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Genetic selection in presence of pathogens such as the lymphoid leukosis virus: computer simulation *, **

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Summary. A computer model was developed to simulate the population dynamics involved when selection is for a trait influenced by the presence of a pathogen in addition to quantitative genetic factors. The lymphoid leukosis virus is such a pathogen, when selection is for egg production in chickens. It is transmitted congenitally from dam to offspring and horizontally from one individual to another. For these simulations, individual selection for high performance in the trait influenced by the pathogen was more effective than family selection for removing infected individuals from populations. The resulting reduction in the incidence of infected individuals in following generations made the overall response to individual selection greater than for family selection. However, the virus would remain in most populations due to horizontal transmission to individuals which later transmit the virus to their offspring. These horizontally infected individuals would not be eliminated in the selection process because their egg production was assumed to be less reduced than that of congenitally infected birds. These simulation results seem to mimic certain experimental results which heretofore have been difficult to explain since they were not consistent with quantitative genetic theoretical expectations from selection.

Key words: Quantitative genetics – Selection response – Chickens – Lymphoid leukosis – Egg production – Computer simulation

Introduction

The theoretical basis and the relative efficiency of various methods of genetic selection have been reviewed and discussed in detail by several authors, including Lush (1948); Cochran (1951); and Falconer (1960). Much of this theory is based on the assumption of independent autosomal additive genetic factors transmitted equally from the sire and dam to offspring. Griffing (1960a, b) extended this theory to allow for linkage and the contribution of additive by additive forms of epistasis to selection response. Lush (1947) compared selection on either individual merit or family merit and developed formulae for predicting the response to either of these forms of selection, including optimum selection criteria involving both individual and family merit. This included the possibility of common environmental effects to family members, but these were not considered as being transmissable. Osborne (1957a, b) extended these results and made them specific for the form of selection, often used in poultry, combining individual, dam family, and sire family information together into an optimum selection criterion.

None of these theoretical developments allows for the transmission from parents to offspring of non-genetic factors, such as pathogens that may be transmitted from the dam via the egg to congenitally infect the offspring. This phenomenon may be implicated in explaining the results of poultry selection studies, especially those whose results are inconsistent with theory and for which alternative explanations do not exist.

Review of literature

Since most chicken populations experience some incidence of the lymphoid leukosis disease, since the LL virus had been found present in most flocks surveyed, and since the quantitative genetic theory previously mentioned does not consider the

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occurrence of congenital transmission of pathogens from dam to offspring, the objective of our research was to determine whether the occurrence of these phenomena might account for the difficult to explain results of poultry selection experiments. This possibility was explored by computer simulation of the population dynamics involved. Because of the detrimental effects of subclinical LL, the poultry breeding industry is working toward reduction or eradication of the LL virus infection. The results of this study were expected to provide information about the changes in the frequency of LL virus infection and the changes in mean level of performance associated with such changes under the various selection conditions simulated.

Numerous experiments have been conducted in egg production chickens to ascertain if the responses to quantitative genetic selection were in agreement with the above mentioned theory. Kinney et al. (1970) contrasted four alternative forms of selection – selection of individual merit, sire family selection, dam family selection, and selection on an index combining individual, sire family, and dam family information. Realized responses to individual selection were close to predicted responses, whereas the realized responses to selection on sire family averages were extremely small relative to predicted responses. The responses to dam family selection agreed more closely but were still considerably less than predicted, while the responses to index selection were greater but still less than one half of the predicted response. Garwood and Lowe (1979) extended the study of Kinney et al. (1970) for three additional generations with similar results.

Dickerson (1963) reported that relaxation of selection following a substantial selection response for a total economic index with percent egg production as a major factor, resulted in a "recombination loss" in the next generation, such that the net genetic change was quite small. The temporary response in egg production attributed to additive by additive epistatic effects is consistent with the theory presented by Griffing (1960a, b). However, since the magnitude of epistatic effects upon egg production is not well documented, alternative explanations are still relevant.

Gowe (1974, 1977); Gowe and Fairfull (1980) and Fairfull and Gowe (1980) reported on several populations continuously selected for many generations for a combination of traits with primary emphasis on egg production. Gowe (1977) suggested that changes in management of the flocks to an all cage rearing and housing system and to a short day length rearing program may have exposed new genetic variation that has led to increases in response to selection in the long-term selected strains. If would seem of interest to investigate these increases in observed response from the point of view of possible involvement of the lymphoid leukosis virus.

Recently, Spencer et al. (1979, 1980) and Gavora et al. (1980) studied the incidence of individuals shedding the lymphoid leukosis (LL) virus in their eggs in the same selected and control strains of egg production poultry described by Gowe and Fairfull (1980) and Fairfull and Gowe (1980). These results showed that transmitters of the LL virus generally have depressed egg production. Thus, selection for egg production resulted in selection against transmitters. Also, selected lines had a lower incidence of the virus than their unselected controls. The following sequential events seem evident from their results:

1. Certain females transmit the LL virus congenitally to a fraction of their progeny.
2. Progeny not congenitally infected with the LL virus from their dams may be horizontally infected from chicks who do receive the virus congenitally.
3. There is a detrimental effect of the virus upon egg production and other traits, occurring even when the individual does not succumb to the disease.
4. To the degree that selection is for greater egg production, there is selection against individuals infected with the virus by either route.
5. Selection for higher egg production, thus, depresses the incidence of transmitters in the breeding population and resulting generations, except for the counteracting tendency for the incidence to recur due to horizontal infection.

Harris et al. (1984) studied the incidence of the virus and its relationship to egg production in populations including both slow-feathering and fast-feathering chickens. The presence of the virus in the blood (viremia) and the incidence of antibody against the virus, as well as transmission of the virus were measured. Their results demonstrated that the detrimental effect of the presence of the virus upon egg production seemed to be much greater for congenitally infected female chickens than for those horizontally infected. Therefore, the individuals infected congenitally will be more likely eliminated by selection for high egg production than those infected horizontally. Garwood et al. (1981) provided confirming evidence that depressed layer performance is associated with virus infection. Gavora et al. (1982) observed similar associations with egg production in meat-type chickens along with a 5% decline in broiler-age body weight for test-positive females.

Thus, three virus categories of progeny are possible (1) congenitally infected, (2) horizontally infected and (3) virus-free. Dams that are congenital transmitters might have all three kinds of progeny, whereas dams that are not congenital transmitters might have only the second and third types. Crittenden (1975) has suggested that hens that were themselves congenitally infected were probably more consistent transmitters of the virus to their embryos than hens infected horizontally.

Crittenden (1975) reviewed the information on the nature of genetic resistance to the LL virus, including four simply inherited genetic factors for resistance to infection at the cellular level. For sub-group A, the major naturally occurring form of viruses, genetic susceptibility is dominant to genetic resistance. This form of resistance should lead to improved performance since resistant hens would not be infected, would lay more eggs, would not be as likely to die, and would thus have a higher probability of being selected. Such a striking form of genetic resistance should have major impact upon selection for resistance, if it were segregating in the population. Unfortunately, many otherwise desirable stocks seemingly do not carry genetic factors for resistance.

Model of simulation

A model was developed to study the population dynamics of selection for a trait, such as egg production, influenced not only by quantitative genetic factors but also by the presence of a pathogen, such as the virus causing lymphoid leukosis. It was assumed that this virus adversely influences the trait under selection, is congenitally transmitted from dam to offspring, and is also horizontally transmitted between contemporaries. Although the computer model may over-simplify the true phenomena, the essential features in such processes were included. For simplicity, a single trait representing hen-housed egg production rate, including effects of sexual maturity and mortality, was considered as the single criterion of selection and the primary trait for which the response was computed. Mortality and the incidence of infection as well as virus transmission were also simulated. In some simulations, the

allelic frequency for a single genetic locus controlling cellular resistance as reported by Crittenden (1975) was included.

Each individual in the population was simulated to have two quantitative genetic characteristics, G_{RST}, representing the additive genetic random variables (normally distributed) for resistance (viability), G_{EP}, representing the quantitative genetic merit of the individual for hen-housed rate of egg production as expressed in a virus-free population. The statistical model for the basic egg production performance of a female is

$$EPS = \mu_i^{EPS} + D_i * G_{RST} + G_{EP} + E_{EPS}$$

where

μ_i^{EPS} represents the mean egg production performance for females that survive throughout the production period for the i^{th} sub-population, $i=1$ for the congenitally infected sub-population, $i=2$ for the horizontally infected sub-population, and $i=3$ for the virus-free subpopulation.

D_i is a coefficient giving the desired regression of egg production upon the genetic resistance factor and

E_{EPS} is a random environmental plus non-additive genetic deviation (normally distributed) affecting individual hens.

D_1 was chosen to be 1., D_2 was chosen to be 0.5, and D_3 was chosen to be 0. This means that the influence upon egg production by the genetic resistance factors for a horizontally infected individual was only one-half ($D_2=0.5$) of that for a congenitally infected individual and that the genetic resistance factors had no influence upon egg production in a virus-free individual ($D_3=0$). However, the genetic resistance factor, G_{RST}, was simulated to also influence the probability of survival through an egg production test. The model was

$$P(LIVE) = \mu_i^L + B_i * G_{RST} + E_L$$

where

P(LIVE) is the prohability that an individual hen lives to the end of the laying test.

μ_i^L represents the mean probability of living for the i^{th} subpopulation for $i=1, 2, 3$ above

B_i is a coefficient chosen to give the desired regression of the probability of living upon the genetic resistance factor and

E_L is a random environmental (non-genetic) deviation (normally distributed).

For the simulation, B_1 was chosen to be 1, B_2 was 0.5, with B_3 equal to 0, so that virus-free individuals ($B_3=0$) are uninfluenced by the genetic resistance factor with the horizontally infected sub-populations having intermediate influence from (regression upon) G_{RST} to that in the sub-population which is congenitally infected ($B_1=1$). Positive deviations for G_{RST} would represent relative resistance (greater viability), and negative deviations would indicate relative susceptibility (greater mortality). However, the simulated hen-housed egg production was influenced by how long the hen lived after housing. The age at death was simulated to occur at random over the length of the egg production period. So the observed egg production with mortality effects was

$EPM = EPS$ if the individual lives and

$EPM = EPS * RU$ if individual dies

where

RU is a random uniform deviate to give the time of mortality as a fraction of the egg production period.

