacement females. But this is highly speculative until it is known how many progeny can be obtained from a bull with sex control. If the same number of cows are settled and all calves are heifers, the rate of genetic trend might be increased dramatically. If the sex separation process resulted in fewer than half of the conceptions otherwise possible, a reduction in the effective use of the best proven sires would occur.

One way to look at the consequences of the number of replacement females per bull is to estimate the annual genetic trend for milk production generated by various young sire sampling programs, if the number of these bulls subsequently needed to service the cow population were doubled or halved. It will be assumed that bulls of equal merit are sampled in all programs, that decisions are based on 50 daughters in 50 herds, that all proven bulls are used equally, and that 25% of the cow population is replaced annually.

This becomes a straightforward problem in population genetics (Lush, 1945; Legates, 1970) in which all the pertinent factors are accounted for by the following equation:

$$\Delta G = \frac{r_{TI} \times \sigma_T \times D}{A} \quad (\text{Eq. 1})$$

In this equation ΔG =annual genetic gain, r_{TI} =the correlation between true breeding value of an individual and our index or estimate of it (accuracy of selection), σ_T =the additive genetic variability of the trait expressed in standard deviation units, D =the selection differential or number of standard deviations that the selected fraction is ex-

pected to be above the original mean, and A =the generation interval in years.

In the current example, $A=5$ years, $\sigma_T=454$ kg (1,000 pounds) and $r_{TI}=0.44$ for future daughters evaluated from a previous sample of 50 paternal half-sibs. Table 4 illustrates the changes in annual genetic trend which would occur if the same number of bulls were tested but the number ultimately selected for heavy service were doubled or halved.

The current rate of genetic trend for milk production from all sources is about 45 kg/year, and this is due almost in its entirety to heavy use of the best A.B. proven sires. This table illustrates that moderate changes in the selection intensity after bulls are proven can have a dramatic impact on the rate of genetic improvement in the cow population. It points out the need to guard against less efficient use of the best proven sires and the need to strive for more effective use of these sires.

Apparently, few bulls currently are used to their physiological limits for siring progeny because of lack of demand for their semen. In this situation, there is some margin for losses during sperm separation to control sex. However, this same lack of demand for semen from the top bulls, due to various factors such as price differences and disagreement as to which bulls are outstanding, could negate any advantage for sex control in improving the genetic merit of sires of herd replacements. A related problem, often heard, is the fear of narrowing the genetic base. Also, when one or a few sires can produce enough sperm to service the entire breed, there is little advantage in doubling the potential number of progeny per sire.

Avenue 5. Perhaps the greatest potential for increased rate of genetic improvement of dairy cattle through sex-control is from choosing which milking cows will leave daughters as herd replacements. This potential can be assessed by computing the increased genetic trend which could result if this selection were

TABLE 4. EXPECTED CHANGE IN ANNUAL GENETIC TREND WHEN ALTERING THE RATIO OF BULLS SAVED TO BULLS PROGENY TESTED

Current program (Bulls saved/ bulls tested)	Annual genetic change in kilogram milk if:		
	No change	Twice as many bulls saved	Half as many bulls saved
All bulls used	0	0	32
1/2	32	0	51
1/3	44	21	60
1/4	51	32	66
1/6	60	44	74
1/8	66	51	80

TABLE 5. RELATIVE GENETIC GAIN DUE TO SELECTING COWS TO PRODUCE ♀ CALVES

Replacement rate, %	Generation interval, A (year)	Selection differential (D)		Relative annual progress, D/A (r_{TI} , σ_T constant)	
		Living ♀		40% ♀	80% ♀
15 ^a	7 2/3	1.01	1.44	0.132	0.188
20	6	0.80	1.27	0.133	0.212
25	5	0.60	1.14	0.120	0.228
30	4 1/3	0.42	1.01	0.097	0.233
40	3 1/2	0.0	0.80	0.0	0.229
50	3	0.60	0.200
60	2 2/3	0.42	0.157
70	2 3/7	0.24	0.099
80	2 1/4	0.0	0.0

^a 15% is probably a minimal involuntary culling rate.

effective. Annual genetic trend can again be computed from equation 1, but r_{TI} , D, and A can be varied.

