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A simple steady-state model for the carry-over of aflatoxins from feed to cows milk

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1 **A simple steady-state model for the carry-over of aflatoxins**
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7 **from feed to cow's milk**
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5 Jan C.H. van Eijkeren^{*}, Martine I. Bakker and Marco J. Zeilmaker

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7 *National Institute for Public Health and the Environment; PO Box 1, Bilthoven, The*
8 *Netherlands*

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10 ^{*} to whom correspondence should be addressed. e-mail:jan.van.eijkeren@rivm.nl

Abstract

A simple steady-state model is derived from two kinetic one-compartment models for the disposition of aflatoxin B₁ (AFB₁) and aflatoxin M₁ (AFM₁) in the lactating cow. The model relates daily intake of AFB₁ in feed of dairy cattle and the cow's lactation status to resulting concentration levels of AFM₁ in milk. Moreover, assuming a linear relation between the cow's lactation status and feed intake, the model relates daily milk production and AFB₁ concentration in total feed to AFM₁ levels in milk. The model explains similar experimental outcomes from different experiments investigating carry-over of aflatoxins from feed to milk. Although it is concluded that it is difficult to set a limit for AFB₁ in feed once and for all, in Europe the European Union (EU) limit of 5 µg AFB₁/kg of concentrate until now has proved to be appropriate to prevent exceeding the EU-limit of 0.05 µg AFM₁/kg milk.

Keywords: aflatoxin B₁, aflatoxin M₁, steady-state model, animal feed

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27 **Introduction**

28 Aflatoxins are known for their carcinogenic, mutagenic and teratogenic properties
29 (Van Egmond, 1989). They have been found, amongst others, in groundnuts, cotton-
30 seed and corn, which are constituents in different formulations of concentrate rations
31 fed to dairy cattle. Aflatoxin B₁ is the most abundant of the aflatoxins. They are sec-
32 ondary metabolites of some *Aspergillus fungi*. In mammals AFB₁ is metabolised to
33 AFM₁, which is excreted in milk. Both AFB₁ and AFM₁ are very toxic and potent
34 liver carcinogens. Several authors, e.g., references in Van Egmond (1989), Frobish *et*
35 *al.* (1986), Veldman *et al.* (1992), Chopra *et al.* (1999), have investigated the relation
36 between intake of aflatoxins in feed of dairy cattle and the resulting AFM₁ levels in
37 milk, depending on (equivalent) AFB₁ level in (total) feed, daily intake of AFB₁ and
38 lactation status. However, no modelling effort, unifying the different investigations
39 and explaining common observations, was made.

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41 A model based on mechanistic considerations was developed. This includes the frac-
42 tional absorption of daily ingested AFB₁ over the gut wall, its metabolism to AFM₁
43 and its elimination by other ways, the corresponding formation of AFM₁ and the ex-
44 cretion of AFM₁ through milk and its elimination by other ways. From the steady-
45 state analysis of this model, the carry-over rate (COR) from AFB₁ to AFM₁, i.e. the
46 ratio of the daily amount of AFM₁ excreted by milk and the daily amount of AFB₁
47 ingested was modelled. Additionally, the bioconcentration factor (BCF), i.e. the ratio
48 of AFM₁ concentration in milk and AFB₁ concentration in feed, follows from the
49 steady state analysis. When it is assumed that feed intake depends linearly on daily
50 milk production, then the BCF could be expressed in terms of lactation status only.

51

Materials and Methods

The number of animals per experimental group for the studies utilised in this paper is low. Frobish *et al.* (1986) used 4 animals per group, Veldman *et al.* (1992) used 12 and 8 animals per group and Chopra *et al.* (1999) used 10 animals in their repeated experiment. But also other authors generally seem to use a number of animals of the same order (van Egmond, 1989). A general remark is that the inter-individual variability regarding the resulting AFM₁-level in milk is great. Moreover, different studies use different races, different composition of concentrate, different source of contamination (naturally contaminated corn, cottonseed or groundnuts) and different composition of additional feed.

