INCORPORATION OF DIRECT SELECTION ON MILK PROTEIN LOCI INTO A NATIONAL DAIRY BREEDING PROGRAM

E. Ezra1, M. Ron2, E. Feldmesser2, and J.I. Weller2
1Israel Cattle Breeders Association, Tel Aviv 62488, Israel
2Institute of Animal Sciences, A. R. O., The Volcani Center, Bet Dagan 50250, Israel

SUMMARY
Cheese quality and quantity is higher for milk derived from cows with the BB genotypes for \( \beta \)-lactoglobulin and \( \kappa \)-casein. Selection for these loci can only be justified if producers are paid accordingly, which requires genotype determination in commercial populations. A method is presented in which producers will be paid according to expected cow genotype based on sire and maternal grandsire genotypes. In populations with extensive artificial insemination (Al), most cows are progeny of a much smaller number of sires. Thus the total number of genotypings required will be economically insignificant. Variances of expected allele frequencies of cows were close to the values postulated by the variances of sire genotypes. Assuming that the economic benefit of the BB genotype over the AA genotypes are 4% for \( \beta \)-lactoglobulin and 5% for \( \kappa \)-casein, selection on the economically optimum index for ten years will result in increases of 2 and 1% in the frequencies of the desirable alleles, respectively for these loci, with virtually no reduction in genetic gains for production traits. The value of this gain for the Israeli Holstein population is $187,000/yr.

INTRODUCTION
Caseins are the principal components of milk protein. Several studies have found that cheese quality and quantity is higher for milk derived from cows with the BB genotypes for \( \beta \)-lactoglobulin and \( \kappa \)-casein (Marziali and Ng-Kwai-Hang, 1986; Rahali and Menard, 1991). A number of studies have also found that milk protein production is positively associated with these genotypes (reviewed by Lin et al., 1992), however recent studies have found no effect in the Dutch (Bovenhuis and Weller, 1994) and Israeli (Ron et al., 1994) populations. Genotypes of cows can be determined by isoelectric focusing of milk extract, and of any individual by DNA restriction fragment length polymorphism (RFLP) analysis after DNA amplification via the polymerase chain reaction (PCR) (Medrano and Aguilar-Cordova, 1990, 1990a; summarized by Schlee, 1993).

Selection indices are based on the economic values of the component traits to the producers. Thus incorporation of these loci in a selection index can only be justified if farmers received differential payment based on their cows' genotype. Optimally this would require genotyping all cows, or quantitative estimation of allele frequencies in milk shipments from each farm. Neither of these alternatives is economically viable. In advanced breeding programs based on Al, most cows will be daughters of a small number of sires, and the expense involved in genotyping only Al sires can be considered negligible. If maternal grandsires (MGS) are also genotyped, then 5/16 of the genetic variance for these loci can be determined.

We propose that differential payment could be applied, based on the expected frequency of desirable genotypes in the milk of each herd, as estimated from sire and MGS genotypes. The objectives of this study were to estimate expected frequencies of the B-allele for \( \beta \)-lactoglobulin and \( \kappa \)-casein in the Israeli population based on sire and MGS genotypes, estimate the between herd variance for expected cow genotype, devise the economically optimum selection index including these loci, and estimate predicted genetic gains based on this index.

METHODS
Genotypes for \( \kappa \)-casein and \( \beta \)-lactoglobulin were determined for 126 and 120 Israeli Holstein sires respectively, by the method of Medrano and Aguilar-Cordova (1990, 1990a). Of 92,040 milk
and protein recorded cows in production on Dec 31, 1993, sire genotypes of 74,698 cows were
determined for \( \kappa \)-casein, and 70,403 cows for \( \beta \)-lactoglobulin. Both sire and MGS genotypes were
determined for 41,071 and 37,916 cows, respectively. Based on the sire and MGS genotypes, the
expected frequency of \( B \) alleles inherited from genotyped ancestors was determined for each cow.
Thus if only the sire was genotyped, then expected frequency of inherited \( B \) alleles was 0 for AA
sires, 0.25 for AB sires, and 0.5 for BB sires. If both sire and MGS were genotyped, then the
expected frequency ranged from 0 for cows with AA sires and MGS to 0.75 for cows with BB sires
and MGS. Herd expected frequency of \( B \) alleles were computed from each cow's genotyped
ancestors based on the expected cow frequencies. The analyses based only on sire genotype
included 755 herds with at least 20 milking cows. The analyses based on sire and MGS included
411 herds, each with at least 20 cows with both ancestors genotyped.