Assume that the sex ratio is exactly 50:50, and that under good management conditions with high fertility and low calf mortality it is possible to produce 40 female replacements annually from a 100-cow herd, i.e., 40 surviving to 2 years of age. With complete sex control, the number of potential female replacements might be double, or 80. Presumably, the dairyman would choose his replacement heifers before they were conceived by choosing which cows would produce heifer calves for future herd replacements. The advantage of sex control in increasing genetic gain through this kind of selection is shown in table 5. These computations were made from equation 1. This takes into consideration the dependency between D and A, wherein the annual replacement rate determines both the generation interval (A) and the number of replacements needed annually (hence D). An optimum herd replacement rate is determined by the ratio D/A. To illustrate, a 100-cow herd with an annual replacement rate of 20% would have a generation interval of 6 years. It would need 20 replacements from among 40 potential heifers ($D=0.80$) without sex control, or 20 from among 80 potential heifers ($D=1.27$) with sex control. The ratio of D/A is a measure of the relative genetic progress which would result from such selection.

Annual genetic progress resulting from selecting dams to produce herd replacements is always greater with sex control (table 5), but the herd replacement rate which maximizes genetic progress is about 20% without sex control and goes up to 30% with complete sex control. It may not be economically feasible to increase replacement rate; this depends upon the cost of raising replacements relative to slaughter value of low producing cows.

TABLE 6. ANNUAL GENETIC GAIN FOR MILK PRODUCTION DUE TO SELECTING COWS TO PRODUCE ♀ CALVES

Replacement rate	Annual increase in milk (kg)			
	$r_{TI}=.20$		$r_{TI}=.30$	
	40% ♀	80% ♀	40% ♀	80% ♀
15%	12	17	18	26
20%	12	19	18	29
25%	11	21	16	31
30%	9	21	13	32
40%	0	21	0	31
50%	..	18	..	27
60%	..	14	..	21
70%	..	9	..	14
80%	..	0	..	0

The annual genetic gain for various levels of r_{TI} (selection accuracy), assuming $\sigma_T=454$ kg, is listed in table 6. Accuracy of selection is low, because future progeny would be selected on the performance of their maternal relatives. Examples of r_{TI} for a few types of pedigree selection are listed in table 7. The upper practical limit for r_{TI} is about 0.40.

In general, a prospective heifer calf in a production tested herd using A.B. proven sires can be ranked with 20% accuracy if the dam is a first-calf heifer, and with 30% accuracy if the dam has completed one or more lactation records. Assuming r_{TI} to be 30%, the potential increase in the maximum rate of genetic progress from choosing cows to be mothers of herd replacements could be increased from 18 kg/year to 29 kg/year, a gain

TABLE 7. EXAMPLES OF THE ACCURACY (r_{TI}) WITH WHICH CALVES CAN BE SELECTED AT THE TIME THEIR CONCEPTION IS PLANNED, USING ONLY INFORMATION ABOUT THE DAM AND HER RELATIVES

r_{TI}	Information available
0.06	No record on cow; one record on her half-sib.
0.12	No record on cow; one record on her dam or one daughter.
0.20	No record on cow; A.B. ^a proof on her sire (30 dau.).
0.23	No record on cow; A.B. proof on her sire (100 dau.).
0.25	One record on cow.
0.29	Two records on cow.
0.31	One record on cow; A.B. proof on her sire (100 dau.).
0.33	Eight records on cow.
0.35	Four records on cow; A.B. proof on her sire (100 dau.).
0.36	Eight records on cow; A.B. proof on her sire (100 dau.).

^a A.B.=artificial breeding.

of 11 kg (24 lb.)/per year, through the use of sex control. This trend could be pushed to 32 kg/year if accompanied by an increase in the replacement rate. Genetic gain from such selection is cumulative. This gain for a single year for 14 million cows would be worth about \$16 million.