The mechanistic model for carry-over of AFB₁ to AFM₁ is shown in **Figure 1**. A fraction, F of the daily intake $\dot{D}$ $\mu\text{g/day}$ of AFB₁ is taken up over the gut wall (in this paper dotted symbols denote quantities per time unit). This fraction may well depend on the matrix/carrier of AFB₁ and thus can be different for different AFB₁ contamination sources (groundnuts, cottonseed and corn), different concentrate composition and different total feed composition. The daily intake $\dot{D}$ of AFB₁-equivalents is the product of the total daily feed intake $\dot{I}_{\text{feed}}$ (kg feed / day) and the total feed concentration

$$C_{\text{feed}} \text{ (}\mu\text{g AFB}_1\text{/ kg feed): } \dot{D} = \dot{I}_{\text{feed}} \cdot C_{\text{feed}}.$$

In the one-compartment model, the amount A_B taken up over the gut wall results in a plasma concentration $C_B = A_B / V_B$, where V_B is the distribution volume of AFB₁, i.e. the equivalent to the body tissues volume of the volume of pure plasma to reach that

concentration. AFB₁ is cleared from plasma by urinary excretion (after GSH-conjugation) or by transformation to metabolites that are of no further toxicological interest (clearance CL_B in L/day) and by transformation to the metabolite of interest AFM₁ (clearance $CL_{B:M}$ in L/day). Once AFM₁ has been formed in the liver, it results in a plasma concentration $C_M = A_M / V_M$, where V_M is the distribution volume of AFM₁. Also AFM₁ is cleared from plasma by elimination through other means than milk (CL_M in L/day) and by excretion through milk: $P_m \dot{M}$ L/day, where P_m is the milk:plasma partition of AFM₁ and $\dot{M}$ is the milk production in kg/day.

A coupled set of mass balances describes the carry-over of AFB₁ in feed to AFM₁ in milk:

$$\begin{aligned} \frac{dA_B}{dt} &= F\dot{D} - (CL_B + CL_{B:M}) \cdot C_B \\ \frac{dA_M}{dt} &= CL_{B:M} \cdot C_B - (CL_M + P_m \dot{M}) \cdot C_M \end{aligned} \quad (1)$$

The first line in equation (1) shows the rate of change of the body burden of AFB₁ dA_B / dt after the fractional systemic uptake F of the daily ingested amount $\dot{D}$ through contaminated feed and the concurrent clearance from plasma by elimination (CL_B) and AFM₁-formation $CL_{B:M}$. The second line shows the rate of change of the body burden of AFM₁ dA_M / dt and its concurrent clearance from plasma by elimination (CL_M) and excretion through milk, $P_m \dot{M}$. Note that the daily milk excretion is $P_m \dot{M} C_M$, which is the product of the daily milk production $\dot{M}$ (kg/day) and the concentration of AFM₁ in milk $P_m C_M$.

In this study we are interested in the case that contamination is sustained and steady state will be reached. From equation (1), setting the rates of change to zero, one obtains readily the steady state concentrations in plasma:

$$C_B = \frac{F\dot{D}}{CL_B + CL_{B:M}} \quad (2)$$

$$C_M = \frac{CL_{B:M} \cdot C_B}{CL_M + P_m \dot{M}} = \frac{CL_{B:M}}{CL_M + P_m \dot{M}} \cdot \frac{F\dot{D}}{CL_B + CL_{B:M}}$$

where in the second line the resulting steady state concentration of AFB₁ is substituted from the first line.