A weakness of this simulation model may be that the G_{RST} factor only influences whether or not the individual lives and does not influence age at death. Both the additive genetic variables for resistance and for egg production were chosen to have mean values of 0 in the initial generation with additive genetic standard deviations of 1.0 for resistance and 1.5 for egg production. The variance of the environmental factors was chosen such that the basic additive genetic heritabilities were 20% for P(LIVE) when $B_i=1$ and for EPS when $D_i=0$. But the heritabilities for observed viability and for EPM would be less than 20% due to the chance occurrences associated with mortality and the subsequent effects upon egg production. Also, the genetic and phenotypic correlations between RST and EPS (survivors egg production) were simulated to be zero. The genetic and phenotypic correlations between RST and EPM (egg production with mortality) would be positive with magnitude determined by the B_i and D_i constants. The mean livabilities for the three sub-populations were chosen to be

$$\mu_1^L = 80\%, \quad \mu_2^L = 85\% \quad \text{and} \quad \mu_3^L = 90\%,$$

The means for egg production without mortality influences were chosen to be

$$\mu_1^{EPS} = 60\%, \quad \mu_2^{EPS} = 62.5\% \quad \text{and} \quad \mu_3^{EPS} = 65\%.$$

Combining these means, the mean egg production with mortality influences for the three sub-populations became

$$\mu_1^{EPM} = 54\%, \quad \mu_2^{EPM} = 57.8\% \quad \text{and} \quad \mu_3^{EPM} = 61.75\%.$$

Such levels are not unreasonable for poultry populations with appreciable mortality and leave opportunity for improvement from the simulated selection.

Further, it was simulated that dams that were themselves congenitally infected by the LL virus (sub-population 1) transmitted the virus to 40% of their progeny and dams that were horizontally infected (sub-population 2) transmitted the virus to 20% of their progeny. Of course, there was no egg transmission from virus-free dams in sub-population 3.

The incidence of horizontal infection was simulated to have a curvilinear relationship to the percentage of chicks congenitally infected, by the formula

$$P(INF) = 1 - \gamma^{V_T}$$

where

P(INF) represents the probability of the non-congenitally infected chicks becoming horizontally infected

V_T is the percentage of chicks congenitally infected by egg transmission and

γ is a constant reflecting the degree of horizontal infectivity from congenitally infected chicks to non-congenitally infected chicks.

This function gives an appropriate curvilinear relationship. Depending upon the conditions being simulated, γ was alternatively chosen to be 0.000001 to represent an extremely high degree of infectivity, 0.0001 to represent an intermediate level of infectivity, and 0.01 to represent a low degree of infectivity.

The genetic relationships between parents and offspring and between full- and half-sibs was simulated by using the statistical relationship for either of the genetic factors, G_{RST} or G_{EP}, as follows:

$$G_{OFFSP} = \frac{1}{2} G_{SIRE} + \frac{1}{2} G_{DAM} + G_{SEGR}$$

where

G_{OFFSP} is the total genetic value for an offspring

G_{SIRE} is the genetic value for the sire

G_{DAM} is the genetic value for the dam and

G_{SEGR} is the additional random genetic effect contributing to the value for a given offspring of a specified sire and dam.

With the variance of G_{SEGR} generated to be one-half of the total genetic variance, the simulated covariances between relatives (as a fraction of the total genetic variance) will be one-half for sire and offspring, one-half for dam and offspring, one-half for full-sibs and one-fourth for half-sibs. These are appropriate for multiple autosomal genetic factors with additive gene action. All simulated populations involved reproduction from 80 sires each mated to 3 dams. Each of these 240 matings produced 2 male offspring and 4 female offspring. Selection among the 480 male offspring and 960 female offspring was for 80 males and 240 females which were mated randomly to become the sires and dams of the next generation.

Selection was varied depending upon the conditions simulated. Female selection was alternatively simulated as being random with no relation to egg production performance (R), mass selection based upon the individual female's hen-housed egg production (M), or full-sib selection based upon the average performance of the family of four full sisters (F). Male selection was either random with no relationship to sister performance (R) or sib selection where males were selected upon the average performance of their four ful-sisters (S).

In some cases, the criterion of selection or the nature of infectivity was changed after 20 generations of selection so that the later 20 generations were of a different type for contrast.

In addition, the option of having the cellular genetic factors for resistance and susceptibility to a single virus type (such as sub-group A) segregating at a single autosomal locus with susceptibility dominant to resistance was examined. Homozygous recessive resistant individuals were then incapable of being infected either congenitally or horizontally. However, susceptible offspring of resistant dams were allowed a greater tendency for being horizontally infected relative to those from susceptible dams reflecting the absence of maternal antibodies from the non-infected resistant dams.

Results

In this study, 26 combinations of simulation parameters were investigated, made, each with five replicate runs, so as to contrast the alternative schemes considered to be relevant. However, because of space limitations, plots of only 13 alternative parameter combinations will be presented. In nearly all cases, the five replicates gave very similar patterns of response. For each characteristic of interest, symbols are plotted representing the generation means for each replicate with a line connecting the average of the five replicate generation means. Table 1 presents the parameter combinations

Table 1. Summary of parameter combinations for various simulations (Note: when parameters were changed after 20 generations the two parameters are shown separated by a slash. With no slash, the same parameters were continued for all 40 generations)

Parameter combination	Selection		Initial shedding	Initial cellular resistance	Unselected control intermingled	Shedding in intermingled control	γ_A	γ_{NA}
Basic quantitative genetic model with random viability and no virus								
2	S	M	–	–	N	–	0.0001	–
3	S	F	–	–	N	–	0.0001	–
Models including viral infection, congenital transmission, and quantitative resistance factor								
4	R	R	25%	–	N	–	0.0001	–
5	S	M	25%	–	N	–	0.0001	–
6	S	F	25%	–	N	–	0.0001	–
Relaxed selection after 20 generations and involvement of unselected control with selected populations								
7	S/R	M/R	25%	–	N	–	0.0001	–
11	S/R	M/R	25%	–	Y	25%	0.0001	–
13	S	M	25%	–	Y/N	25%	0.0001	–
14	S	M	25%	–	Y/N	25%	0.0001/0.01	–
Effects of cellular genetic resistance against virus infection								
20	S/R	M/R	25%	10%	Y	25%	0.0001	0.000001
22	S/R	F/R	25%	10%	Y	25%	0.0001	0.000001
25	S/R	M/R	25%	2%	Y	25%	0.0001	0.000001
26	S/R	F/R	25%	2%	Y	25%	0.0001	0.000001

S = Sib, M = Mass, F = Family, R = Random, N = No, Y = Yes
γ_A = parameter of horizontal infection for individuals susceptible to type A LL virus from susceptible dams
γ_{NA} = parameter of horizontal infection for individuals susceptible to type A LL virus but from resistant (antibody negative) dams
Note: smaller numerical values of γ indicate greater degrees of horizontal infections

used in the simulations for which the results are presented in subsequent figures.

Basic quantitative genetic model with random viability and no virus

In parameter combination number 2 plotted in Fig. 1, the population was virus-free with mass selection of females on their hen-housed egg production and with sib selection of the males. Hen-housed egg production steadily increased from original values near the expected mean of 61.75% to over 80% after 40 generations of selection. The change in the percent viability from the expected 90% is nil in this simulation because there was no selection for the G_{RST} genetic variability. Parameter combination number 3 (Fig. 2) also simulates a virus-free population but with the selection for both females and males being based upon the full-sib female average. Percent viability again fluctuates but shows no response to selection. For the moderate heritability (20%) for the hen-housed egg production trait, individual and family selection give responses very similar to each other over the 40 generations.

Models including viral infection, congenital transmission and quantitative resistance factor

Parameter combination number 4, presented in Fig. 3, simulated random selection in both sexes, but with a 25% incidence of congenitally infected individuals in the initial population. The incidence of individuals infected either congenitally or horizontally by the LL virus is also shown. Their incidence increased to an equilibrium of around 90% infected individuals. The initial generation means for hen-housed egg production and viability were lower than for the virus-free population. However, both remained stable after the equilibrium of virus incidence was reached. In parameter combination number 5, shown in Fig. 4, mass selection in females and sib selection in males were simulated with 25% initial incidence of infected chicks. In this plot, the incidence of infected birds was reduced until it went to zero at from generation ten to generation nineteen for the different replicates. Response to selection increased the mean for egg production to above 80, similar to the final level for selection in virus free populations.