A word of caution should be interjected, however, because considerable circumstantial evidence indicates that dairymen are realizing very little of the potential 12 to 18 kg genetic gain from selecting dams of herd replacements. This should be both a warning and a challenge—a warning because sex-control produces no genetic change without selection, and a challenge because sex-control may be the instrument to educate breeders to the potential gains which would accompany selection of dams of replacement heifers.

Avenue 6. Selection among heifer calves after birth presents a management problem, but sex control would provide the potential for producing up to 80 heifers each year per 100 cows in the population. Pedigree selection before breeding has been discussed. Pedigree selection could be used also after the calves are born, and the genetic gain resulting could be predicted from the tables presented previously. In addition, there is potential gain from using performance information on the calf to augment pedigree information. This presumes that extra heifers will be raised and either (1) milked for a part lactation before choosing herd replacements, or (2) their correlated traits, such as growth rate or conformation, would be utilized. Correlated traits have not proven very useful. Of course, raising more replacement heifers lowers selection intensity for pedigree selection.

The success of raising extra replacement

heifers and milking them for part of their first lactation before choosing herd replacements is largely a function of the cost of raising heifers, the sale price of newborn calves and of cull cows, and the effectiveness of labor, equipment and building utilization. Only the extreme case where all cows produce heifer calves will be considered. If 25 heifers are needed annually for a 100-cow herd and 80 are produced, the annual genetic gain can be predicted from equation 1, where, $A=6$ years, $\sigma_T=454$ kg, $D=1.14$. The r_{TI} for a 305 day lactation is 0.5, but the r_{TI} would be 0.30, 0.38, 0.43, 0.45, or 0.47 for part lactations of 1, 2, 3, 4 or 5 months, respectively (J. F. Keown and L. D. Van Vleck, unpublished data). Assuming 3-month lactation records, ΔG would be 37 kg/year, compared with 31 kg/year for pedigree selection. The optimum would probably be some combination of the two sources of information.

Additional phenotypic gain could be achieved by obtaining part lactation information, as shown in table 8. This gain is not cumulative, since it represents selection for permanent environmental and non-additive genetic effects.

In summary, substantial additional genetic and phenotypic gain in dairy cattle could be achieved if sex could be controlled, and if the gain was accompanied by proper testing and selection. Most extra genetic gain could probably result from choosing which cows would become dams of replacement heifers.

Intersexes (free-martins) could be eliminated. Currently about 1% of the cows carry twins of opposite sex. The female usually is sterile and can be raised for meat. Sex control would become much more important if twinings were increased either through selection,

TABLE 8. EXTRA PHENOTYPIC GAIN IN SELECTED FEMALES IF ONE LACTATION IS COMPLETED BEFORE SELECTIONS ARE MADE

Replacement rate	D value		(r-h) (D) (σ_p) ^a		Relative gain from selection
	40% ♀	80% ♀	40% ♀	80% ♀	
	(Milk, kg)				
15%	1.01	1.44	183	262	1.43
20%	0.80	1.27	145	231	1.59
25%	0.60	1.14	109	207	1.90
30%	0.42	1.01	76	183	2.40
40%	0	0.80	0	145
50%	0.60	109
60%	0.42	76
70%	0.24	44
80%	0	0

^a Formula for calculating phenotypic gain, where r=repeatability, h=heritability, D=selection differential and σ_p =within herd phenotypic standard deviation. The table has been computed on the basis of r=0.45, h=0.25 and σ_p =908 kilograms.

controlled superfetation or embryo transfer (Hendy and Bowman, 1970; Rowson, Lawson and Moor, 1969). Twinning is considered uneconomic because reproductive problems of the dam increase and calf survival and performance are reduced. Improved management may largely overcome these problems according to Hendy and Bowman, 1970.