The corresponding AFM₁-level in milk at steady state is:

$$C_{milk} = P_m C_M = \frac{P_m CL_{B:M}}{CL_M + P_m \dot{M}} \cdot \frac{F\dot{D}}{CL_B + CL_{B:M}} \quad (3)$$

Dividing through the milk:plasma partition coefficient P_m and defining the constants

$$\alpha = \frac{F \cdot CL_{B:M}}{CL_B + CL_{B:M}}, \quad \beta = \frac{CL_M}{P_m} \quad (4)$$

the resulting steady state AFM₁ concentration in milk can be expressed in terms of the “free” variables of daily dose and lactation status:

$$C_{milk} = \frac{\alpha \dot{D}}{\beta + \dot{M}} \quad (5)$$

Two additional quantities can be derived from equation (5): the carry-over-rate (COR), which is the relation between the daily AFB₁ intake and the daily AFM₁ excretion through milk and the bio-concentration factor (BCF), which is the ratio between the AFM₁-level in milk and in AFB₁-level in total feed:

$$COR = \frac{\dot{M}C_{milk}}{\dot{D}} = \frac{\alpha\dot{M}}{\beta + \dot{M}}, \quad BCF = \frac{C_{milk}}{C_{feed}} = \frac{\alpha\dot{I}_{feed}}{\beta + \dot{M}} \quad (6)$$

Note that the COR is only dependent on lactation status and the BCF only on daily feed intake and lactation status.

Additionally, when it is assumed that there exists a linear relationship between daily milk production and feed intake:

$$\dot{I}_{feed} = A \cdot \dot{M} + \dot{B} \quad (7)$$

($\dot{B}$ is intake for self maintenance when no milk is produced) then C_{milk} in equation (5) can be expressed in terms of lactation status and feed concentration, and so the corresponding BCF of equation (6) is no longer dependent on feed intake and lactation status, but on the latter only:

$$C_{milk} = \frac{\alpha \cdot (A \cdot \dot{M} + \dot{B})}{\beta + \dot{M}} \cdot C_{feed}, \quad BCF = \frac{\alpha \cdot (A \cdot \dot{M} + \dot{B})}{\beta + \dot{M}} \quad (8)$$

Results

Van Egmond (1989; chapter 2) shows a compilation of data from Sieber and Blanc (1978) which clearly indicates that there is a linear relationship between AFB₁ intake and AFM₁ levels in milk. This is consistent with model equation (5), be it that it may be expected that the slope of the linear relationship differs from the different investigations, which it does, mainly depending on the kind of contamination and lactation status.

The model of equation (5) has been fit to data, concerning concentrate containing naturally contaminated cottonseed, from Frobish *et al.* (1986), see Figure 2. The resulting empirical parameter values found are $\alpha = 0.032$, $\beta = 17$. Of the six data points, one appears to be an outlier: its low milk level would indicate cows at high production, while in fact production is low. Frobish *et al.* also present AFB₁ levels in total feed and thus daily intake of feed can be estimated. The result of linear regression of daily intake versus production status is presented in Figure 3. The resulting optimised parameter values are $A = 0.43$, $\dot{B} = 10$. Note that, because of their clustering the data do not allow for a definite conclusion that a linear relation exists between intake and production level. However, for the range of milk production levels the model may assumed to be adequate. If so, the model for milk levels and bio-concentration factors of equation (8) apply.

In a second trial, concentrate containing contaminated cottonseed was used again, as well as concentrate containing naturally contaminated corn. In Table 1 observed AFM₁-levels in milk are compared with levels estimated by applying the models in equation (5) and (8). For cottonseed all the estimated levels exceed observed level, but