Figure 5 shows parameter combination number 6 wherein family selection of females and sib selection of males were simulated with 25% initial incidence of individuals congenitally infected. In spite of the selection, the incidence of the infected birds increased for the first several generations, but to a level not as high as the level for random selection in parameter combination number 4 (Fig. 3). Concurrent with this increase in the number of infected birds was a decline in viability. The response to selection for hen-housed egg

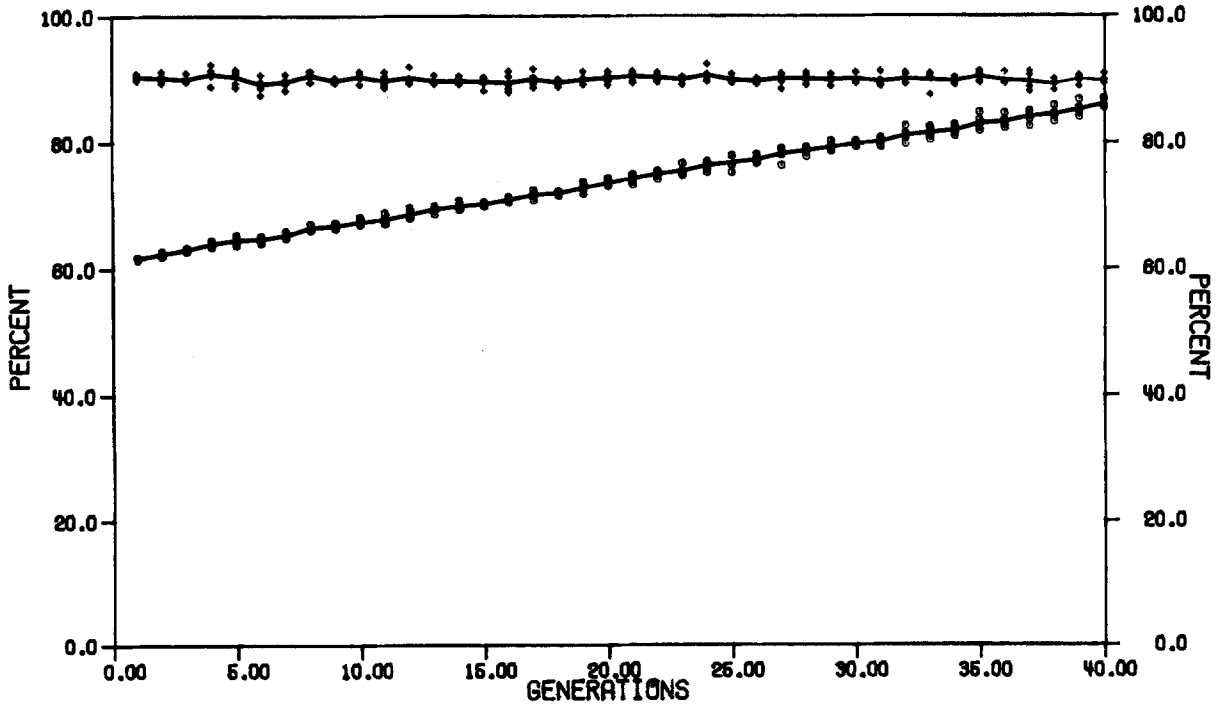

Fig. 1. Simulated selection responses for parameter combination no. 2 with sib selection of males and mass selection of females with 0% incidence of congenital infection for 40 generations. (Octagons denote % hen-housed egg production and diamonds denote % viability, with lines connecting generation means for five replicates)

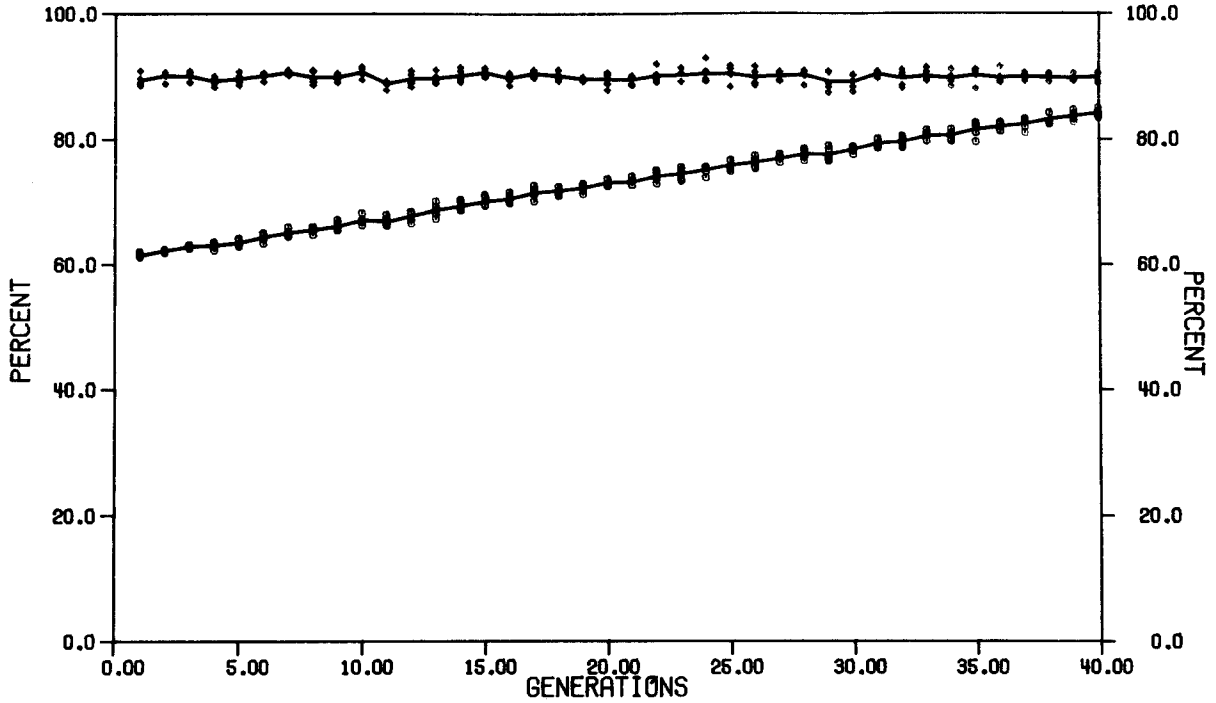

Fig. 2. Simulated selection responses for parameter combination no. 3 with sib selection of males and family selection of females with 0% incidence of congenital infection for 40 generations. (Octagons denote % hen-housed egg production and diamonds denote % viability, with lines connecting generation means for five replicates)

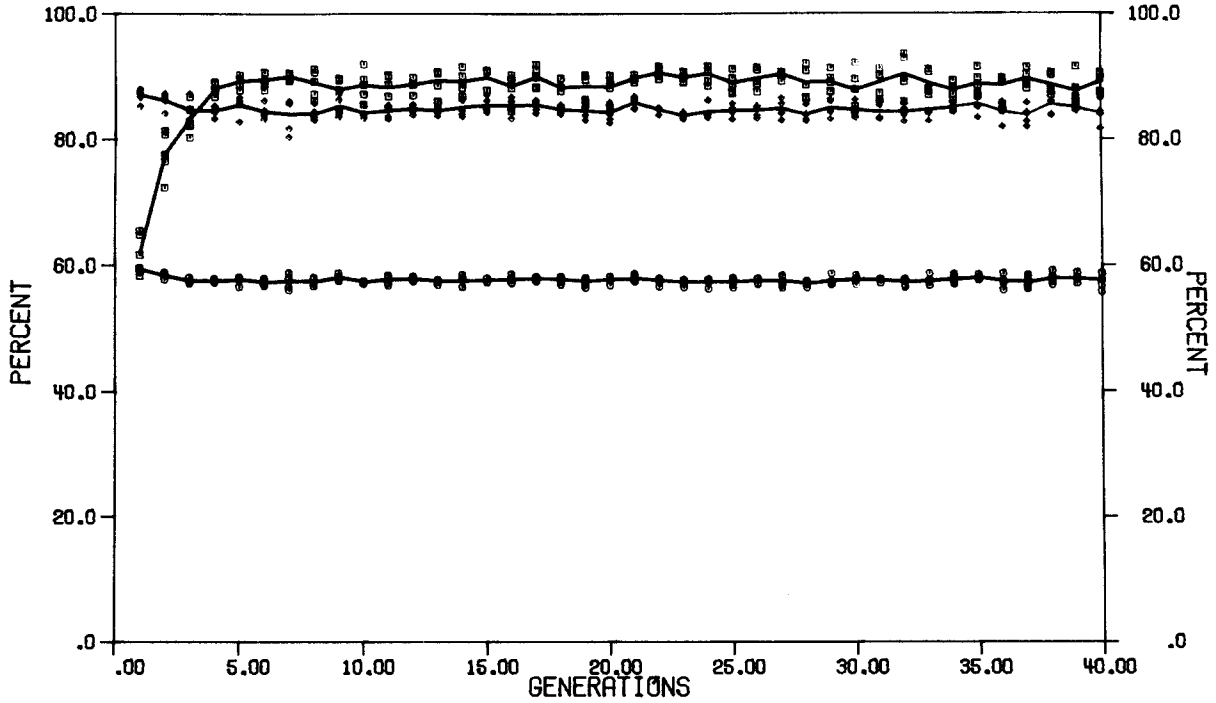

Fig. 3. Simulated selection responses for parameter combination no. 4 with random selection of males and females with 25% initial incidence of congenital infection and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for 40 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares donote % infected individuals, with lines connecting generation means for five replicates)

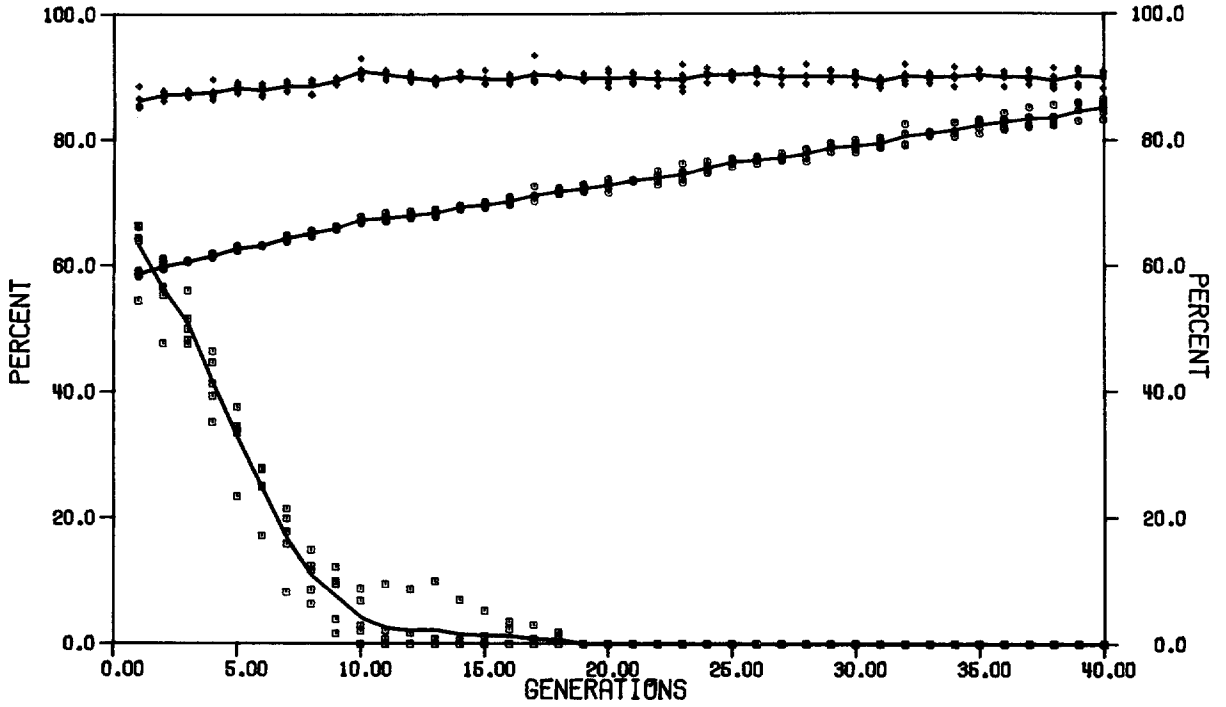

Fig. 4. Simulated selection responses for parameter combination no. 5 with sib selection of males and mass selection of females with 25% initial incidence of congenital infection and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for 40 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares denote % infected individuals, with lines connecting generation means for five replicates)