Beef Cattle. The gigantic beef cattle industry (table 1) is growing. Currently about 15 million female progeny are born each year; many are used for herd replacements. By 1980, it is estimated that about 10 million heifers will be needed in the feed lots to meet the demands for beef in the U.S. Steer calves wean heavier than females and also gain more efficiently in the feed lot. The total economic advantage for the steers over heifers by the time they are marketed is about \$20 each. If 10 million heifer calves were replaced by males through sex control, the annual potential benefit might reach \$200 million. The total cost of applying sex control might reduce this figure greatly.

As market conditions change, there may be less advantage of steers over heifers. Also, drugs may be used to alter the physiology of the animal and minimize advantages of one sex for meat production. However, because of the potential hazards of additives, biological control likely will be preferred, at least as a public policy.

If the industry and consumer accept bulls, increased efficiency of meat production could be as much as 10%. More of the carcass would be lean meat, but part of this gain will be in the less desirable cuts. Also, marketing bulls is more difficult. Steers can be held somewhat longer, if necessary, to balance supply with demand; whereas, management problems increase as bulls become older.

At the same time, if bulls can be raised for the meat market, there would be incentive to performance test more bulls, increasing the pool from which breeding bulls could be selected. Most bulls for performance testing should come from the best cows bred to top sires. Other outstanding cows in the herd would be selected to produce female progeny as herd replacements. The rest of the cows would be "sex-controlled" to produce males for meat primarily. Although some genetic gain would be realized, the major potential economic benefits in beef cattle from sex control would be phenotypic.

Another advantage of sex control (table 3) would be in crossbreeding programs. For ex-

ample, if it were known that A x B crosses produced outstanding dams, then a minimum number of B-line females could be utilized to produce all females by A-line sires. The next cross with C-line sires would be controlled to produce males for meat.

Eliminating intersexes in multiple births is another advantage, but of somewhat lesser importance than in dairy cattle. If twinning can be increased considerably, like-sexed twins would be especially important when producing breeding stock.

Sheep. The major potential advantages of sex control are producing more males than ewe lambs for meat, and its use in crossbreeding programs. Wethers are about 10% heavier than ewes at weaning; equivalent to a net gain of about 4 to 5 kilograms. There is no premium for wethers. The increased value per head at current prices would be about \$3, and if two-thirds of this reflects increased efficiency the net value might be \$2. If 5 million more males could be produced annually, the total value would be \$10 million. If the market accepts ram lambs the gain will be greater. Nevertheless, the cost of sex control per animal would have to be low to be economical.

Sex control in breeding flocks and in crossbreeding would have advantages similar to those already described for beef cattle. In breeds where the females are noted for their production, a minimum number of males would be produced. Conversely, in some other breeds where males are noted for their performance, and in crossbreeding, mostly males would be produced for market. In introducing new genetic stock, indigenous females might be inseminated with sex-controlled semen to produce all females. These crossbred females would be used for subsequent breeding.

Swine. Sex control in swine appears to be of limited value from a genetic standpoint. The gain from having more male or female progeny from the top sow x boar crosses to select future breeding stock would be small, because with the high reproductive rate the potential pool without sex control is large. For market, gilts are preferred over barrows because they produce 1 to 2 kg more lean meat at slaughter. With about 45 million barrows slaughtered per year, the total value of replacing them with gilts could exceed \$50 million. If boar meat were acceptable, the value would be approximately doubled. Again, sex control would have to be cheap and convenient, because having about five more progeny of one

sex per litter would be worth about \$5 to \$10.

Other Farm Mammals. Sex control in horses could be extremely valuable in the limited population of high priced stock. Generally, colts produced for sale would command a much higher price than fillies. When replacing brood mares, the breeder would want females if sex control were possible.

For the lady of the house, production of mostly male mink kits would be nice. The male pelts are worth about \$4 to \$6 more than pelts from females. In an average litter of five, producing all males would increase the total value per litter by \$10 to \$15. On the basis of current mink pelt production in the U.S., sex control would be worth about \$12 million annually. What the net economic gain, if any, might be, depends on the cost of implementing sex control technology.