Selection index weights for these loci under Israeli production conditions were derived based
on the following assumptions: Mean protein production per cow per lactation is 300 kg. The
economic benefits of the BB genotypes as compared to the AA genotypes were 4% for \( \beta \)-lactoglobulin, and 5% for \( \kappa \)-casein. The economic values were additive and codominant for both
loci. Total national milk production is 900 million liters, of which 55% is directed to cheese making.
The farm price for milk protein is $8.25/kg, and milk averages $0.33/liter. In addition to the
genotypes for these two loci, the selection index includes kg milk, fat, and protein, with respective
economic weights of -0.274, 6.41, and 34.85. The vector of expected gains from selection, \( d \),
were derived from the following equation:

\[
d = \left( \sqrt{\sigma_i^2} \right) G b
\]

Where \( i \) is selection intensity, \( \sigma_i \) is the standard deviation of the selection index, \( G \) is the genetic
variance matrix, and \( b \) is the vector of index weights. \( \sigma_i^2 = b^T P b \), where \( P \) is the phenotypic
variance matrix. \( i \) was set equal to 2, which is comparable to about 10 years of selection. It is
assumed that selection is based on genetic evaluations. Thus the vector of economic values will
be equal to the index coefficients. The genetic and phenotypic matrices for milk, fat, and protein
were derived from Pasternak and Weller (1993), and are given in Table 1. The genetic variance for
these loci was the expected variance of \( B \) alleles inherited from sire and MGS, and the phenotypic
variance was estimated as the variance of the allele frequency among sires. Milk protein loci were
assumed to have zero correlations to each other and productions traits.

<table>
<thead>
<tr>
<th>Genetic</th>
<th>Phenotypic</th>
</tr>
</thead>
<tbody>
<tr>
<td>milk</td>
<td>fat</td>
</tr>
<tr>
<td>Milk</td>
<td>527,076</td>
</tr>
<tr>
<td>Fat</td>
<td>6879</td>
</tr>
<tr>
<td>Protein</td>
<td>9973</td>
</tr>
</tbody>
</table>

RESULTS

Sire genotype frequencies are given in Table 2. Frequencies of the \( B \) alleles were 0.12 for
\( \kappa \)-casein and 0.48 for \( \beta \)-lactoglobulin. The genotype frequencies were close to the Hardy-Weinberg
equilibrium values. Assuming that these frequencies are representative and binomially distributed,
the expected genotype variances are 0.053 and 0.125, respectively. Estimated cow frequencies,
their standard deviations and ranges are given in Table 3. Estimated frequencies for the two loci
were computed for all cows with genotyped sires, and for cows with both sire and MGS genotyped.
The variances of the expected cow allele frequencies based on sires and MGS were close to the
expected values of 5/16 of the variances derived from the sire frequencies. Assuming the same allele frequencies in cows, the expected mean allele frequencies including contributions of ancestors that were not genotyped can be derived by dividing the means by 0.75 if both sires and MGS were genotyped, and 0.5 if only sires were genotyped. The results are 0.086 and 0.085 for \( \kappa \)-casein and 0.468 and 0.464 for \( \beta \)-lactoglobulin, which are slightly lower than the sire allele frequencies.

Table 2. Distribution of sire genotypes for \( \kappa \)-casein and \( \beta \)-lactoglobulin.

<table>
<thead>
<tr>
<th>Locus</th>
<th>Total</th>
<th>AA</th>
<th>AB</th>
<th>BB</th>
<th>frequency of B</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \kappa )-casein</td>
<td>126</td>
<td>98</td>
<td>26</td>
<td>2</td>
<td>(0.78) (0.21)</td>
</tr>
<tr>
<td>(proportion)</td>
<td></td>
<td>(0.02)</td>
<td></td>
<td></td>
<td>(0.12)</td>
</tr>
<tr>
<td>( \beta )-lactoglobulin</td>
<td>120</td>
<td>35</td>
<td>54</td>
<td>31</td>
<td>(0.29) (0.45)</td>
</tr>
<tr>
<td>(proportion)</td>
<td></td>
<td>(0.26)</td>
<td></td>
<td></td>
<td>(0.48)</td>
</tr>
</tbody>
</table>

Table 3. Estimated frequencies of \( \kappa \)-casein and \( \beta \)-lactoglobulin B alleles among Israeli-Holstein cows.