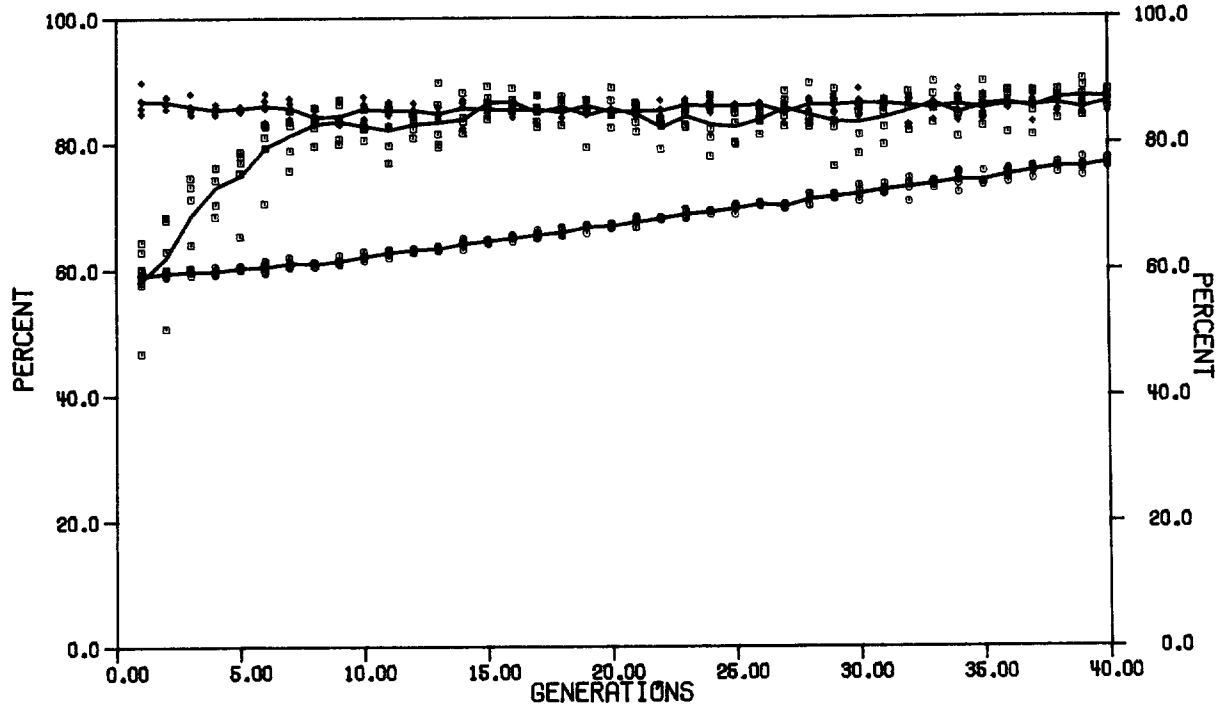

Fig. 5. Simulated selection responses for parameter combination no. 6 with sib selection of males and family selection of females with 25% initial incidence of congenital infection with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for 40 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares denote % infected individuals, with lines connecting generation means for five replicates)

production during these early generations was quite small resulting from the depressing effects of the increased incidence of infection cancelling out the probable response in G_{EP} in the first few generations. The response to selection was still not large, even after reaching the equilibrium point. Hence, the overall response was somewhat less than for family and sib selection in virus-free populations (Fig. 2) and was less than for mass and sib selection in the virus-contaminated populations (Fig. 4). Thus, whereas mass selection and family selection of females were approximately equally effective in the virus-free situation, mass selection was more effective than family selection in the virus-contaminated situation.

Relaxed selection after 20 generations and involvement of unselected control with selected populations

Parameter combination number 7 presented in Fig. 6 involves a situation equivalent to parameter combination number 5 of Fig. 4 for the first 20 generations (mass and sib selection in males and females, respectively). After 20 generations, selection was random for both males and females (relaxed selection). Since, in these instances, the virus was eliminated by from generation 9 to 15, the response after generation 20 was stable. However, parameter combination number 11 in Fig. 7 shows a quite different result. The characteristics of selection and initial infection were identical to parameter combination number 7. The difference was that the offspring of selected parents were simulated to be brooded intermingled with an equal number of birds from an unselected control population with 25% incidence of congenital infection to induce more horizontal infection to the progeny. Thus, even though the number of congenitally infected birds was reduced by the selection of their parents for egg production performance, the total incidence of infection was still large and the virus remained in the population for the first 20 generations of selection. When selection was relaxed after 20 generations, the incidence of the virus increased for a few generations until it reached an equilibrium value somewhat less than 80%. During the generations from 20 to 24 when the virus incidence was increasing, a decline in the mean egg production was noted in the average for the five replicates. The magnitude of the decline per generation in egg production was roughly equivalent to the magnitude of the response per generation prior to generation 20 and relaxation. Thus, there was a "relaxed selection effect" that cancelled the response to selection in the immediately prior few generations.

Parameter combination number 13 presented in Fig. 8 involves 40 generations of selection with mass

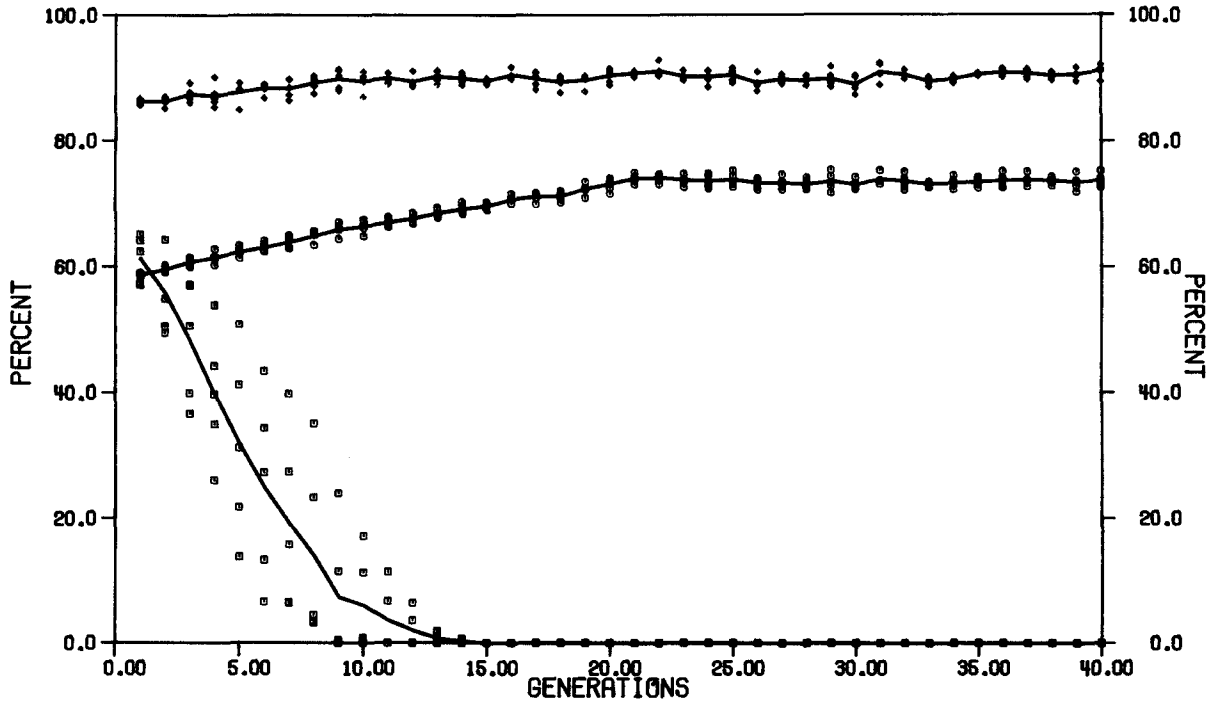

Fig. 6. Simulated selection responses for parameter combination no. 7 with sib selection of males and mass selection of females with 25% initial incidence of congenital infection and with intermediate degree of horizontal infection ($\gamma = 0.0001$) for first 20 generations followed by random selection of males and females for remaining 20 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares denote % infected individuals, with lines connecting generation means for five replicates)