Poultry. Since the female is the heterogametic sex, control of the sex ratio in birds would require a distinctly different method than is most commonly envisioned for mammals. Cloning would be a possibility as has been demonstrated for a plant (Steward, 1967). In egg laying strains, the male chicks (cockerels) are essentially worthless, whereas the females (pullets) are worth about \$0.25. With sex control, sexing of baby chicks would not be required and only half as large a total breeding and hatchery operation would be needed to produce pullets. At 300 million pullets, sex control would be worth \$75 million. Greater uniformity of product resulting in a one-sex operation also would be preferred by the large processors.

In the broiler industry, the 1.5 billion cockerels used are worth about \$0.05 each more than pullets for a total value of \$75 million. In the turkey industry, males are worth more, have a higher yield and are preferred by the commercial processing industry. Sex control might be worth \$20 million. Again, clearly the cost of applying the technology to the breeding stock must be relatively small.

Humans. Should an effective method be developed for animals there almost certainly would be some demand to adapt it to humans. In fact, already there is one report (Rorvik and Shettles, 1970) of extensive advice given to couples for assistance in choosing the sex of their child.

Etzioni (1968) discussed potential problems if a choice is possible. Evidence suggests that there is a preference for boys. If more boys were produced men would find wife hunting more difficult. There may be more prosti-

tution and homosexuality, or a man might have an urge to "rob the cradle" unless he were content to wait for a widow.

Assuming that an optimal balance in sex ratio could be maintained in the population, there could be a real advantage of choice within the family. It would be especially nice if family size is to be limited to have some choice—say a boy and a girl. Or, if two children of the same sex result "naturally" and a third child is allowed, choice of one of the opposite sex might be strongly desired.

In the past, data collected (Thomas, 1951; Freedman, Freedman and Whelpton, 1960; Etzioni, 1968) suggest that when all the children are of one sex a state of disappointment may exist which induces the couple to try again, thus accounting for some of the larger families rather than the sex ratio being altered by family size (Mussali, 1970). Thomas (1951) states that "I might quite properly ask what the parents of the future would do if sex determination became possible. If the motives which appear to have been exposed by the analysis of our data continue to influence parents, the family size of the future may be somewhat smaller than it is at present, as many parents will choose to have a boy and a girl."

On the other hand, if this becomes a woman's world, Parkes (1963) has computed that there is excess male biomass from the standpoint of efficient reproduction. He states that, "a fertile man . . . could easily father 500 children, or considerably more if he got himself properly organized."

Conclusions

1. Sex control would permit the livestock industry to produce the optimum proportion of males to females to take advantage of sex-limited and sex-influenced traits. The benefits can result from both phenotypic and genotypic selection, particularly from the former, in producing food for the world more efficiently and biologically.

2. The potential benefits are enormous, but the optimum schemes have not been established.

3. Furthermore, to be applied widely, any sex control technology must be effective, must result in high fertility and must be reasonably inexpensive and convenient to apply in animals.

4. In humans, any predictions of the price

people will pay, or the consequences of paying the price are highly speculative, but the possibility of sex control with family size limitations demands careful consideration.

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DISCUSSION

Question: Kiddy

I wonder if you considered the laboratory animal industry and what effect controlling the sex would have in that industry?

R. H. Foote: I didn't objectively try to gather information on it. Certainly there are many cases where one would like to produce all females or males for certain kinds of experiments and this would be valuable. This would be true in both large and small animals. At other times, in breeding experiments, in order to perpetuate certain lines and provide for crosses and selection in a controlled fashion, it would be desirable to have males and females produced in equal numbers. Due to the vagaries of chance this often doesn't happen.

Question: Casida

What did you mean by the use of cloning in poultry?

R. H. Foote: By cloning I was referring to asexual reproduction. This would represent culturing somatic cells from the female or male, depending upon the desired sex, under suitable conditions. Eventually such cells might dedifferentiate, as in carrot cells cul-

tured by Dr. Steward. Then they might be transferred to unfertilized eggs (after laying) in poultry or to the uterus of farm animals. This would result in control of sex. Also, and perhaps more important, reproduction of a known highly selected and desirable genotype would occur.

