

## Chapter 21

### *Inbred Lines for Heterosis Tests?*

The justification for considering heterosis tests in breeding work rests on the mode of action and interaction of the genes responsible for genetic variability in the material available to the geneticist. The nature of this genetic variability may vary widely between species or populations in response to differences in the degree of inbreeding and kind of selection, natural or imposed, that has characterized the population over an extended period. For any given trait or combination thereof, structure of genetic variation will depend upon how consistent, intense, and prolonged selection has been.

It follows that choice of the system of mating and selection appropriate for most rapid improvement in economic attributes of any given plant or animal population should be guided by as complete knowledge of the kind of genetic variation in the population as analysis of all available data affords. The discussion which follows is an attempt (1) to interpret the evidence presently available concerning the sort of genetic system which underlies important economic traits, using swine as the example; and (2) to compare expected effectiveness of several alternative breeding methods.

#### NATURE OF GENETIC VARIATION IN ECONOMIC TRAITS

Types of association between the genotype and its phenotypic expression have been classified logically as intra-allelic and inter-allelic. The former includes all degrees of dominance or levels of expression for the heterozygote relative to the corresponding homozygotes. The concept of heterozygote advantage or overdominance differs from the usual ideas of dominance in that each gene is visualized as exerting certain dominant favorable effects lacking in its allele. Inter-allelic gene action or epistasis includes all effects of a gene in one set of alleles on the expression of genes in other sets of alleles. Complementary, inhibiting, duplicate dominant, and duplicate recessive gene interactions are extreme examples.

By definition, epistasis is universal in the sense that expression of every gene is to some degree dependent on and modified by the effects of genes in other sets of alleles. Epistasis would include fixed multiplicative or proportional effects of each gene on the expression of non-allelic genes. Such epistasis, although unlikely to be important, would be of a highly predictable sort and would disappear if phenotypes were measured in log scale units. A potentially much more important sort of epistasis would be that involved whenever a phenotypic maximum is associated with an optimum genetic intermediate (Wright, 1935). Here a given gene may have either a positive or a negative selective value, depending on whether the individual's average genotype is above or below the optimum genetic intermediate.

Some of the evidence concerning the kind of genetic variability with which we must deal in seeking to improve economic characters of swine has been considered earlier (Dickerson, 1949, 1951) and may be summarized here as follows:

#### **Inbreeding and Crossbreeding Effects**

Proportion of heterozygous loci has a major influence on total performance, affecting most the highly important but lowly heritable characters for which selection has been consistently in one direction. Take for example, an intra-season comparison of 538 inbred and 325 linecross litters from the same lines in four projects of the Regional Swine Breeding Laboratory (Dickerson *et al.*, 1947). This showed a decline in performance per 10 per cent increased inbreeding of litter amounting to 2.6 and 7.8 per cent, for litter size at birth and weaning, respectively; 2.6 per cent for pig weight at 154 days of age; and 11.4 per cent for total weight of litters at 154 days. Similar estimates per 10 per cent increased inbreeding of dam, based on sixty-three inbred and fifty linecross dams at the Iowa Station, were 2.1 and 5.0 per cent for litter size at birth and weaning; 1.6 per cent for pig weights at 21 days; and 5 per cent for total weight of litters at 154 days.

Results from studies of regression of performance on inbreeding of dam and litter within line and season (Blunn and Baker, 1949; Stewart, 1945; Comstock and Winters, 1944; and Hetzer *et al.*, 1940) agree quite well with the figures given. Inbreeding of dam and litter together greatly depresses prolificacy, suckling ability, pre- and post-natal viability and growth rate, and particularly their product—total litter weight. Inbreeding effects on carcass composition, body conformation, and efficiency of food utilization were relatively minor (Dickerson *et al.*, 1946).

The results of the earlier crossbreeding experiments have been summarized by Lush (1939) and Winters (1936). When the mean of the two purebred stocks crossed is compared with the crossbred litters, the results of many experiments summarized by Carroll and Roberts (1942) indicate that the average performance of crossbred individuals is increased about as much as it would be by a 10 per cent reduction of inbreeding (see Table 21.1). More

recent studies of crossbreeding using inbred strains (Hazel *et al.*, 1948; Sierk, 1948) verify the earlier conclusions.

Some degree of dominance is the most obvious genetic mechanism by which change in heterozygosity from inbreeding or crossbreeding would affect the level of performance. Inbreeding decline due to dominance would be a function of  $2q(1 - q)k f$ , where  $q$  is frequency of the dominant allele,  $f$  is Wright's inbreeding coefficient, and  $k$  is the degree of dominance (Hull, 1945) defined in terms of phenotypic scale as  $(2 Aa-AA-aa)/(AA-aa)$ .

TABLE 21.1  
RESULTS OF CROSSBREEDING EXPERIMENTS SUM-  
MARIZED BY CARROLL AND ROBERTS (1942)

Factors of Production	No. of Expts.	Mean of Two Pure Breeds	Mean of Crossbreds	Relative Performance of Crossbreds with Purebreds = 100
No. pigs per litter . . . . .	12	9.74	9.48	97.3
Birth weight of pigs (lbs.) .	6	2.77	2.79	100.6
Survival ability (%) . . . . .	15	76.3	80.2	105.1
Weaning wt. of pigs (lbs.) .	15	32.5	33.12	101.8
Weaning wt. of litters (lbs.)* . . . . .	13	235.6	254.1	107.9
Av. daily gain (lbs.) . . . . .	9	1.381	1.436	104.0
Feed for 100 lbs. gain (lbs.)	6	374.1	368.6	98.5
Danish pig-testing stations:				
Av. daily gain . . . . .	32	1.359	1.381	101.5
Feed per 100 lbs. gain . .	32	345.4	344.3	99.7

\* From the original publications of these experiments.

If genetic intermediates in one or more primary functions produce maximum performance, the increased total genetic standard deviation ( $\sqrt{1 + f}$ ) associated with inbreeding would tend to increase the average deviation from optimum genotype and hence depress performance roughly in proportion to  $(\sqrt{1 + f} - 1)$ . Inbreeding alone would not alter mean level of performance without dominance, if only epistatic factors of the complementary or duplicate sort were involved.

Inbreeding depression and crossbreeding advantage indicate some degree of dominance or of genetic intermediate optimum, but, alone, they fail to distinguish between the two or to indicate the probable degree of dominance.