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168 within 20% at maximum. The estimations for carry-over from corn are about 1.5-fold
169 greater than determined experimentally. As the animals got the same diet, but with the
170 corn portion contaminated instead of the cottonseed portion, this must be due to dif-
171 ference in the typical aflatoxin mix of naturally contaminated corn as compared to that
172 of cottonseed. This implies a difference in the factor α in equation (5).
173
174 Given the parameterisation in equation (5), the maximum carry-over-rate possible
175 $= \alpha = 0.032$ (3.2%). Values of milk production in the study or cottonseed ranged
176 from a minimum of 14.6 L/day to a maximum of 32.9 L/day, and consequently the
177 model calculated COR (for cottonseed) should range from 0.015 (1.5%) to 0.021
178 (2.1%). Values of 1.38% to 2.33% are reported, except for 15.2 kg milk per day pro-
179 ducing lot (which is also exceptional in Figure 2). In concordance with our model, it is
180 remarked that AFB₁-level in feed did not affect COR (equation (6)), but that COR was
181 positively correlated with increased milk production (equation (6)).
182
183 Also, it is reported that milk production did not affect AFM₁-levels in milk. When
184 feed intake is linearly dependent on milk production and equation (8) applies, this
185 should imply that, at least within the range of milk production in the study, BCF is
186 (almost) independent of $\dot{M}$. In the range $\dot{M} = 14.6 - 32.9$, BCF ranges between the
187 values 0.0155 and 0.0165. So, an explanation of the independence of AFM₁-levels on
188 milk production may lie in the validity of both the models in equation (5) (derived
189 from mechanistic considerations) and (7) (assuming linear relationship between daily
190 feed intake and milk production). Linear dependence of AFM₁-level in milk on AFB₁-
191 level in feed is implied both by equation (5) and (8).

193 In a two experiment study of Veldman *et al.* (1992), concentrate with naturally con-
194 taminated groundnuts was used. Note that also in this case, quantitative model calcu-
195 lations using the parameters found above, notably the parameter α , need not be simi-
196 lar to experimental observations. Qualitative model aspects however, should not dif-
197 fer. Nevertheless, application of model equation (5) to experimental results of experi-
198 ment 1 do not fit: while daily intake for high and low producing cows are similar (39
199 and 34 $\mu\text{g/day}$, respectively), mean AFM_1 -level in milk of the high producing cows
200 exceeds 1.5-fold the corresponding mean level in low producing cows: one would ex-
201 pect the reverse, because of the more efficient excretion route through milk. This ex-
202 perimental result is also not consistent with the result of the second experiment, nor
203 with experimental results of other researches. The results of experiment 2 are consis-
204 tent with the model, indicating that the BCF of AFB_1 to AFM_1 from groundnuts to be
205 a factor of 1.6 greater than the BCF from cottonseed.

206
207 From the second experiment it is concluded by the authors that 1. COR is positively
208 correlated with milk production (our equation (6)), 2. given a fixed AFB_1 intake the
209 corresponding AFM_1 -level in milk is negatively correlated to milk production (our
210 equation (5)) and 3. COR is independent of AFB_1 -level in feed (our equation (6)).

211
212 Model calculations (equation (5)) with the parameterization as found above applied to
213 result from Chopra *et al.* (1999) can reasonably explain their findings. However, cal-
214 culated concentrations appear to be 2-fold (± 0.5) higher than the concentrations found
215 experimentally. The cows were fed concentrate with naturally contaminated ground-
216 nuts, as in the research of Veldman *et al.* This last research found concentrations that
217 appear to be about 1.6 higher than the calculated concentrations based on parameters

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found for Frobish *et al.* So, concentrations found by Veldman *et al.* exceed those found by Chopra *et al.* by a factor of about 3.2. This may be partly due to matrix effects: apart from different concentrate compositions, cows in Chopra *et al.* were fed green maize and wheat straw, cows in Veldman *et al.* grass and maize silage. Moreover, it is not clear whether the ration was contaminated naturally. Applebaum *et al.* (1982) report an increased AFM₁-level in milk when naturally contaminated portion was administered compared to an equivalent contamination level with pure AFB₁.