Question: Hafs

Have you considered the total value of genetic gain possible from sex control? What would this amount to relative to the 1 or 2% annual genetic gain that we think we now obtain in dairy cattle? Secondly, how would the phenotypic gain compare, either in dollars and cents or on any other basis that you care to relate it?

R. H. Foote: I'll have to answer that in a general way. The different components that we considered here result in several times the present rate of genetic gain. So, it would be a very large factor, perhaps representing 200 million dollars from an economic standpoint. The phenotypic gain could be of similar magnitude. However, the net value really cannot be estimated until we know the cost of sex control.

PHENOTYPE OF SPERMATOOZOA IN RELATION TO GENETIC CONTENT

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IT has long been an attractive thought that experimental manipulation of spermatozoa in relation to their genetic content might afford a new means of controlling the transmission of genetic factors from parent to offspring. A prerequisite for any success in this line of research is that the spermatozoan phenotype should vary in accordance with its own genetic content, and my mandate is to discuss this possibility.

Phenotype and Genotype in the Male Germ Line

The male germ cell differentiates through the successive stages of primordial germ cell, spermatogonium, spermatocyte, spermatid, spermatozoon and male pronucleus. At all stages it has an observable phenotype. There are three elements to the genetic background. After meiosis, the germ cell has its own haploid genotype. Before meiosis it has its own diploid genotype. The same diploid genotype characterizes the body cells that constitute a biological environment within which the germ cells differentiate.

My task today is to speak of the association between genotype and phenotype in germ cells with particular reference to the haploid genotype, and with some emphasis on that part of the genotype contained in the sex chromosomes. Our immediate interest is in whether the different haploid genotypes of the germ cells in a single animal do or do not endow the spermatozoa with different phenotypes. If they do so affect spermatozoan phenotype, then a way is open for elaborating appropriate technologies for the differential separation, inactivation, or destruction of individual spermatozoa according to their genetic content.

Let us visualize the exact moment in time when the genetic material segregating into one daughter germ cell is not the same as the material segregating into the other daughter cell. It is at this time that the possibility of corresponding phenotypic differences first arises.

The segregation may be of "billiard-ball" genes; or of structural re-arrangements and abnormalities, such as translocations; or of entire segments of chromosomes, such as differential segments of sex chromosomes; or of whole chromosomes, such as X and Y. The segregation of unlike genetic material into daughter cells can occur at either the first meiotic division ("pre-reduction") or the second meiotic division ("post-reduction"). In male *Drosophila*, segregation of all factors is pre-reductional. This means in *Drosophila* that different X and Y-bearing cells arise at the end of the first meiotic division, and these cells will also differ in respect of all autosomal factors for which the male happens to be heterozygous. In virtually all mammals, segregation of X and Y chromosomes also takes place at the first meiotic division and some autosomal factors will also segregate at this time. But the segregation of autosomal factors in mammals is sometimes delayed until the second meiotic division, and cells differing in genotype in respect of these factors do not exist until the very end of meiosis. I will recall this timing of segregation a little later.

I would like to indicate a short terminology. *Somatic genetic action* is the activity of the normally diploid genotype of the body cells at any time relative to meiosis, and also of the same genotype in the pre-meiotic germ cells. *Post-segregational genetic action* is the activity of the genetic material after segregation (i.e., after either the first or second meiotic division). I have used the term genetic action because we often want to refer simultaneously to *gene action*, which must be defined strictly in terms of synthesis of messenger RNA; and to *gross genetic action*, mediated by the gross structural, physical or chemical nature of the chromosomes. I hope that this indicative terminology will do for the time being. Frankly, the older terms genotype and phenotype and the newer terms of molecular biology are irreconcilable, but I am not at the moment prepared to invent a new set of terms meaningful at all levels of thought.