#### Effectiveness of Selection within Inbred Lines

Selection within mildly inbred lines has been only slightly effective. Decline in performance with mild inbreeding (2 to 4 per cent per generation) has been much the same as would have been expected from inbreeding without selection. These statements are based largely on a study<sup>1</sup> of time trends

1. To be published in more detail, separately.

in litter size and growth rate in 49 inbred lines from five projects with an average of 9 seasons per line (see also Dickerson, 1951). In Figure 21.1 the average actual linear time trend (*solid line*) is negative for both litter size at weaning and for pig weight at 154 days of age. An estimate of the effectiveness of selection was made by adjusting the time trends for the effect of the increased inbreeding, using corrections derived from the intra-season comparison of inbreds and linecrosses from the same inbred lines involved in the time trends. The adjusted time trend (*dashed line*) indicates that selection

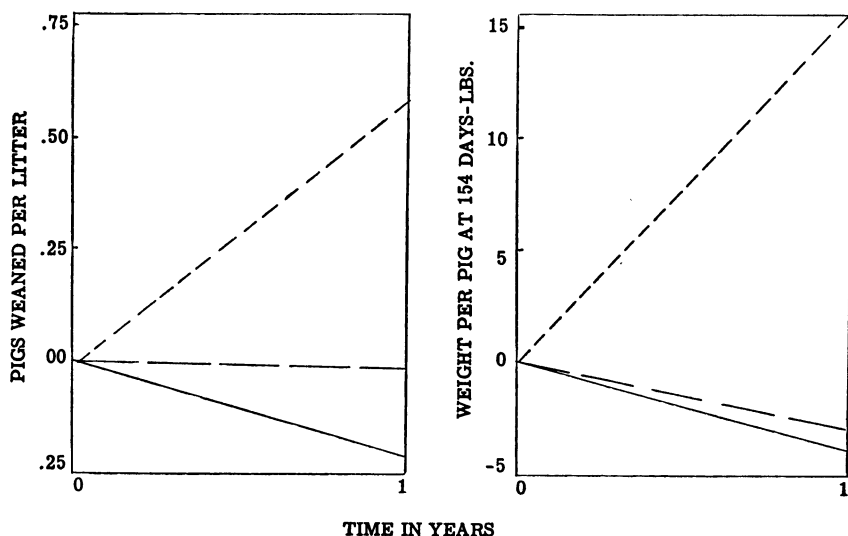


FIG. 21.1—Linear time trend within mildly inbred strains for pigs weaned per litter and 154-day weight per pig. Solid line is actual trend, dashed line is trend adjusted for effect of inbreeding trend to non-inbred basis, and the top broken line indicates mean superiority of selected parents.

has failed to improve genetic merit for litter size and has allowed growth rate to decline, although selection of parents per year has averaged about .6 pigs for size of litter weaned by the dam and sixteen pounds for pig weight at 154 days (*top broken line*).

These results must be accepted with caution, because time trends can be influenced by trends in nutrition, parasites, disease, management, or other factors. Also, the correction for inbreeding effects may have been underestimated. It seems clear that improvement has been at best only a small fraction of what would have been expected from the heritability of these traits and the amount of selection practiced for each. Evidence from comparison of intra-breed linecrosses with representative purebreds is meager but does not suggest any major improvement. Intra-herd comparisons of viability and growth rate of progeny from inbred and from representative purebred boars

(Hazel *et al.*, 1948) likewise have shown little advantage accruing from selection during development of the inbred lines.

The apparent inability of selection to offset the decline in performance from mild inbreeding casts doubt on the assumption that epistasis or ordinary dominance (between none and complete) can account for the major influence of inbreeding on performance in swine. Unless one assumes a preponderance of tight repulsion phase linkages, selection should have increased the frequency of favorable dominant genes. Similarly, under epistasis in which the genetic intermediate is optimum, selection should have prevented fixation of the more extreme homozygous combinations, particularly if a rather large number of loci determine the genetic range for each primary function.

The type of genetic mechanism that would most surely produce an inbreeding decline relatively unresponsive to selection is heterozygote superiority ( $k > 1$ ). Here selection would maintain gene frequency near some intermediate equilibrium value, rather than move it toward fixation of any one allele ( $q_A$  smaller). Linear regression of genotype on phenotype (heritability) would be lower than for lesser degrees of dominance, making selection relatively ineffective. Inbreeding depression for dominance, which is proportional to  $2 q_A(1 - q_A) k f$ , would increase with  $k$ , particularly since  $q_A$  would be smaller and  $q_A(1 - q)$  larger than under partial or complete dominance.

#### "Controlled" Selection Experiments

Results have been published from two "controlled" experiments on selection with minimum inbreeding in swine. In both the Illinois study of growth rate (Kridler *et al.*, 1946) and the Alabama study of feed efficiency (Dickerson and Grimes, 1947), the high and low selection lines separated appreciably and significantly. However, it is difficult to judge from the time trends whether the difference came partly from improvement in the high line or almost entirely from decline in the low line. Taken at face value, the time trends indicate that the separation was due to decline in growth rate of the low line in the Illinois experiment, but that efficiency increased in both lines in the Alabama study.

In these experiments, the low line involved a reversal in the usual direction of selection. This amounted to assigning new selective values to genes affecting growth and feed utilization, and hence selection might be expected to be unusually effective for the first few generations in moving toward some new equilibrium. In both experiments, selection was most effective in the first generation.

In Goodale's (1938) and in MacArthur's (1949) selection for size in mice, there is no question that a steady increase in size was produced. However, these experiments with adult size in mice are not directly analogous to those

with prolificacy, viability, and growth rate in swine, for several reasons. First, the history of selection prior to the beginning of the experiment presumably had not been consistently positive for adult size in mice, as it was for prolificacy, viability, and rate of growth in swine. Second, selection for increased size of the organism may be quite different from selection for a further increase in efficiency within the same adult body size. Adult size is generally highly heritable but not consistently selected for in either direction in farm animals. The steady decline in effectiveness of selection without reduction in variability for size in MacArthur's study suggests approach to an equilibrium similar to that postulated for total performance in swine.

#### Heritability Estimates

Heritability, the portion of observed variance linearly associated with genotype, ranges from about 10 to 50 per cent for individual characters of economic importance. But heritability is found to be lower for the highly important characters such as prolificacy and viability, for which selection has been appreciable and always in one direction, than for traits such as carcass composition or external dimensions, for which selection has been mild or in opposite directions in different portions of the breed or during different periods of time. Heterozygote superiority is more likely to be important for genetic variability in the highly important characters, since selection would have had greater opportunity to fix those genes whose homozygotes were equal or superior to alternative genotypes at the same locus, leaving at intermediate frequencies (larger  $q_A[1 - q_A]$ ) genes exhibiting heterozygote advantage.

Ineffectiveness of selection for heritable traits suggests that degree of dominance may be higher and heritability lower for total performance than for its individual components. This has been shown for grain yield and its components in corn by Robinson *et al.* (1949) and by Leng *et al.* (1949). In swine, Cummings *et al.* (1947) found heritabilities of 22 per cent for size of litter at birth, 40 per cent for survival from birth to weaning, but only 7 per cent for total litter weight at weaning. Heritability of total weaning weight jumped from 7 to 59 per cent when effects of size of litter at birth and of survival were held constant. These results could have arisen from negative genetic-physiological or from high positive environmental correlations, or both, between numbers per litter and weight per pig at weaning.

Positive estimates of heritability for economic characters may be obtained, even though selection is ineffective due to heterozygote advantage. If  $k > 1$  and rates of reproduction were proportional to phenotypic levels, equilibrium frequency for the more favorable allele would be  $q_A = (1 + k)/2k$ . At this point, the linear regression of genotype on phenotype in an unselected population would be zero, and all intra-allelic genetic variability would be due to

dominance deviations (Fig. 21.2). Here both paternal  $\frac{1}{2}$ -sib correlation and regression of progeny on parent would yield zero estimates of heritability, if only dominance were involved.