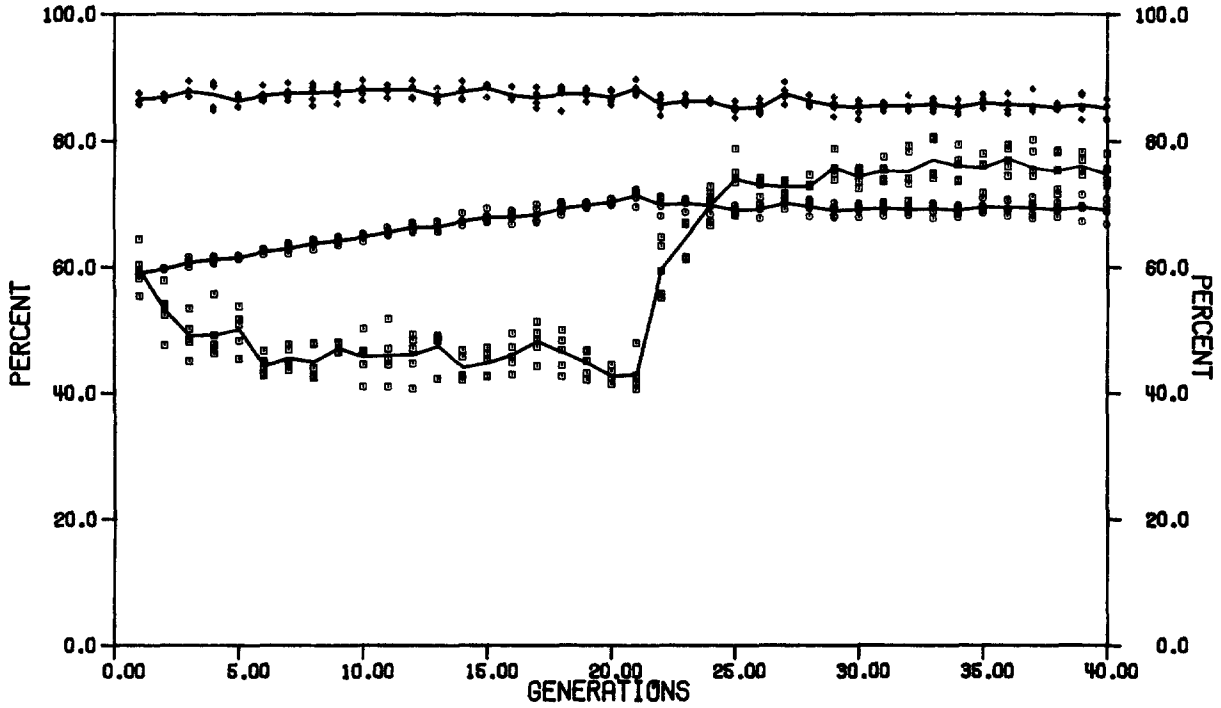

Fig. 7. Simulated selection responses for parameter combination no. 11 with sib selection of males and mass selection of females with 25% initial incidence of congenital infection with an unselected control with 25% incidence of congenital infection intermingled brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for first 20 generations followed by random selection of males and females for remaining 20 generations with contact with unselected control continuing. (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares denote % infected individuals, with lines connecting generation means for five replicates)

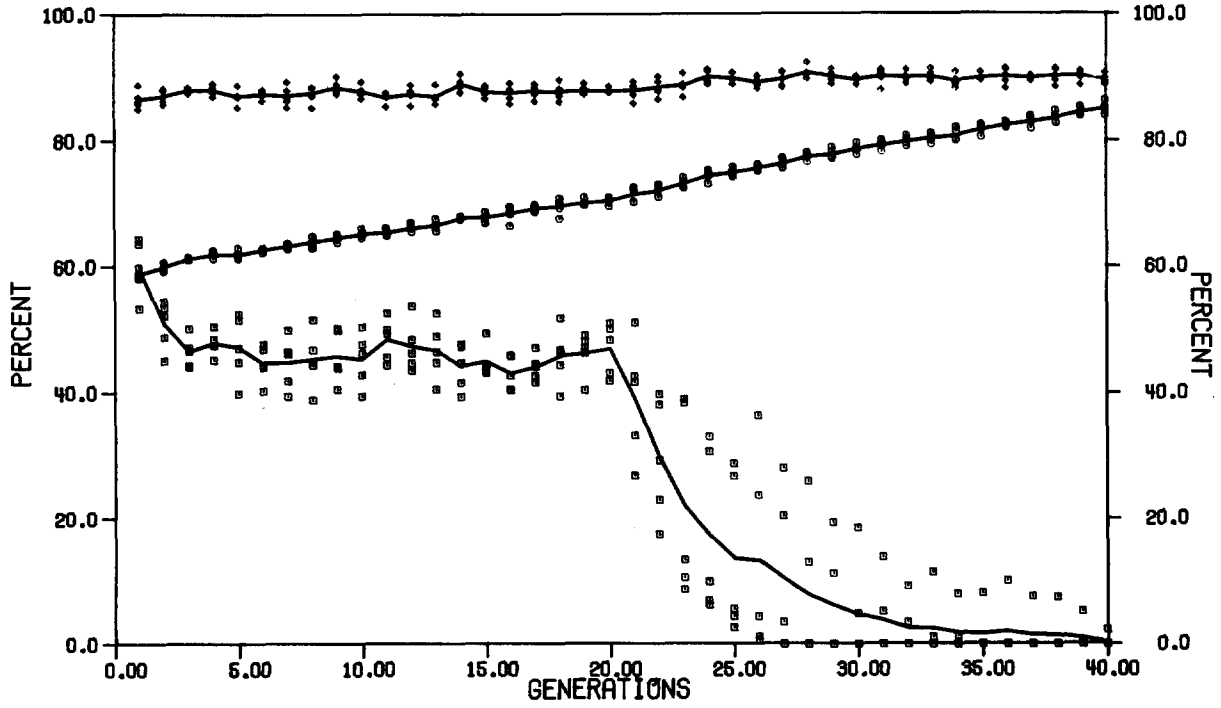

Fig. 8. Simulated selection responses for parameter combination no. 13 with sib selection of males and mass selection of females with 25% initial incidence of congenital infection with an unselected control with 25% incidence of congenital infection intermingled during brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for first 20 generations followed by no intermingled control for remaining 20 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares denote % infected individuals, with lines connecting generation means for five replicates)

selection of females and sib selection of males for the 40 generations. However, the intermingled control during brooding was removed after the first 20 generations. The infection remained in the population at a level somewhat above 40%, similar to parameter combination number 11 up to generation 20. Following removal of the control, the incidence of virus declined until it was eliminated from all except one population by generation 35. During this period of elimination, there was a greater rate of increase in hen-housed egg production corresponding to the declining influence of the virus infection upon performance. There was also a slight increase in livability during this same period. Parameter combination 14 in Fig. 9 shows similar selection with an intermingled control during brooding for the first 20 generations and with this intermingled control removed after generation 20. Also at generation 20, the degree of horizontal infection of the virus was reduced by changing the parameter from the 0.0001 to 0.01, giving a lower degree of horizontal infection. This was done to simulate a presumed change in degree of horizontal infection representing the change in growing conditions from floor growing to cage growing. Under these conditions, the virus was eliminated from all populations by generation 29. Since much of the horizontal infection between chicks during growing is through virus shed in the feces (Spencer et al. 1977), it may be presumed that horizontal infection is greater under floor conditions than under cage growing conditions since the contact of non-infected chicks with excreta would be greater on the floor than in cages.

Effects of cellular genetic resistance against virus infections

In parameter combination number 20 in Fig. 10 and for parameter combination number 22 in Fig. 11, the incidence of cellular resistant (homozygous recessive) individuals who are incapable of being infected by the virus (Crittenden et al. 1975) was added to the simulation. All prior simulations presumed a zero incidence of such cellular resistance to virus infection in the populations. In these two simulations, the initial incidence of birds resistant to infection (homozygous recessives for the cellular resistance factor) was 10%. In addition, it was simulated that the susceptible progeny of resistant dams were more vulnerable to horizontal infection by assigning them a γ value of 0.000001 representing the lack of neutralizing maternal antibodies from the

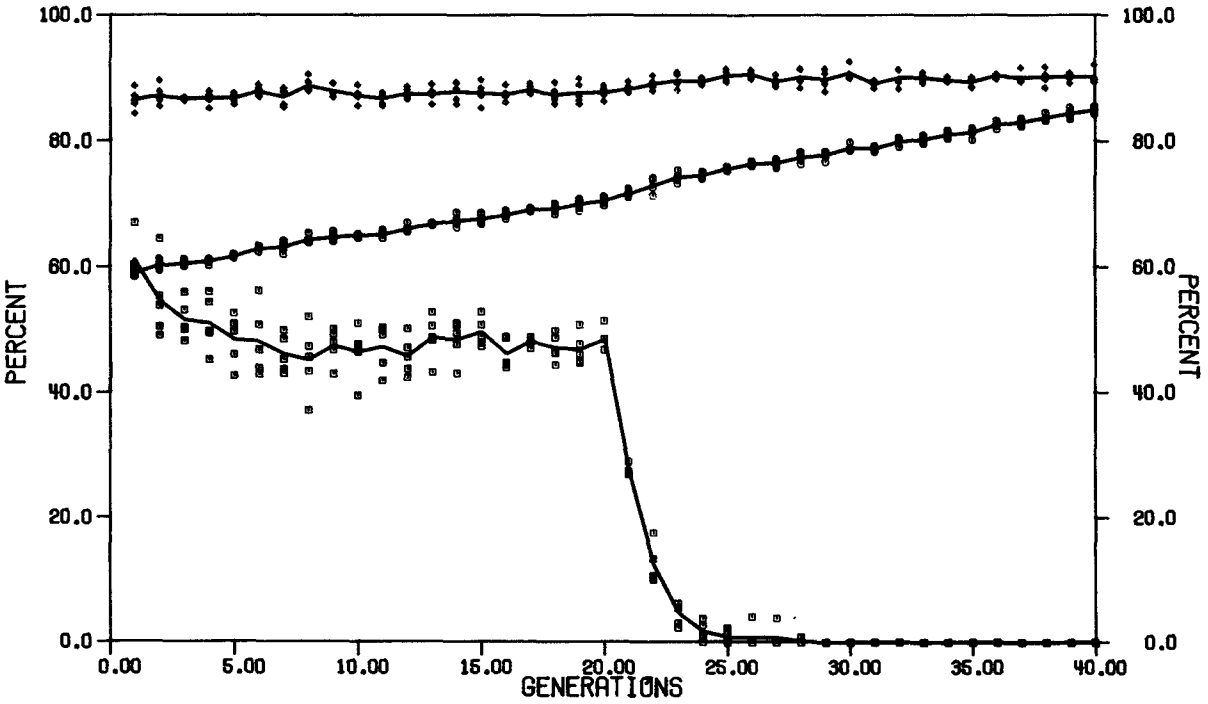

Fig. 9. Simulated selection responses for parameter combination no. 14 with sib selection of males and mas selection of females with 25% initial incidence of congenital infecton with an unselected control with 25% incidence of congenital infection intermingled during brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for first 20 generations followed by no intermingled control with low degree of horizontal infectivity for remaining 20 generations ($\gamma = 0.01$). (Octagons denote % hen-housed egg production, diamonds denote % viability, and squares denote % infected individuals, with lines connecting generation means for five replicates)