Returning then to the problem of immediate interest—can the post-segregational genotype

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affect the phenotype of the male germ cell? I will first review some genetic evidence that this effect does occasionally occur, and then other evidence of various kinds that on the whole says that it cannot occur. I will confine myself to illustrative results and general concepts, and refer you for detail to my recent review (Beatty, 1970).

Overall Genetic Effects on Spermatozoa

I will first mention briefly a large body of evidence in which genetic effects on the spermatozoan phenotype are certainly demonstrated, but one is not able formally to distinguish between the somatic genotype effect and the post-segregational genetic effect (Beatty, 1970). Studies of this kind provide material in the search for post-segregational effects but do not prove the existence of such effects. There is now a good deal of evidence that strains of mammals, whether inbred or outbred, differ characteristically in the morphology of their spermatozoa (Braden, 1959; Beatty and Sharma, 1960) and that patterns of inheritance emerge when strains are crossed. The balance of factors affecting the spermatozoan phenotype seems to be as follows. There is often a genetic effect, sometimes quite large. There is very little environmental effect attributable to age of male, season, identity of the litter, and so on. Superimposed on this is a relatively large "random" variability of spermatozoa from the same male. There is often a pronounced additive effect in breeding experiments, yielding high heritabilities of the order of 0.7 to 0.9 (Napier, 1961; Woolley and Beatty, 1967; Woolley, 1970). It is probable that spermatozoan dimensions have little connection with reproductive fitness of the cells, since this lack of connection is a general characteristic of traits with a high heritability. High heritability means that it should be relatively easy to conduct a successful programme for the genetic selection of spermatozoan dimensions. This has been verified in the mouse, where selection for midpiece length proceeded smoothly and brought into existence strains of mice with either a long or a short midpiece (Woolley and Beatty, 1967; Woolley, 1970). The change in length was caused by an alteration in the number of gyres of mitochondria that compose most of the midpiece. The experiment had two unusual features, since it was a selection for the gametic phenotype, and also a selection for the amount or arrangement of an intracellular organelle, the mitochondrion.

Strain differences in spermatozoan dimensions are so characteristic that males of different strains of mice can be distinguished from one another by studying microscope preparations of their spermatozoa. They can sometimes be distinguished virtually without error. It is more difficult to identify individual spermatozoa of one strain from those of another because of the natural variability of these cells. The most contrasted strain pair so far known is JBT and A, whose individual spermatozoa can be distinguished with only some 6% error (Williams, Beatty and Burgoyne, 1970). In none of these quantitatively defined strain differences is there any reason to call one strain "abnormal" in comparison with another. Certain inherited sperm defects characteristic of mutant strains homozygous for recessive alleles affecting spermatozoan morphology will be mentioned later.

Distorted Mendelian Ratios in "Tailless" Mice Interpreted as a Post-Segregational Genetic Effect on Spermatozoan Fertility. The fertility of a spermatozoan is as much an aspect of its phenotype as are dimensionally-defined characteristics, and I would now like to recall the well-known facts of the inheritance of alleles at the *T* locus of the mouse, a locus whose most obvious effect is on the length of the mouse's tail. Studies of this locus have provided a unique and apparently well-established demonstration of a post-segregational genetic effect on spermatozoa. There are several alleles, but for simplicity I will speak as if all experiments were conducted with *t* and with its wild-type allelomorph, *+*.

Now the Mendelian expectation is that a heterozygote such as a *+**t* should produce two kinds of gamete in equal number, *+* and *t*. Mating of the heterozygote to a *++* animal should give two kinds of offspring in equal number, *++* and *+**t*. In other words, simple Mendelian expectation is a 50% transmission rate of *t* to offspring. It has been known for a long time that transmission through a heterozygous female parent gives the expected 50% transmission rate. But transmission through the heterozygous male parent does not, the ratios being generally higher than 50%, according to the particular allele of *t* used, and the ratio may even be of the order of 95%.