Equilibrium gene frequency actually will be determined by degree of dominance expressed in terms of relative selective values or reproductive rates ( $k'$ ) rather than in terms of relative performance levels ( $k$ ) of the several genotypes. Conceivably,  $k'$  could be either larger or smaller than  $k$ . If culling is mild, difference in reproduction rates will be smaller between  $Aa$  and  $AA$  and larger between  $AA$  and  $aa$  than if proportional to phenotypic levels, and effective  $k'$  will be smaller and equilibrium  $q_A$  larger. Conversely if phenotypic selection is intense, differences in reproduction rates between

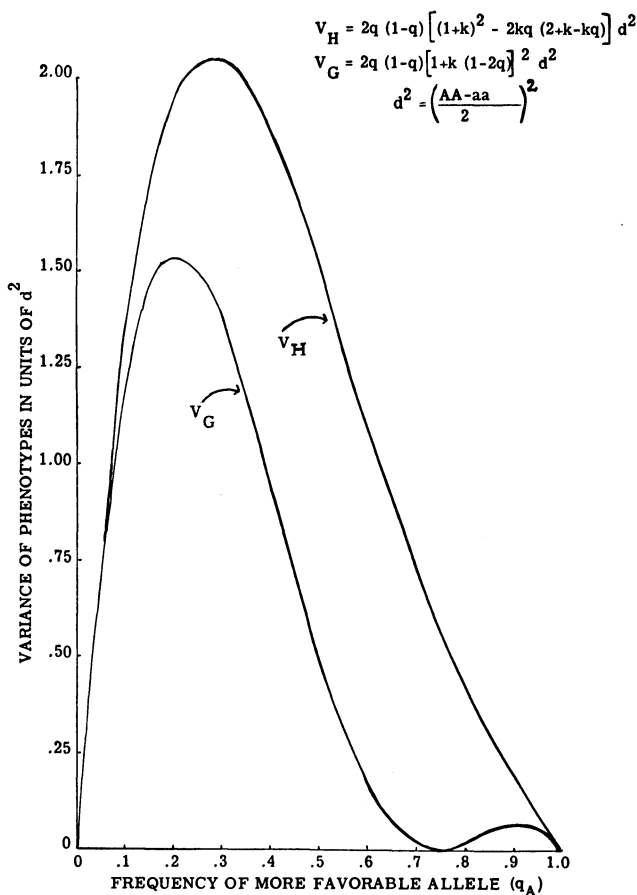


FIG. 21.2—Total variance in phenotype ( $V_H$ ) and portion linearly associated with genotype ( $V_G$ ) in a random breeding population for a single chromosomal unit and heterozygote advantage of  $k = 2$ , at varying frequencies for the more favorable of two alleles.

$Aa$  and  $AA$  will be magnified and those between  $AA$  and  $aa$  minimized, making  $k'$  larger than  $k$  and equilibrium  $q_A$  smaller than  $(1 + k)/2k$ . The larger the number of genes controlling genetic variation in the basis of selection, the less difference intensity of culling will introduce between  $k'$  and  $k$ .

Estimates of heritability from regression of offspring on parent will increase positively as equilibrium  $q$  becomes larger than  $(1 + k)/2k$ , and assume larger negative value as  $q$  becomes smaller than  $(1 + k)/2k$ . Larger positive heritability estimates based on paternal  $\frac{1}{2}$ -sib correlation will be obtained as  $q$  becomes either larger or smaller than  $(1 + k)/2k$ , since this method estimates fraction of the phenotypic variance linearly associated with genotype regardless of the sign of the regression of offspring on parent (Fig. 21.2).

It seems clear that positive estimates for heritability of individual characters do not rule out the possibilities (1) that heterozygote advantage obtains, especially for net selective advantage or total performance; and (2) that effectiveness of selection may be only a small fraction of that indicated by the estimates of heritability for individual characters. More attention needs to be given estimates of heritability for total performance indices and their components.

#### Negative Genetic Correlations between Components of Total Performance

Existence of negative genetic correlations would correspond to heterozygote superiority. This is in the sense that an increase in frequency of genes with partially or completely dominant favorable effects on one character would amount to a decrease in frequency of their alleles having partially or completely dominant favorable effects on one or more other characters. This involves the reasonable assumptions that genes have manifold end effects and that selection maintains at intermediate frequencies—where contribution to genetic variability is larger—only those genes having dominant favorable but recessive unfavorable effects on performance. MacArthur's (1949) experiment provided ample evidence that selection for a single character (adult size) produces many important changes in other characters.

Direct evidence for negative genetic correlations is not plentiful. Much data must be analyzed to estimate genetic correlation with precision, particularly when the traits correlated are of low heritability. Also, it is difficult to avoid bias from environmental correlations. If leaner hog carcasses are considered desirable, the genetic correlations of .3, .7, and  $-.7$  for ratio of fat to lean cuts with 180-day weight, daily gain, and feed requirements per unit of weight gain found in a study of Iowa Record of Performance data (Dickerson, 1947) need to be considered. In the same and in another study (Dickerson and Grimes, 1947) evidence for genetic antagonism between



good milking ability and rapid, economical fattening in swine is presented.

Other reasons for expecting negative genetic correlations that might be mentioned are (1) lower heritability for total performance than for its components, as outlined previously, and (2) approach to some physiological maximum, where increase in one function must necessarily reduce others, as in division of nutrient energy available between milk production and fleshing.

Negative genetic correlation, in some degree, is maintained by the process of selection itself and would disappear if selection were relaxed. Animals mediocre in any one respect are retained as breeders only if superior in several other characters. Thus selection leads to a negative correlation between characters among the animals selected as parents. To a much lesser degree, these negative relationships would appear among the progeny, where fresh selection would magnify them again. Such negative character relationships may explain in part the discrepancy between rates of improvement "expected" and obtained, and could exist quite apart from any real heterozygote advantage.

#### Analogy between Results with Corn and with Swine

In both corn and swine, (1) inbreeding has been slight during domesticated history, until recently at least, (2) degree of heterozygosity exerts a major influence on performance, (3) effectiveness of continued phenotypic selection is questionable in stocks with a long history of selection for the same complex of characters in which further improvement is sought.

Hull (1945) has postulated overdominance or heterozygote superiority, with additive interaction of non-alleles, to explain corn breeding results. He does so on the basis that (1) yields of parental,  $F_1$ ,  $F_2$ , and backcross populations are linearly related to proportion of loci heterozygous (Neal, 1935), (2) yields are usually less than one half as large for homozygous lines as for their  $F_1$  crosses, (3) regression of  $F_1$  yield on parental inbred yield among  $F_1$  crosses having one parent in common often is zero or negative for the higher yield levels of the common parent. Robinson *et al.* (1949) have obtained estimates indicating heterozygote advantage ( $k = 1.64$ ) for grain yield but only partial to complete dominance for components of yield. Crow (1948) has shown that under complete dominance ( $k = 1$ ) of favorable genes combining additively, average superiority of maximum hybrid over the variety at equilibrium gene frequency would be the product of mutation rate and number of loci, or less than 5 per cent, whereas potential hybrid advantage under some degree of heterozygote advantage ( $k > 1$ ) at even a small proportion of loci could be many times greater, in agreement with results already obtained.