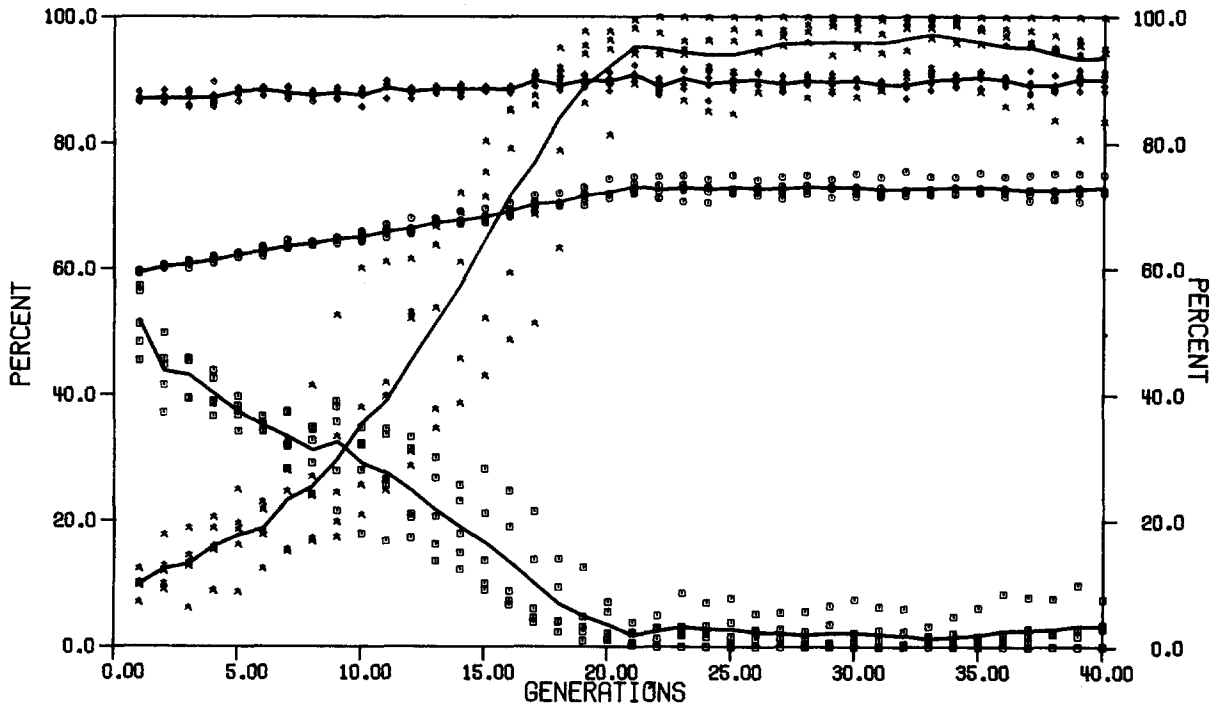

Fig. 10. Simulated selection responses for parameter combination no. 20 with sib selection of males and mass selection of females with cellular resistance segregating starting at 10% with 25% initial incidence of congenital infection with unselected control with 25% incidence of congenital infection intermingled during brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for susceptible progeny of susceptible dams and high infectivity ($\gamma = 0.000001$) for susceptible progeny of resistant dams for first 20 generations followed by random selection of males and females with continued intermingled control for remaining 20 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, squares denote % infected individuals, and stars denote % cellular resistant (homozygous recessive) individuals, with lines connecting generation means for five replicates)

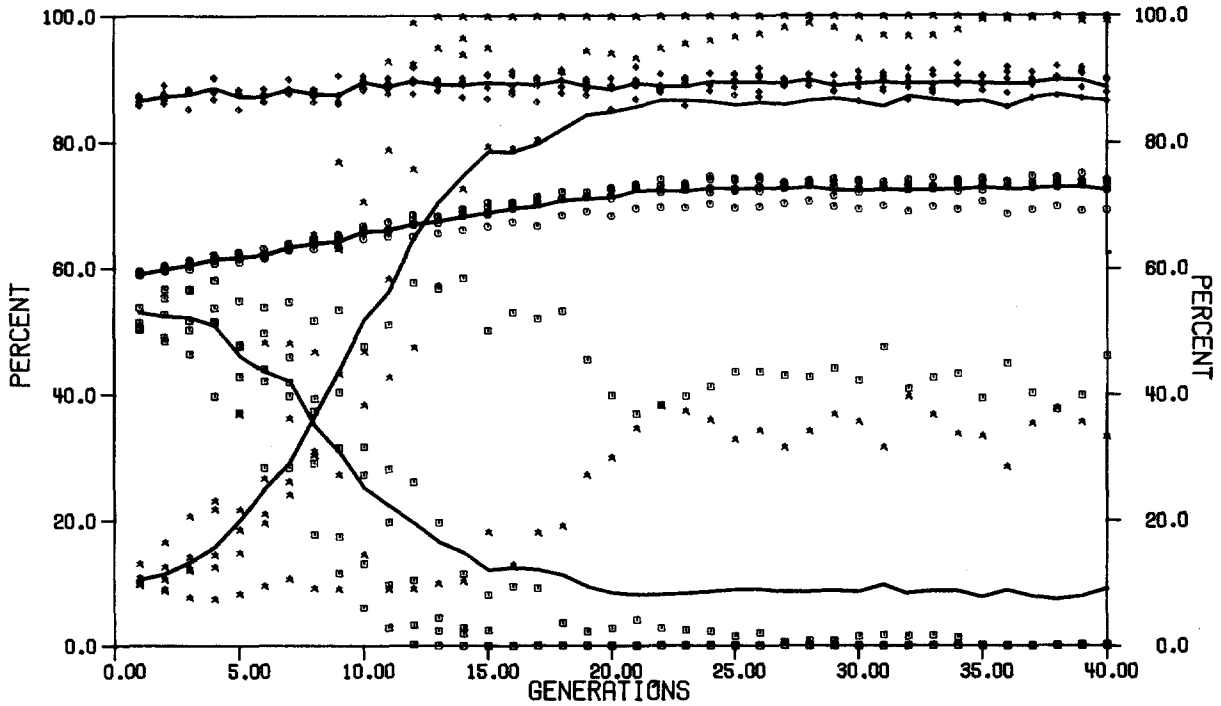

Fig. 11. Simulated selection responses for parameter combination no. 22 with sib selection of males and family selection of females with cellular resistance segregating starting at 10% with 25% initial incidence of congenital infection with unselected control infection intermingled during brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for susceptible progeny of susceptible dams and high infectivity ($\gamma = 0.000001$) for susceptible progeny of resistant dams for first 20 generations followed by ramdom selection of males and females with continued intermingled control for remaining 20 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, squares denote % infected individuals, and stars denote % cellular resistant (homozygous recessive) individuals, and stars denote % cellular resistant (homozygous recessive) individuals, with lines connecting generation means for five replicates)

resistant dams that did not get infected (Crittenden et al. 1975). Parameter combination number 20 (Fig. 10) represents mass selection of females and sib selection of males for the first 20 generations followed by relaxed selection. In all five replicates, cellular resistance increased and virus shedding decreased for the 20 generations although fixation of cellular resistance and elimination of the virus was not quite complete in any of the replicates by generation 20. After relaxation of selection at generation 20, one replicate did drift to fixation and elimination. For parameter combination number 22 (Fig. 11) the selection was for family mean production in both sexes and the responses were quite variable. Four of the five replicates yielded appreciable increases in cellular resistance and declines in virus shedding. However, one replicate did not show response for cellular resistance and decline in shedding before generation 15 and both remained at intermediate levels until generation 40 even though the other four achieved fixation and elimination by generation 35 with one replicate achieving that state at generation 13. The replicate with less response for cellular resistance and thus less reduction in virus infection showed less improvement in egg production.

To further investigate the relationship of response to selection to frequency of cellular resistance, parameter combinations 25 (Fig. 12) and 26 (Fig. 13) are equivalent to combination 20 and 22, respectively, except that the initial incidence of cellular resistance was only 2%. For mass and sib selection (parameter combination 25, Fig. 12), there was negligible response of cellular resistance in any of the five replicates and the pattern of response for the five replicates was quite similar to parameter combination number 11 (Fig. 7) with mass selection for females and sib selection for males. For parameter combination number 26 (Fig. 13) selection was on female family averages for both sexes. For four of the five replicates cellular resistance remained low and virus incidence high, but for one replicate, cellular resistance went to fixation and the virus was eliminated.

Two other parameter combinations (23 and 24) were simulated with initial cellular resistance of 5%. These figures are not presented, but for both mass and family selection the results were quite variable. Some replicates went to high levels for cellular resistance (with corresponding low levels for the virus) and with cellular resistance remaining at low levels (with high virus levels) for some replicates.