Differential embryonic mortality was ruled out early in this work as a possible cause of the distorted segregation ratio. This left two possibilities—either a differential production of *t* and *+* spermatozoa in the testis, or else a differential fertility of the two kinds of

gamete caused by their different post-segregational genetic contents. A critical experiment by Braden (1958) supported the postulate of differential fertility. In a control series, he mated heterozygous $+t$ male mice to $++$ females in the usual way and obtained a 77% transmission. In an experimental series he imposed an experimental challenge (late mating relative to oestrus) and obtained a 60% transmission rate that differed significantly from that of the control. The main point of this experiment is that an experimental challenge applied to mature spermatozoa *altered their relative fertility*. This must mean that the two genetic kinds of spermatozoa have correspondingly different phenotypes as defined by their differential response to the experimental challenge. Finally, it could be supposed that the different fertility phenotypes of the two kinds of spermatozoa were responsible for the distorted transmission ratios even after normal mating. The results have been fully confirmed (Yanagisawa, Dunn and Bennett, 1961; Braden and Weiler, 1964).

This important work on tailless mice appeared to establish several things. There was an exception to the Mendelian law of random union of the gametes. There was a unique demonstration of an effect on the gametic phenotype of the post-segregational genotype. There was an experimental control of a transmission ratio. The work was an exact precedent for what many would like to achieve with the segregation of sex. And the work was also a precedent for conceivable medical applications, since there had been a reduction in incidence of a factor causing an anatomical disaster to a mouse; namely, taillessness.

Distorted Mendelian Ratios in Drosophila Melanogaster Interpreted as "Meiotic Drive". In *Drosophila* also there is a well-known example of disturbed segregation through the male parent. The facts are very like those for tailless mice. Males of *Drosophila* heterozygous for the SD factor transmit SD to more than 50% of their progeny; for example to 99%. Meiosis is completely normal, and differential zygotic mortality is not involved. The straightforward explanation would seem to be the same as in mice; that there is post-segregational genetic effect whereby spermatozoa bearing the SD factor are relatively more fertile than those not bearing it.

But a wholly different explanation of the SD effect has developed in terms of a phenomenon named "meiotic drive" (Peacock and Erickson, 1965). Two postulates are made.

First, it is postulated that of the four products of a male meiosis, all are motile, but only two are functional in the sense of being able to fertilize an egg. Second, an orientated segregation of SD and $+$ chromosomes is postulated, such that SD chromosomes tend to enter preferentially the meiotic cells destined to become functional spermatozoa, whereas $+$ chromosomes tend to enter the cells destined to become non-functional. In short, SD and $+$ factors tend to find themselves respectively in functional and non-functional spermatozoa, but do not themselves affect function. The result is a distorted transmission rate of SD to offspring which does not involve any hypothesis of post-segregational genetic action.

The postulate that it is normal for two of the four products of male meiosis in *Drosophila* to give rise to non-functional gametes, a postulate basic to the theory of "meiotic drive", originated with Novitski and Sandler (1957). These authors also had encountered a disturbed transmission of certain translocation products through the male parent. Once again, a simple explanation of their results could have been a post-segregational genetic effect. This explanation was not favoured by the authors. Their actual observational evidence against post-segregational genetic effects was rather slight, and their decision to set aside the possibility of such effects was influenced by a long-standing dogma among Drosophilologists originated by Muller and Settles (1927), and stating that post-segregational genetic effects *cannot* occur in animals. The dogma certainly has a high general validity. But we now reach an interesting paradox: when occasional but apparently real evidence of a post-segregational genetic effect finally emerges, as in the inheritance of the SD factor, it has to be interpreted in some other way, because the dogma says that such effects cannot occur.

Latterly, there has been a re-interpretation of the SD effect in terms of post-segregational genetic action (Hartl, 1969). He measured the fecundity of SD/ $+$ and SD/SD males. On the theory of meiotic drive, the fecundity of the males should be normal, since SD is not supposed on that theory to affect sperm fertility, and fecundity would be preset by the postulated natural occurrence of 50% functional sperm. On the hypothesis of post-segregational genetic action, however, fecundity would be proportional to the degree of segregation distortion characteristic of different SD factors, and would be particularly low in the