The impossibility of accounting for the 15 to 25 per cent advantage of better corn hybrids over open-pollinated varieties through complete dominance of favorable genes combining additively can be demonstrated (Dicker-

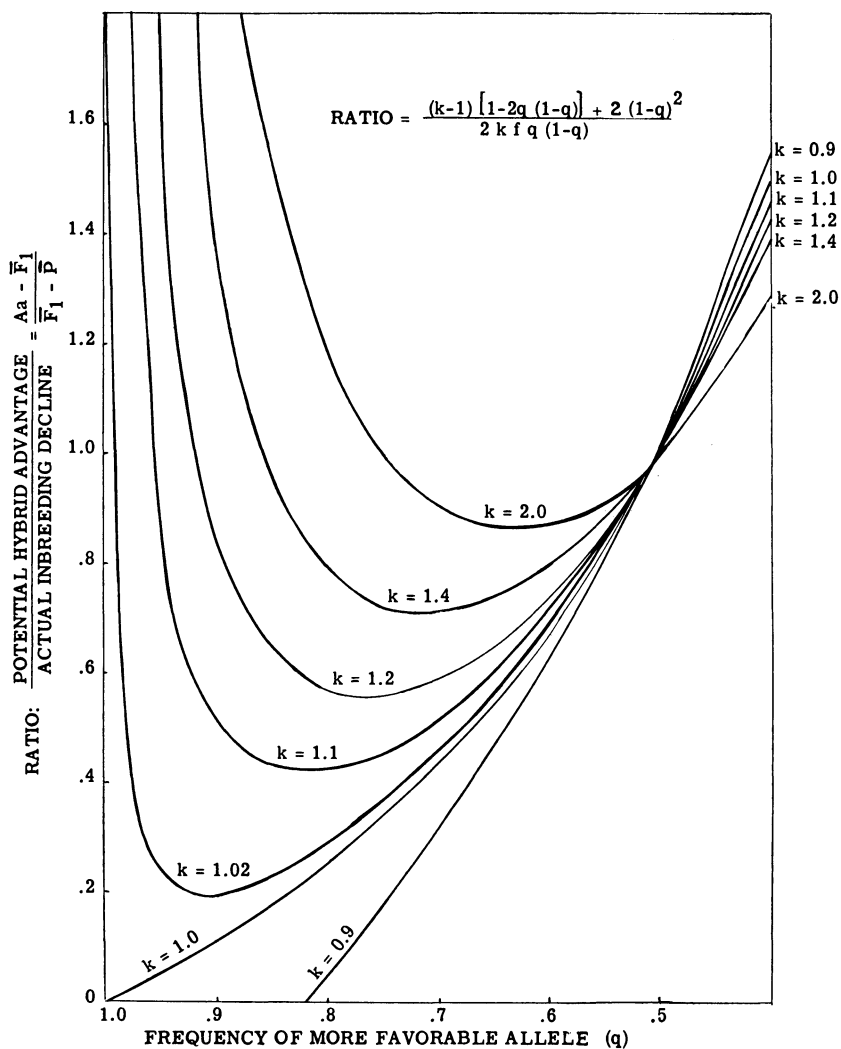


FIG. 21.3—Potential hybrid advantage per locus ( $Aa - \bar{F}_1$ ) as a proportion of observable inbreeding decline ( $\bar{F}_1 - \bar{P}$ ), for varying degrees of dominance and frequencies of the more favorable allele in a population of homozygous ( $f = 1$ ) lines and their  $F_1$  crosses.

son, 1949) from the average ratio per locus of maximum potential superiority of hybrid over average of all possible  $F_1$ 's to the observable mean advantage of the  $F_1$ 's over the inbred lines themselves (Fig. 21.3). Using  $(1 - q)$  for frequency of the less favored allele,  $f$  for Wright's inbreeding coefficient,  $k$  for degree of dominance, as before, and  $d = (AA - aa)/2$ :

$$\bar{H} = \text{Maximum heterozygote} = C + (1 + k) d$$

$$\bar{F}_1 = \text{Mean of } F_1 \text{ crosses} = C + 2q [1 + k(1 - q)] d$$

$$\bar{P} = \text{Mean of inbred lines} = C + 2q [1 + k(1 - q)(1 - f)] d$$

$$\text{Hence, } \frac{(\bar{H} - \bar{F}_1)}{\bar{F}_1 - \bar{P}} = \frac{(k - 1)[1 - 2q(1 - q)] + 2(1 - q)^2}{2kfq(1 - q)}$$

Under partial or complete dominance, equilibrium  $(1 - q) = (k - 1)/2k = 0$ , except for reverse mutation pressure. When the parental lines are homozygous ( $f = 1$ ), mean  $(1 - q)$  lies between .05 and .1 and mean inbred yield is about 40 per cent of that for  $F_1$  crosses, the maximum increase of hybrid over average  $F_1$  would lie between 3 and 7 per cent. There is little reason to suppose that present better hybrids approach the maximum. The potential maximum increase over open-pollinated varieties increases rapidly with degree of heterozygote advantage ( $k$ ), approaching  $(\bar{F}_1 - \bar{P})$  or about 50 per cent in corn yield.

The evidence thus far obtained in swine suggests that the genetic basis of variation in net productivity is fundamentally quite similar to that in corn. This indicates challenging possibilities for increasing productivity of swine by utilizing potential heterosis.

#### Heterozygote Advantage for Single Loci and Chromosome Segments in Other Species

Dobzhansky (1949) has shown experimentally that natural selection favors individuals heterozygous for inversion chromosome segments in *Drosophila*. He also has shown that the resulting equilibrium between frequency of alternative homologous segments fluctuates with locality and season of the year, depending on relative selective advantage of alternative "homozygous" segments. He postulates natural selection for increased *coadaptation* between alternative segments in heterozygotes within each interbreeding population. Demonstration of heterozygote advantage at individual loci would be difficult, since any one locus usually would account for only a small part of the total variability in selective value or in any complex character. However, some cases of presumably single gene mutations exhibiting heterozygote advantage have been reported (Jones, 1945; Gustafsson, 1946, 1947). The "yellow" gene of the agouti series in mice (Danforth, 1927; Dickerson and Gowen, 1947) provides a classic example of manifold effects

of genes and of heterozygote superiority in food utilization, if not in selective value.

It seems inevitable that manifold effects of genes and equilibrium between frequencies of alternative alleles are commonplace, with relative selective values shifting with the characters given emphasis in selection at each stage of development from conception through maturity.

### EFFECTIVENESS OF METHODS OF SELECTING FOR MAXIMUM HETEROSIS

The evidence presented provides several related assumptions concerning the nature of genetic variability in economic characters of swine as the basis for considering how selection for maximum heterosis can be made most effective. These are: (1) Heterozygote advantage ( $k > 1$ ) is important for total performance when its components are characters that have had consistently positive selective values, although lesser degrees of dominance may obtain for individual characters. (2) Average gene frequency approaches an intermediate equilibrium near  $q_A = (1 + k)/2k$ , whose value and stability depend on the intensity, consistency, and duration of selection. (3) Performance levels attainable by selection in outbred populations are far below the maximum heterozygote, because more than one-half of the individuals are homozygous at each locus. (4) Inbreeding decline may be considered as due largely to the reduced number of genes useful to the species that can be carried by the more homozygous individuals, rather than to fixation of unfavorable recessive genes.