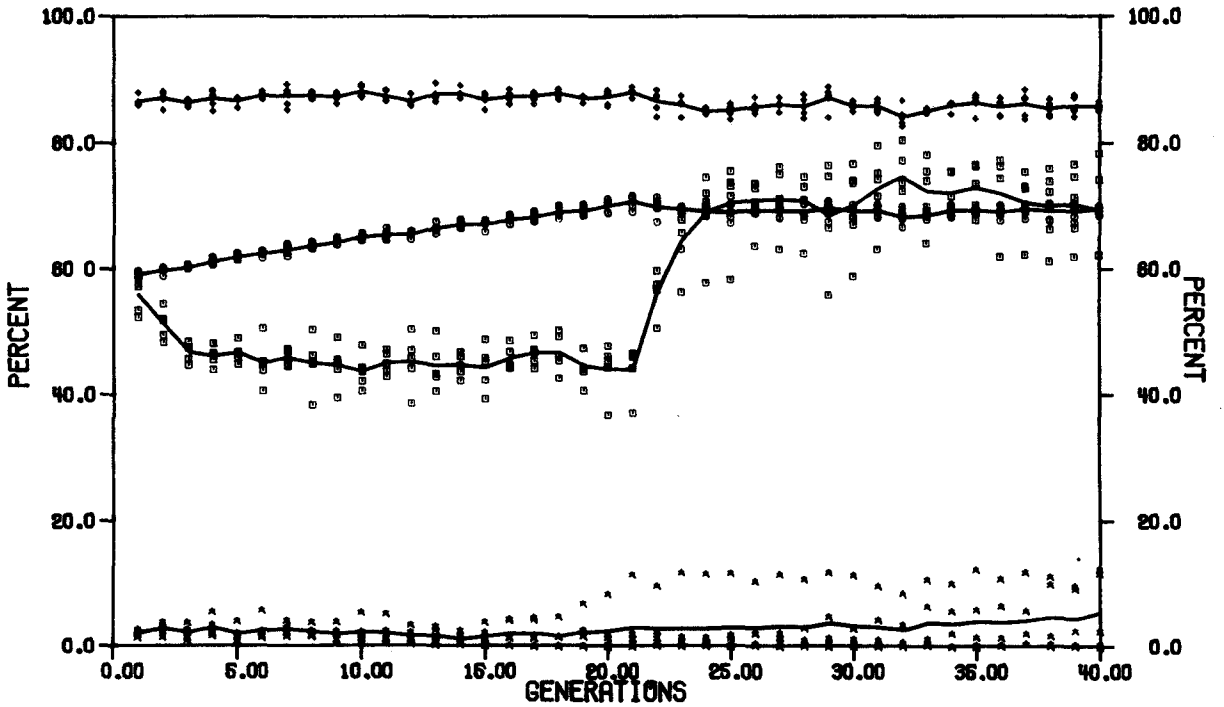

Fig. 12. Simulated selection responses for parameter combination no. 25 with sib selection of males and mass selection of females with cellular resistance segregating starting at 2% with 25% initial incidence of congenital infection with unselected control with 25% incidence of congenital infection intermingled during brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for susceptible progeny of susceptible dams and high infectivity ($\gamma = 0.000001$) for susceptible progeny of resistant dams for first 20 generations followed by random selection of males and females with continued intermingled control for remaining 20 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, squares denote % infected individuals, and stars denote % cellular resistant (homozygous recessive) individuals with lines connecting generation means for five replicates)

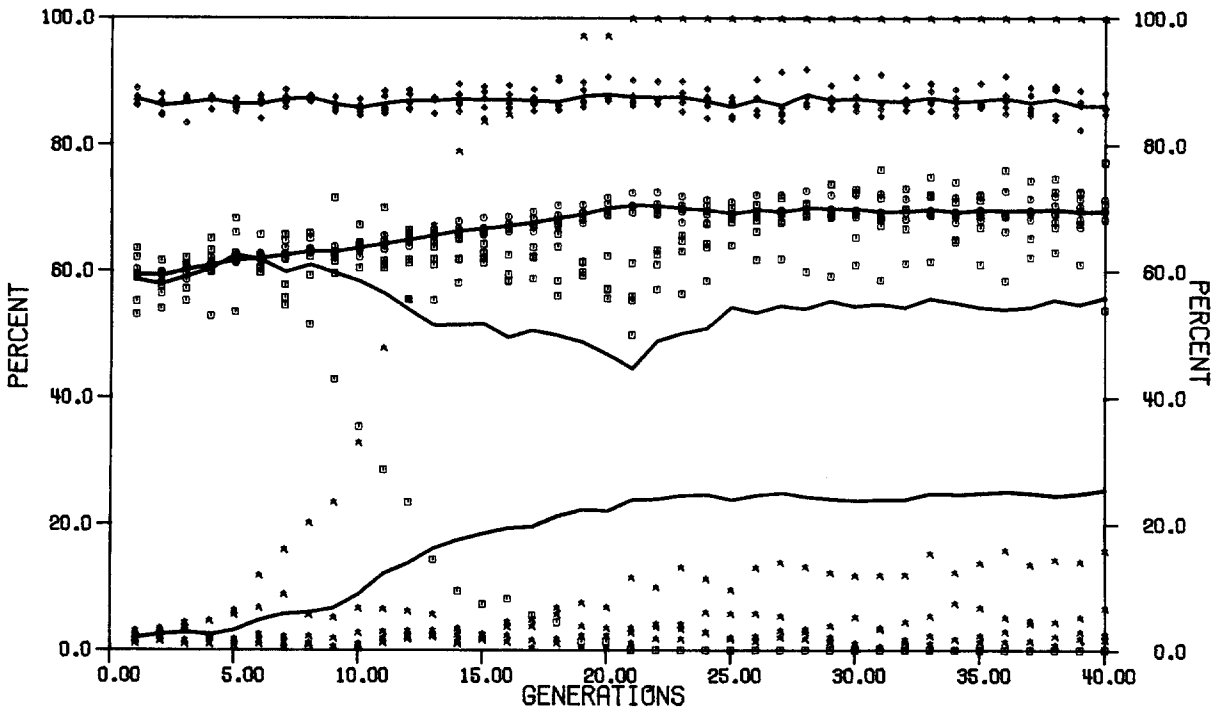

Fig. 13. Simulated selection responses for parameter combination no. 26 with sib selection of males and family selection of females with cellular resistance segregating at 2% with 25% initial incidence of congenital infection with unselected control with 25% incidence of congenital infection intermingled during brooding and with intermediate degree of horizontal infectivity ($\gamma = 0.0001$) for susceptible progeny of susceptible dams and high infectivity ($\gamma = 0.000001$) for susceptible progeny of resistant dams for first 20 generations followed by random selection of males and females with continued intermingled control for remaining 20 generations. (Octagons denote % hen-housed egg production, diamonds denote % viability, squares denote % infected individuals, and stars denote % cellular resistant (homozygous recessive) individuals with lines connecting generation means for five replicates)

Discussion and conclusions

Even though the precise interpretation of simulation results depends upon the completeness of the model, the simulations provide plausible explanations of phenomena which have been difficult to explain in the past. The simulation parameters used in this study were largely based upon the results of Spencer et al. (1979, 1980) and Gavora et al. (1980). Those studies did not differentiate between congenitally infected and horizontally infected individuals. Thus, the computer simulation of both types of infection required parameters not estimated in the experimental results. Some guesses were made as to the relative consequences of the two forms of infection. The results of the Harris et al. (1984) experimental study, although conducted concurrently with this simulation study, were not fully analyzed until after the simulation study. Thus, the latter results did not specifically contribute to the parameters used in the simulation. In retrospect, the Harris et al. (1984) results suggest detrimental effects upon egg production resulting from horizontal infection not as great as those simulated. The qualitative effects which were demonstrated seem to be justified, but the quantitative differences may not be a precise reflection of the quantitative differences that would occur in experimental populations.

Basic quantitative genetic model with random viability and no virus

The near-equivalence of responses to family selection and individual selection for females in virus-free populations (Figs. 1 and 2) with 20% heritability was consistent with the theoretical findings by Lush (1947) and others. This consistency with theory was not surprising since the simulation model was equivalent to the theoretical model underlying the cited expectations.

Models including viral infection, congenital transmission and quantitative resistance factor

Under the theoretical considerations of Lush (1947), the added variability due to infection and mortality should have reduced effectiveness of selection with family selection becoming more effective than individual selection. The difference occurring in the simulation was in the opposite direction.

The increase in virus incidence in Fig. 3 (parameter combination 4) expressed the tendency of virus infection to increase under no selection until a maximum infection is reached. The decline in virus incidence observed for parameter combination 5 was evidently due to selection against the infected individuals because of the adverse effects of either congenital or horizontal infection upon their hen-housed egg production. Since the adverse effects were greater for congenitally infected individuals than for horizontally in-

fected ones, the selection pressure would have been greater against those congenitally infected. Thus the 40 generation response to selection for parameter combination number 5 was very similar but slightly less than the virus-free population (parameter combination 2) and the viability after elimination of the virus was also quite similar.

The contrast of the observed relative effectiveness of individual selection and family selection as simulated in parameter combinations 5 and 6 seemed to parallel the experimental results of Kinney et al. (1970), where individual selection is more effective than various forms of family selection. This parallel offers a plausible explanation of those unexplained results so inconsistent with theoretical expectations. In particular, it seems, both experimentally and in the simulations that responses for various forms of family selection are more reduced from the expectations for virus-free populations relative to mass selection. Very likely, lymphoid leukosis was present in the populations in that experimental study. Most poultry populations are known to carry the LL virus and the Harris et al. (1984) study was conducted on the same poultry farm, even though years later. It seems likely that the family selection, both full-sib family and half-sib family, in the Kinney et al. (1970) study was adversely influenced by added variability due to the greater presence of LL infected birds in those populations such that the effectiveness of selection was greatly diminished by reduced effective heritabilities. Individual selection would have been more effective in removing the infected birds from the populations so there was less disturbance to the expected response to selection.

The occurrence of congenital and horizontal transmission of the LL virus infection suggest that the quantitative genetic theories of Lush (1947) and Osborne (1957a, b) are not completely relevant to predict response to selection (non-genetic as well as genetic) and to compare the relative effectiveness of individual and family selection since these theories are based on models that do not include such phenomena. This theory may, however, be adequate in virus-free populations.