<table>
<thead>
<tr>
<th>Locus</th>
<th>Ancestors genotyped</th>
<th>No. of cows</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \kappa )-casein</td>
<td>Sires</td>
<td>74,698</td>
<td>0.043</td>
<td>0.110</td>
<td>0.</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Sires and MGS</td>
<td>41,071</td>
<td>0.064</td>
<td>0.125</td>
<td>0.</td>
<td>0.75</td>
</tr>
<tr>
<td>( \beta )-lactoglobulin</td>
<td>Sires</td>
<td>70,403</td>
<td>0.234</td>
<td>0.200</td>
<td>0.</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Sires and MGS</td>
<td>37,916</td>
<td>0.349</td>
<td>0.212</td>
<td>0.</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Expected herd mean frequencies for the B alleles are given in Table 4. The standard deviations and ranges of the herd means are also given. As expected, means and variances were higher for \( \beta \)-lactoglobulin, and higher when both ancestors were genotyped. In the proposed payment system the standard deviations among herds with sires and MGS genotyped will be: \((8.25/\text{kg})(300 \text{ kg})(0.05)(0.55)(0.028)\) = $1.91/cow for \( \kappa \)-casein, and for \( \beta \)-lactoglobulin will be: \((8.25/\text{kg})(300 \text{ kg})(0.04)(0.55)(0.043)\) = $2.34/cow.

Table 4. Estimated mean herd frequencies of \( \kappa \)-casein and \( \beta \)-lactoglobulin B alleles as estimated from genotyped cow ancestors.

<table>
<thead>
<tr>
<th>Locus</th>
<th>Ancestors genotyped</th>
<th>No. of herds</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \kappa )-casein</td>
<td>Sires</td>
<td>755</td>
<td>0.043</td>
<td>0.021</td>
<td>0.</td>
<td>0.147</td>
</tr>
<tr>
<td></td>
<td>Sires and MGS</td>
<td>411</td>
<td>0.064</td>
<td>0.028</td>
<td>0.</td>
<td>0.166</td>
</tr>
<tr>
<td>( \beta )-lactoglobulin</td>
<td>Sires</td>
<td>755</td>
<td>0.235</td>
<td>0.034</td>
<td>0.</td>
<td>0.354</td>
</tr>
<tr>
<td></td>
<td>Sires and MGS</td>
<td>411</td>
<td>0.351</td>
<td>0.043</td>
<td>0.</td>
<td>0.524</td>
</tr>
</tbody>
</table>
The economic benefit of BB genotype for κ-casein over the AA genotype in index units is: (34.85 units/kg)(300 kg)(0.05)(0.55) = 288 selection index units. Likewise the economic benefit of the BB genotype for β-lactoglobulin is: (34.85 units/kg)(300 kg)(0.04)(0.55) = 230. The expected genetic gains for ten years selection with and without inclusion of these loci in the index are given in Table 5. Inclusion of these loci had virtually no effect on response for production traits. Responses were slightly less than 1% for κ-casein and nearly 2% for β-lactoglobulin.

### TABLE 5. Index coefficients and expected genetic gains under the current and the proposed indices.

<table>
<thead>
<tr>
<th>Index</th>
<th>Traits</th>
<th>Milk (kgs)</th>
<th>fat protein (kgs)</th>
<th>κ-casein (frequency)</th>
<th>β-lactoglobulin (frequency)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>Coefficients</td>
<td>-0.274</td>
<td>6.41</td>
<td>34.85</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Expected gains</td>
<td>445.0</td>
<td>18.0</td>
<td>17.1</td>
<td>0</td>
</tr>
<tr>
<td>Current</td>
<td>Coefficients</td>
<td>-0.274</td>
<td>6.41</td>
<td>34.85</td>
<td>288</td>
</tr>
<tr>
<td></td>
<td>Expected gains</td>
<td>444.3</td>
<td>18.0</td>
<td>17.1</td>
<td>0.008</td>
</tr>
</tbody>
</table>

The annual economic value of this gain is: 
(900,000,000 kg/yr)(0.55)(0.33/kg)(0.05)(0.0081) + (0.04)(0.0185)) = $187,000/yr. Similar to any genetic gain, it should be noted that this gain is cumulative and eternal. Since expenses would consist only of genotyping about 50 sires per year, and data analysis, this slight change in breeding objectives can be readily justified.

**CONCLUSIONS**

By genotyping only A1 sires, cow frequencies for milk protein loci can be estimated. These frequencies can be used to differentially pay farmers for expected cheese yield. Under Israeli conditions the standard deviations among herds for differential payments would be $1.91/cow for κ-casein, and $2.34/cow for β-lactoglobulin. A selection index based on the economic benefits of the B alleles for these loci would result in 1% and 2% gains respectively after ten years of selection, with virtually no reduction in gains for fat and protein production. This increase has an economic value of $187,000/yr, and justifies the cost of genotyping sires and data analysis.

**REFERENCES**