Under these assumptions, any method of selecting for maximum performance will involve (1) selection for maximum proportion of heterozygous loci in crosses of complementary strains, and (2) selection based on progeny tests of individuals or lines in crosses. These methods are indicated only when individual and family selection become relatively ineffective, because the intensity of selection per unit of time is much lower for selection based on test-cross progeny performance.

#### Importance of Recurrent Selection to Achieve Maximum Heterosis

Hull (1945) has emphasized the great importance of utilizing cumulative gains from recurrent selection for heterosis in crosses, rather than relying on a single selection among  $F_1$  crosses of a group of homozygous lines. This principle may be illustrated by contrasting the observed distribution for number of heterozygous loci in a population of  $F_1$  crosses among inbred lines with the potential range (Fig. 21.4). It can be shown that the standard deviation in proportion of heterozygous loci is:

$$\sigma_{Hw} = \sqrt{\frac{2q(1-q)(1-f)[1-2q(1-q)(1-f)]}{n}}$$

within linecrosses, and

$$\sigma_{Hb} = \sqrt{\frac{2q(1-q)f[1-2q(1-q)(2-f)]}{n}}$$

among linecrosses, where  $f$  is the inbreeding of the population of lines and  $n$  is the effective number of segregating chromosomal units.

Range in degree of heterozygosity among all  $F_1$  crosses of a population of lines for likely values of  $n$  ( $n = 100$  and  $f = 1$  in Fig. 21.4) is small rela-

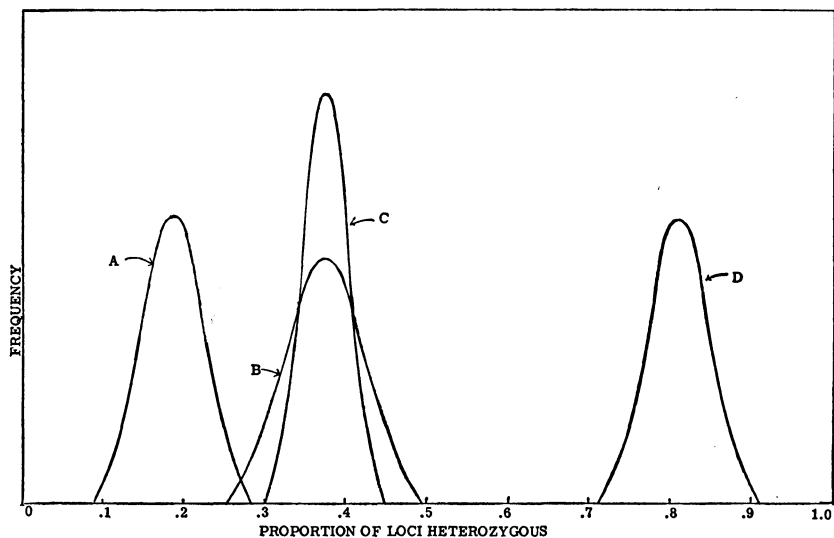


FIG. 21.4—Frequency distribution for proportion of 100 loci heterozygous when  $k = 2$  and initial  $\bar{q}_A = .75$  within lines 50 per cent inbred (A), between  $F_1$  crosses of homozygous lines or in a non-inbred population (B), between  $F_1$  crosses of lines inbred only 50 per cent (C), and in a cross between complementary strains ( $\bar{q}_1 = .95, \bar{q}_2 = .15$ ) attainable only through recurrent selection for cross performance (D).

tive to the potential range. Hence recovery of  $F_1$  crosses much above the average for all  $F_1$ 's or for non-inbred stock cannot be expected. Inbreeding provides a means for steadily reducing the proportion of heterozygous loci. What is needed is recurrent selection in complementary strains to make them steadily approach opposite extremes in gene frequency at each locus exhibiting heterozygote advantage. The best  $F_1$  of a population of 100  $F_1$  crosses would average about  $2.6 \sigma_{Hb}$  above the mean, whereas the best 1 of 10 would average about  $1.54 \sigma_{Hb}$  above the mean and cumulative selection of the best 1 of 10 in each of 10 recurrent cycles of selection would amount to choosing  $F_1$ 's that were  $10 (1.54) \sigma_{Hb} = 15.4 \sigma_{Hb}$  above the original mean.

#### Homozygous Tester versus Reciprocal Selection

Hull (1945) has proposed recurrent cycles of selection in crossbred material based on progeny test in crosses with a single homozygous line (alternatively, with two related lines or their  $F_1$ ) as a method of producing highly comple-

mentary lines to be used in production of commercial hybrids. Comstock *et al.* (1949) have compared expected effectiveness of Hull's plan with that for reciprocal selection for cross performance between two foundation stocks of divergent origin, avoiding inbreeding in both stocks. They point out that the potential limits of improvement are the same for the two methods, except for loci exhibiting only partial dominance ( $k < 1$ ), where the use of a tester homozygous for any of the less favorable alleles would reduce potential hybrid performance. Existence of important epistatic effects also would tend to make limits lower for use of a homozygous tester.

There is no reason to expect initial cross performance to differ between reciprocal and homozygous tester selection, other than because of the performance of the inbred tester line itself (inbreeding effects on maternal environment of the litter in swine). If anything, it would be easier to find a population differing materially in gene frequency at individual loci from a homozygous tester than to find two similarly complementary non-inbred populations.

Relative rates of improvement expected from the two plans depend on (1) selection pressure applied, and on (2) size of regression of gene frequency in the material under selection on performance of test-cross progeny. Hull's homozygous tester plan limits selection to only one of the parental stocks. Hence selection applied will be only  $\frac{1}{2}$  as great as in reciprocal selection. However, as long as frequencies of the more favorable alleles ( $q$ ) are anywhere near their expected equilibrium of  $(1 + k)/2k$ , progress toward complementary gene frequencies (toward maximum proportion of heterozygous loci in the cross) per cycle of selection will be far less for reciprocal than for homozygous tester selection.

Comstock (1949) has shown that improvement in performance of random crosses between two segregating populations per generation of selection, at a given locus, is:

$$\Delta P_r = [\Delta q_1 (1 + k - 2kq_2) + \Delta q_2 (1 + k - 2kq_1) - 2k \cdot \Delta q_1 \cdot \Delta q_2] d \quad (1)$$

The change in gene frequency at a given locus within each of the two selected populations ( $\Delta q_1$  and  $\Delta q_2$ , respectively) will be determined by (1) the intensity of selection based on the test-cross progeny means ( $s$  = selection differential in  $\sigma$  units), (2) the correlation between  $q_1$  and the mean progeny performance ( $P$ ), and (3) the size of  $\sigma_{q_1}$  among the tested individuals, as follows:

$$\Delta q_1 = s r_{q_1, P} \sigma_{q_1} = s \frac{\text{Cov}_{q_1 P}}{\sigma_P} = \frac{s d}{2 \sigma_P} q_1 (1 - q_1) (1 + k - 2kq_2) \quad (2)$$