Relaxed selection after 20 generations and involvement of unselected control with selected populations

The "relaxed selection effect" observed for parameter combination 11 (Fig. 7) seems to mimic the situation described by Dickerson (1963) and suggests that this effect may be due to an increase in virus incidence when selection is relaxed, especially when there is a source of reinfection, such as an unselected population being brooded intermingled with the selected population. Dickerson's experimental procedure for evaluating the response to selection involved keeping some unselected breeders from the prior generation. Also, several populations of chickens were brooded together under floor growing conditions, where populations with a high incidence of LL virus could have been the source of horizontal infection to other populations.

In addition to this suggestion of selection against congenitally transmitted detrimental effects (maternal selection responses), two additional explanations have been proposed for relaxed selection effects. One of these is antagonistic natural selection in a direction opposite to the prior directional selection that returns the population towards its origin upon relaxation of intentional selection. This explanation may not be pertinent for egg production since natural selection would be, at least partially, in the same direction as the directional selection. Secondly, Griffing (1960a, b) pointed out that there can be a temporary response to selection for additive by additive epispastic effects which would give a relaxed selection effect when directional selection ceases. Bennett et al. (1980), in an experiment in earlier generations on the same genetic strains of birds as studied by Spencer et al. (1979, 1980) and Gavora et al. (1980), indicates that both temporary epistatic effects and maternal selection responses contribute to relaxed selection effects. Temporary maternal environmental effects of dam selection account for 18% of the response in early egg number and 36% of the response in full year egg number and temporary epistatic superiority from selection accounts for 73% of the early egg number response and 40% of the full year egg number response. The earlier study by Dickerson (1963) indicated consistent loss of performance in the first generation of relaxed selection, but was not designed to separate maternal (disease) and epistatic effects of relaxed selection. The temporary maternal selection effects include the congenital transmission of the LL virus. Thus, both of these explanations seem to be involved in relaxed selection effects in chickens following selection for egg production.

The Gowe studies involved a change in growing conditions from floor to cages at a generation near the beginning of renewed response to selection relative to that experienced under the floor-litter conditions. In addition to the shift from floor to cage growing, during the rearing period each of the several strains of birds including the control strains was assigned to a different set of cages separated by sheet metal partitions. Therefore, it seems that parameter combination number 14 simulated, at generation 20, changes in conditions of horizontal infection similar to what occurred in the Gowe (1974, 1977) experiment. The increased response to selection in the simulation somewhat resembled the observed increase reported by Gowe (1977). Could it be that the greater response reported by Gowe in recent generations comes from more effective elimination of the lymphoid leukosis virus under cage growing conditions than was accomplished in the preceding years under intermingled floor-litter growing conditions? Does this also account for the low incidence of the virus as found in the Spencer et al. (1979) and Gavora et al. (1980) studies, since they were done in 1976 and 1977 in the Gowe populations? The incidence of the LL virus may have been greater in both the selected and the control populations prior to the change in environments. Was this due to a greater incidence of horizontal infection in a more infectious floor environment with greater contact between selected and control individuals? Known characteristics of the LL virus plus the simulations provide suggestive evidence that the answer to all of these questions is the affirmative.

Alternatively, Gowe (1974, 1977) proposed that the increased response following the shift in environments to cage growing was due to some variability in production following cage rearing that did not influence performance under floor conditions. This explanation cannot be discounted and may be part of the explanation, but since Spencer et al. (1979) and

Gavora et al. (1980) showed the presence of the effects of lymphoid leukosis in these same populations, the explanation involving LL seems more complete and to have greater experimental support.

Gavora et al. (1980) developed some calculations to show that the total response in the Gowe (1974, 1977) population involved a 25 to 60 egg increase per hen-housed due to genetic changes. In addition, there was a three or four egg increase associated with the reduction of the incidence of LL virus shedding in the selected populations relative to the control populations. However, it seems that the genetic response to selection for egg production might have been greater than the indicated 25 to 60 eggs if the disturbing (heritability reducing) influences of congenital and horizontal infection had not been present in the populations. If the conjecture that the disturbing influences were one of the factors responsible for the near-plateau in the floor growing years prior to 1968 is true, the genetic response to selection probably would have been greater without these influences. The McAllister (1977) analysis of the selection in retrospect indicates that the selection practiced in the Gowe populations placed considerable emphasis upon individual performance. Thus, as indicated above in simulations 5 and 6, the disturbing influences were probably less than might have occurred with greater emphasis upon family selection as practiced in some other chicken populations.

The question has been raised relative to the Spencer et al. (1979, 1980) and Gavora et al. (1980) results indicating the severe effect upon performance of transmitters – Why has genetic selection not reduced or eliminated the lymphoid leukosis virus from selected populations? The additional results from the Harris et al. (1984) study, coupled with the simulation results in this study, suggest that selection may be quite effective in eliminating from poultry populations those individuals that are congenitally infected, especially if the selection places considerable emphasis on individual egg production. However, it seems that those individuals which are horizontally infected do not suffer a severe depression in egg production performance (Harris et al. 1984). Thus, some of them may be selected in spite of a small depression, and they will then be transmitters infecting the next generation and, thus, perpetuating the presence of the virus. Also, it has been suggested that unselected control populations which, for experimental purposes, are often brooded on the floor intermingled with selected populations can be the source of infection to the selected populations.

Effects of cellular genetic resistance against virus infection

The results for parameter combinations 20, 22, 25, and 26 demonstrate a potential for effective genetic selection for resistance if the cellular resistance genetic factors are present at a modest level in the populations being selected. Unfortunately, many egg production populations are either not segregating for these cellular resistance factors for the type A virus which seems to be the more virulent form (Crittenden 1975) or, are segregating at low frequencies. The simulation results suggest that when the frequency of cellular resistance is at quite low levels, the detrimental effects of no maternal antibodies can offset the advantages of cellular resistance, especially when selection is on family egg production performance. When cellular resistance frequencies are higher, say above 10%, responses of greater cellular resistance, lower virus incidence, and greater egg production seem to be readily obtained. Does this simulation result explain why cellular resistance is at low levels in some populations which have been selected strongly for egg production for many generations?

Approaches to LL virus eradication

Thus, we see two problems involved with the presence of lymphoid leukosis in poultry breeding populations. (1) The direct impact is the detrimental effects upon egg production performance. (2) A secondary influence is the disturbing influence upon genetic selection for egg production performance. The practical question is raised – How can poultry breeders overcome both of these two problems? The first suggested answer seems to be reducing the incidence of the virus in the population. An approach for the reduction seems to be strong selection upon egg production performance with greater emphasis upon individual performance than traditional quantitative genetic theory might suggest. However, the procedure proposed by Spencer et al. (1977, 1980) for evaluating congenital transmission by testing for the virus in egg albumen seems a simple way of detecting most of the infected birds that have been unable to eliminate the virus and thus are transmitters. Techniques such as this would be most useful for detecting individuals that have been horizontally infected and thus may have only a small depression in egg production, such that the usual selection for high egg production does not eliminate all of them. Therefore, the second suggested approach would be to combine selection for performance with testing for LL virus infection to serve as a basis for eliminating those infected birds not eliminated by selection on their egg production performance.

However, reducing the level of the virus (without eradication) by selection and/or virus testing may be only temporary. The detrimental effects upon performance may return with relaxation of selection if the simulation results are indicative of the true nature of the situation. Nearly all poultry breeding operations involve relaxation of selection in the generations of multiplication and crossing between the selection programs and the commercial egg production stocks. Also, the level of horizontal contagion may be less under cage growing. Thus, cage growing and laying should be an effective environment for a testing and selection program to reduce the level of virus infection in the multiplication, crossing and commercial populations.

Because of the risk of a relaxed selection effect in the intervening generations between selection and commerical production, the desirability of completely eradicating the LL virus from poultry breeding popula-

tions is strongly suggested. Accomplishing this is made difficult by incomplete accuracy of either egg production or direct virus testing as indicators of virus presence and transmission.

A third suggestion for overcoming these problems of lymphoid leukosis would involve the incorporation of genetic cellular resistance for the sub-group A LL virus into the populations. The incorporation of genetic factors for resistance seems a more secure form of achieving eradication because the resistant stocks could not be infected from outside sources. The effectiveness of such an approach depends also upon whether only sub-group A virus is of major importance in influencing egg production. Developing cellular resistance also for sub-groups B, C and D could make this an extremely complex genetic procedure. Current information is that sub-groups C and D are not important. Unfortunately, as mentioned above, many otherwise desirable stocks (most of those of pure Leghorn origin) do not have the sub-group A cellular resistance segregating as a portion of their genetic variability (or have it at a low frequency). Thus, the introduction (or increase) of the cellular resistance allele in such populations prior to selection to increase its frequency would be a necessary preliminary step.

Implications for poultry breeding plans

The results of this simulation study bring into question the continued use of traditional quantitative genetic selection theory to develop optimum selection schemes in egg production poultry populations. The theories as presented by Lush (1947) and Osborne (1957a, b) are based upon inadequate models and the procedures suggested for achieving optimum response to selection are only valid when phenomena such as the virus infection dealt with in this study are not present. It would seem, from the results of this simulation study, that greater emphasis needs to be placed upon individual performance than is theoretically implied in order to overcome the disturbing influences of virus presence. This conclusion is at least indirectly supported by experimental results (Kinney et al. 1970). The relative effectiveness of individual and family selection also depends upon the consistency of congenital transmission by infected dams and the degree of horizontal contagion, as well as upon the magnitude of the detrimental effects. All of these parameters were probably not assessed completely accurately in developing the simulation model, and their magnitude may differ from population to population and from environment to environment. Thus, further study needs to be made so that optimum selection schemes can be reliably re-evaluated. The eradication of the virus would leave only the solely genetic considerations of Lush (1947) and Osborne (1957a, b) unless there are other pathogens which behave similarly and have similar effects. At this stage of knowledge, with the exception of the *Mycoplasma* (Carpenter et al. 1980), there are no additional egg transmitted pathogens present in most poultry populations that are known to have effects similar to those found for LL.

Perhaps many poultry geneticists have been naive in not realizing earlier that the egg transmission of lymphoid leukosis, which has been known for decades, might have major implications for genetic selection procedures.

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