Hence, as Comstock indicates, improvement in cross performance from one cycle of reciprocal selection and for any one locus is:

$$\Delta P_r = \frac{s d^2}{2 \sigma_P} [q_1 (1 - q_1) (1 + k - 2kq_2)^2 + q_2 (1 - q_2) (1 + k - 2kq_1)^2] - 2k \cdot \Delta q_1 \cdot \Delta q_2 \quad (3)$$

However, equation (3) is not applicable for evaluating Hull's (1945) plan of recurrent selection for cross performance with a homozygous tester line. Here, cross performance will improve as  $q_i \rightarrow 0$  for loci at which the more favorable homozygote ( $AA$ ) is fixed in the tester, and as  $q_j \rightarrow 1$  for loci at which the tester is homozygous for the less favorable allele ( $aa$ ). If  $\bar{q}_T$  repre-

TABLE 21.2  
MEANS, VARIANCES, AND COVARIANCES FOR GENOTYPES OF  
SELECTED POPULATION AND PHENOTYPES OF TEST-CROSS  
PROGENIES FROM HOMOZYGOUS TESTER

SELECTED POPULATION GENOTYPES ( $q_s$ )			MEAN PHENOTYPES OF PROGENIES FROM HOMOZYGOUS TESTER	
			$AA$ at $\bar{q}_T$ of Loci ( $G_i$ )	$aa$ at $(1-\bar{q}_T)$ of Loci ( $G_j$ )
$AA$	Means Dev. Freq.	1.0 $1-q_s$ $q_s^2$	$2d$ $(1-q_i)(1-k)d$ $q_i^2 q_r$	$(1+k)d$ $(1-q_j)(1+k)d$ $q_j^2(1-q_r)$
$Aa$	Means Dev. Freq.	.5 $.5-q_s$ $2q_s(1-q_s)$	$\frac{(3+k)d}{2}$ $(\frac{1}{2}-q_i)(1-k)d$ $2q_i(1-q_i)q_r$	$\frac{(1+k)d}{2}$ $(\frac{1}{2}-q_j)(1+k)d$ $2q_j(1-q_j)(1-q_r)$
$aa$	Means Dev. Freq.	0 $-q_s$ $(1-q_s)^2$	$(1+k)d$ $-q_i(1-k)d$ $(1-q_i)^2 q_r$	0 $-q_j(1+k)d$ $(1-q_j)^2(1-q_r)$
Means		$q_s$	$[1+k+q_i(1-k)]d$	$q_j(1+k)d$
Variances		$\frac{q_s(1-q_s)}{2}$	$\frac{q_i(1-q_i)(1-k)^2 d^2}{2}$	$\frac{q_j(1-q_j)(1+k)^2 d^2}{2}$
Covariances		$(q_s, G)$	$\frac{q_i(1-q_i)(1-k)d}{2}$	$\frac{q_j(1-q_j)(1+k)d}{2}$

sents the proportion of loci segregating in the stock under selection that are homozygous  $AA$  in the tester, then it can be shown (Table 21.2) that average progress in cross performance per locus is:

$$\Delta P_h = [\bar{q}_T \cdot \Delta q_i (1-k) + (1-\bar{q}_T) \cdot \Delta q_j (1+k)] d \quad (4)$$

For loci fixed  $AA$  in the tester:

$$\Delta q_i = s \cdot r_{PG_i} \cdot r_{G_i q_i} \cdot \sigma_{q_i} = \frac{s d \sqrt{\bar{q}_T}}{2 \sigma_P} \cdot q_i (1-q_i) (1-k) \quad (5)$$

Similarly for loci fixed  $aa$  in the tester:

$$\Delta q_j = s \cdot r_{PG_j} \cdot r_{G_j q_j} \cdot \sigma_{q_j} = \frac{s d}{2 \sigma_P} \cdot \sqrt{(1-\bar{q}_T)} \cdot q_j (1-q_j) (1+k) \quad (6)$$

From equation (4) we can now express average progress per locus from selection for cross performance with a homozygous tester as:

$$\Delta P_h = [\bar{q}_T^{3/2} q_i (1 - q_i) (1 - k)^2 + (1 - \bar{q}_T)^{3/2} q_j (1 - q_j) (1 + k)^2] \frac{s d^2}{2 \sigma_P} (7)$$

Rate of improvement in cross performance from reciprocal selection (equation 3) approaches zero as gene frequencies approach the equilibrium expected if rates of reproduction of individuals were directly proportional to their phenotypes (i.e.,  $q = [1 + k]/2k$ ). Hence, progress from reciprocal selection may be expressed more usefully in terms of the deviation of gene frequencies from  $(1 + k)/2k$ , as follows:

$$\Delta P_r = \frac{s d^2}{2 \sigma_P} \left[ q_1 (1 - q_1) \left( \frac{1 + k}{2k} - q_2 \right)^2 + q_2 (1 - q_2) \left( \frac{1 + k}{2k} - q_1 \right)^2 \right] 4k^2 - 2k \cdot \Delta q_1 \cdot \Delta q_2 d \quad (8)$$

Comparisons of expected progress per generation from homozygous tester and from reciprocal selection may be made from equations (7) and (8), respectively. The comparison may be visualized by plotting rate of improvement against deviations of gene frequencies from an initial equilibrium value of  $(1 + k)/2k$ , using  $q_1$  and  $q_2$  for the two populations under reciprocal selection, and  $q_i$  and  $q_j$  for loci that are  $AA$  and  $aa$ , respectively, in the tester, for homozygous tester selection.

In Figure 21.5, it is assumed that  $k = 2$ , and  $q_i$  is shown approaching 0  $(k + 1)/(k - 1)$  times as fast as  $q_j$  approaches 1. Actually,  $q_i$  would move more slowly than  $q_j$  at first because  $(Aa - AA) = (k - 1)d$  and  $(Aa - aa) = (1 + k)d$ . However,  $\Delta q_i$  increases as  $q_i$  falls from .75 toward .5 because of the increased variance of  $q_i$  and consequent increase in genetic variance and in covariance with progeny means, and then  $\Delta q_i$  declines as  $q_i$  moves from .5 toward 0. There is a steady decline in  $\Delta q_j$  as  $q_j$  rises from .75 toward 1.0.

Under reciprocal selection, if  $q_1$  and  $q_2$  are near an equilibrium of  $(1 + k)/2k$  at the outset, initial progress will be slight compared with that from homozygous tester selection and will not equal  $\Delta P_h$  until  $q_1$  and  $q_2$  differ, in opposite directions from  $(1 + k)/2k$ , by an average of about .50. Only during the late generations of selection will reciprocal selection surpass homozygous tester selection in effectiveness.

Another possible disadvantage of reciprocal selection is that gene frequencies at most loci for which  $k > 1$  may be somewhat below  $(1 + k)/2k$ . This will occur if the advantage of  $Aa$  over  $AA$  and  $aa$  individuals in rate of reproduction is made greater by intensive individual or family selection than it would be if reproductive rates were directly proportional to phenotypic levels of performance. This would amount to increasing the effective degree



of heterozygote advantage from  $k$  to  $k'$ , and hence making actual equilibrium  $q$  nearer to .5 (i.e.,  $\hat{q} = [1 + k']/2k'$ ).

If actual equilibrium frequencies for the more favorable allele are generally below  $(1 + k)/2k$  in both populations, reciprocal selection will tend to raise both  $q_1$  and  $q_2$  toward  $(1 + k)/2k$ , but at an ever decreasing rate, until  $q$  chances to go beyond  $(1 + k)/2k$  in one of the populations. However,  $q_1$  and  $q_2$  are unlikely to be equal, even when both are smaller than  $(1 + k)/2k$ . If  $q_1 > q_2$ , then  $q_1$  will be closer than  $q_2$  to  $(1 + k)/2k$  and will move faster in that direction ( $\Delta q_1 > \Delta q_2$ ). Consequently  $q_1$  will become larger than  $(1 + k)/2k$  and direction of  $\Delta q_2$  will be reversed without reducing  $\Delta q_1$  to zero. Only

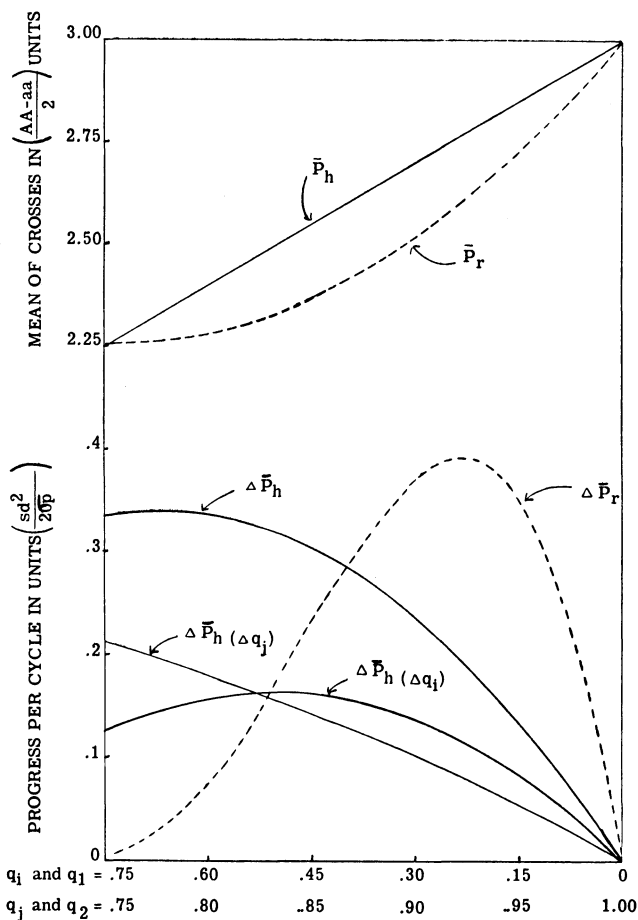


FIG. 21.5—Mean performance of crosses (*upper*) and rates of progress per cycle (*lower*) for homozygous tester (*solid lines*) and for reciprocal (*broken lines*) selection when  $k = 2$  and  $\bar{q}_T = .75$ , as  $q_i$  and  $q_1$  approach 0 and  $q_j$  and  $q_2$  approach 1.

then can the slow-starting reciprocal selection begin moving  $q_1$  and  $q_2$  toward opposite extremes.

### Use of Partially Inbred Tester Lines

In large animals, or even in poultry, discussion of selection utilizing homozygous tester lines is still largely academic. Few very highly inbred and usable lines of swine and chickens exist. However, there are many partially inbred lines of swine and poultry whose average cross performance has been or is now being tested. These partially inbred lines should be extremely useful in overcoming the initial disadvantage of reciprocal selection, because inbreeding will have pushed frequencies of individual genes in these lines much further away from equilibrium than in non-inbred stocks. Since effectiveness of reciprocal selection (equation 8) increases with

$$\left( \frac{1+k}{2k} - q_2 \right)^2,$$

even a moderately inbred line used as one of two populations under reciprocal selection would materially increase initial progress per cycle from  $\Delta q_1$ .

Of course, further selection within the inbred line itself on the basis of cross performance would be relatively ineffective ( $\Delta q_2$  small) until the selection on cross performance has had time to shift  $q_1$  at individual loci in the non-inbred population away from  $(1+k)/2k$  in the opposite direction from  $q_2$ . It might be wise to ignore cross performance in selecting replacements within the inbred line for a number of cycles to allow time for  $q_1$  to make this shift at loci where initial  $q_1$  and  $q_2$  chance to deviate from  $(1+k)/2k$  in the same direction. Beyond this point, progress from reciprocal selection between the partially inbred and the non-inbred populations should approach and finally exceed that from selection for cross performance with a homozygous tester.

In selecting a partially inbred line for use in reciprocal selection, one instinctively would choose a line known to be superior in its average cross performance and in its usability as an inbred strain. This seems desirable to assure that the line carries at high frequencies any genes whose favorable effects on total performance are incompletely dominant. In addition, it would be helpful to try a number of different partially inbred lines in crosses with a given non-inbred stock, choosing finally for reciprocal selection the line showing best initial cross performance. Diversity of origin and previous crossing data would of course aid in selecting the lines more likely to be initially complementary to a given non-inbred stock.

Presumably, both initial cross performance and rate of progress from reciprocal selection are likely to be greater if the two populations are of different breeds. However, Dobzhansky's (1949) finding of greater heterozygote advantage from alternative homologous chromosome segments within a single population than in crosses between non-interbreeding populations of

*Drosophila* suggests the need for further investigation of the importance of diversity of origin for attainment of maximum heterosis in crosses.

### Use of an $F_1$ Cross as the Tester

Hull (1945) also has suggested selection to complement the  $F_1$  cross of two homozygous lines as a means for developing new lines to replace the poorer ones presently used in successful corn hybrids. Here, expected rate of improvement in performance of the 3-line cross ( $\Delta P_f$ ) would be a composite of that expected from selection for cross performance with a homozygous tester, and with a non-inbred strain in which gene frequency is  $\frac{1}{2}$  at each locus:

$$\Delta P_f = [q_T^2 \cdot \Delta q_i (1-k) + (1-q_T)^2 \cdot \Delta q_j (1+k) + 2q_T(1-q_T) \cdot \Delta q_f] d \quad (9)$$

where  $q_T$  is average proportion of loci homozygous for the more favorable allele in the lines represented in the  $F_1$  tester;  $q_i$ ,  $q_j$ , and  $q_f$  are average frequencies of the more favorable alleles at loci that are  $AA$ ,  $aa$ , and  $Aa$ , respectively, in the  $F_1$  tester. The  $F_1$  tester is  $AA$  at  $q_T^2$ ,  $aa$  at  $(1-q_T)^2$ , and  $Aa$  at  $2q_T(1-q_T)$  of the loci. Hence,

$$\Delta q_i = \frac{sd}{2\sigma_P} q_T q_i (1-q_i) (1-k), \quad \Delta q_j = \frac{sd}{2\sigma_P} (1-q_T) q_j (1-q_j) (1+k)$$

and

$$\Delta q_f = \frac{sd}{2\sigma_P} \sqrt{2q_T(1-q_T)} \cdot q_f (1-q_f).$$

Substituting in equation (9), we obtain as estimated progress per cycle:

$$\begin{aligned} \Delta P_f = & \{q_T^3 q_i (1-q_i) (1-k)^2 + (1-q_T)^3 q_j (1-q_j) (1+k)^2 \\ & + [2q_T(1-q_T)]^{3/2} \cdot q_f (1-q_f)\} \frac{sd^2}{2\sigma_P} \quad (10) \end{aligned}$$

Apparently one might expect that selection to complement an  $F_1$  tester (of 2 homozygous lines) would be about one-half as effective as selection to fit a single homozygous tester.

In selection for complementary strains in livestock, the  $F_1$  tester may be a cross of two partially inbred lines,  $M$  and  $N$ . Selection of a population,  $L$ , to complement  $M \cdot N$  would tend to improve the  $L(M \cdot N)$  cross at a rate intermediate between one-half that for reciprocal selection ( $\Delta P_r$ )/2 and that for use of an  $F_1$  cross of homozygous lines as the tester ( $\Delta P_f$ ), depending on the degree of inbreeding in lines  $M$  and  $N$ .

If  $M$  and  $N$  were being selected to complement each other, gene frequency in the  $(M \cdot N)$  linecross tester would tend to be lowered from equilibrium  $(1+k)/2k$  toward  $\frac{1}{2}$  as the limit. Consequently, rate of improvement in the  $L(M \cdot N)$  cross from selecting  $L$  to fit  $M \cdot N$  should approach that expected from selecting in population  $L$  to complement a non-inbred tester in which

$q = .5$  at each segregating locus. Progress per cycle when  $q_2 = .5$  should approach

$$q_1(1 - q_1) \cdot \frac{s d^2}{2 \sigma_P}.$$

Since  $q_1$  would be increased above initial equilibrium of  $(1 + k)/2k$ , maximum progress per cycle should be

$$\frac{(1 + k)(k - 1)}{4k^2} \frac{s d^2}{2 \sigma_P},$$

and rate of progress would decline as  $q_1$  became larger than  $(1 + k)/2k$ . The maximum rate of progress, then, for selecting population  $L$  to complement the cross of two highly complementary strains  $M$  and  $N$ , is expected to be little more than one-half that for selection to complement a homozygous tester.

### Other Considerations

Under heterozygote advantage and selection toward complimentary strains by either the reciprocal or the homozygous tester method, the strains themselves may be expected to decline in performance for characters that are depressed by inbreeding. The less favorable allele would tend to become fixed at about half of the loci segregating in the foundation stocks. The effectiveness of this sort of selection in moving gene frequencies toward opposite homozygous extremes in the complementary strains would be greater for those traits in which heterozygote advantage ( $k > 1$ ), and hence inbreeding depression, is larger. That portion of the inbreeding depression arising from loci at which there is no heterozygote advantage ( $k \leq 1$ ) would not be produced by selection for cross performance without inbreeding, because selection would favor the dominant allele in both strains. Therefore, any serious decline in performance of the strains themselves, while under selection for cross performance, is indicative of heterozygote advantage and should be accompanied by compensatory improvement in performance of the cross.

In order to develop complementary strains whose own performance would make them usable in commercial production of crosses, some compromise may be necessary between selection based on test-cross and on individual performance. There is much opportunity for selection in choosing young breeders, especially males, to be tested in the strain-cross. Individual selection for characters little affected by inbreeding would be least apt to impair the effectiveness of the complementary selection. Some selection for individual performance characters important for both the strains and their cross may become necessary to prevent fixation of rare genes with major detrimental effects in the homozygote, but advantageous in the heterozygote. Selection for fertility and maternal influences (e.g. hatchability, prolificacy, or suckling ability) in test-cross matings should help maintain usable strains.

## SUMMARY

### Genetic Variability in Economic Characters of Swine

1. Inbreeding and crossbreeding effects indicate that degree of heterozygosity exerts a major influence on the important performance characters, and that a high degree either of dominance or of epistacy due to deviations from an optimum genetic intermediate, or both, characterizes genetic variability in performance.

2. Relative ineffectiveness of selection within mildly inbred strains makes ordinary dominance or epistasis doubtful as an explanation of inbreeding decline, and suggests heterozygote advantage for net desirability in prolificacy, suckling ability, viability, and growth rate.

3. "Controlled" selection experiments with swine show that high and low lines for growth rate or feed utilization can be separated, but indicate little improvement of high line over foundation stock, particularly for net performance in all characters.

4. Lower heritabilities and larger inbreeding declines for characters long and intensely selected in one direction, compared with those selected toward an intermediate or in varying directions, indicate a higher degree of dominance for the former.

5. Some sort of negative relationship between components of total performance is indicated by lower heritability for total performance than for its component characters and by direct estimates of correlation. This would correspond to heterozygote superiority, in that increased frequency of genes with dominant favorable effects on one character would constitute decreased frequency of their alleles having dominant favorable effects on other characters.

6. The genetic basis of performance appears to be similar in corn and in swine, as indicated by natural degree of inbreeding, extent of inbreeding decline in performance, and the effectiveness of phenotypic selection. Ordinary dominance is inadequate to account for heterosis already achieved in corn, and by analogy, is unlikely to be adequate in swine.

7. Examples of manifold effects and heterozygote advantage for specific chromosome segments or loci support their inferred importance for quantitative economic characters.

### Methods of Selecting for Maximum Heterosis

1. Intensity of selection per unit of time is lower when based on progeny performance in test-crosses than when based on individual and family performance. Hence, methods of selecting for maximum cross performance between complementary strains are indicated only when individual and family selection have become relatively ineffective, and when there is evidence for

important heterozygote advantage with attendant intermediate equilibrium gene frequencies.

2. Cumulative gains from recurrent selection pressure are necessary to obtain efficiently crosses heterozygous for anywhere near the potential maximum proportion of loci, since distribution of  $F_1$  crosses within any generation is narrow relative to the potential range when numbers of loci are large.

3. Expected effectiveness of reciprocal recurrent selection between two populations and recurrent selection for cross performance with a homozygous tester may be compared as follows:

- a. They are alike in potential limits of cross performance for loci exhibiting heterozygote advantage, but use of a homozygous tester would be more likely to limit ultimate cross performance if partial dominance or special epistatic effects were important.
- b. They would be similar in initial cross performance, except that it should be easier to deliberately select a stock differing materially from a homozygous tester in gene frequency at individual loci than to select two equally complementary non-inbred stocks.
- c. As long as gene frequencies in the selected populations are anywhere near their expected equilibria, improvement in cross performance per cycle will be far greater for the homozygous tester than for the reciprocal selection plan. The difference between progenies from  $A$  and  $a$  gametes under selection approaches zero as frequency of  $A$  in the non-inbred tester approaches an equilibrium of  $(Aa - aa)/(2Aa - AA - aa)$ , but discrimination between  $A$  and  $a$  gametes under selection is maximum when the tester is homozygous  $aa$  or  $AA$ .
- d. Rate of progress from reciprocal selection accelerates as the difference in frequency of homologous chromosomal units in the two populations becomes larger, and surpasses homozygous tester selection when  $q_1 - q_2$  exceeds about .5.

4. Use of a partially inbred line as one of the two populations in reciprocal selection would greatly increase progress in early cycles, since individual gene frequencies will be further away from equilibrium in inbred strains than in non-inbred stocks.