Discussion

Different investigators studied the carry-over of AFB₁ (in fact AFB₁-equivalents of a natural mixture of aflatoxins) from feed to cows milk under different conditions such as lactation status, source of contamination, contaminated concentrate composition and total feed composition. From the pharmacological and toxicological literature, it is well known that the carrier of the contamination [i.e., in the following order, source of contamination (corn, cottonseed, groundnuts), concentrate composition and total feed composition] generally influence its absorption over the gut wall. As the natural contamination is expressed in terms of AFB₁-equivalents and only AFB₁ will be transformed to AFM₁, both feed composition and kind of source will lead to different quantitative outcome of the different experiments. Indeed, different recommendations with respect to daily intake per animal and of corresponding concentrate contamination level may be expected. e.g., Veldman *et al.* (1992) recommend a daily intake of AFB₁ per cow below 40 µg, Munksgaard *et al.* (1987) below 60 µg and Chopra *et al.* (1999) below 70 µg. Corresponding recommended AFB₁-levels in concentrate in Munksgaard *et al.* (1987) and Veldman *et al.* (1992) are 10 µg/kg and 3 – 4 µg/kg, respectively. As daily concentrate intake in Chopra *et al.* is about 3 kg/day, one could

243 derive a recommended concentrate contamination level of 23 $\mu\text{g/kg}$. Scaling the result
244 in Frobish *et al.* to the current AFM₁ EU-limit in milk of 0.05 $\mu\text{g/kg}$ (0.5 $\mu\text{g/kg}$ milk
245 in 1986), the recommended level would be 3.3 $\mu\text{g/kg}$ concentrate. This assumes the
246 conversion in the liver of AFB₁ to AFM₁ to be non-saturated within a tenfold range
247 (see also Veldman *et al.* (1992))

248
249 Despite the expected different quantitative outcome, a qualitative outcome similar to
250 all experiments is reported. In order to unify these studies, a simple steady state model
251 has been developed [see equation (5)]. This model is based on the steady state analy-
252 sis of a mechanistic model describing the kinetics of carry-over of AFB₁ in feed to
253 AFM₁ in milk [see figure 1 and equation (1)]. Though this model lacks an accurate
254 description of the initial phase of contamination, when AFB₁-levels in plasma and,
255 consequently, AFM₁-levels in milk probably change rapidly, it may offer a sufficient
256 description of the terminal phase of contamination, when levels change slowly and
257 reach steady-state.

258
259 The simple model, derived from the steady-state analysis contains two experimentally
260 observable parameters, the contamination rate and the milk production rate, and two
261 empirical constants. These constants will depend on the cows race, the source of con-
262 tamination (cottonseed, corn, groundnuts, *etc.*), and the composition of concentrate
263 fed together with the composition of total feed. *E.g.*, races will most probably differ in
264 their metabolism (both pathways available and kinetics), which influences both pa-
265 rameters [see equation (4)]. Different sources of AFB₁, will lead to different fractions
266 of the amount of the mixture of aflatoxins that, eventually, may be transformed to
267 AFM₁, thus influencing the parameter α in the model. In the same cow, regardless of

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the source, the parameter β is a given constant. The contaminated material that is applied to the concentrate does not only determine the typical natural contaminating aflatoxin composition, but also serves as a different matrix/carrier. This aspect is further influenced by concentrate composition and, indeed, by the total feed composition.

Nevertheless, from the model one can derive the observed aspects of carry-over from AFB₁ in feed to AFM₁ in milk. Milk levels C_{milk} of AFM₁ are independent of feed levels C_{feed} of AFB₁ when the rate of contamination in $\dot{D} = \dot{I}_{feed} \cdot C_{feed}$ is a constant [equation (5)]. Carry-over rate is higher in high milk producing cows than in low producing ones [equation (6)]. Correspondingly, AFM₁-levels in milk are higher in low producing cows than in high producing ones at the same rate $\dot{D}$ of AFB₁ contamination [equation (5)]. Carry-over rate is independent of the rate of contamination [equation (6)].

Furthermore, it was assumed that, at least in the range between low and high milk production, total feed intake was linearly related to milk production level [equation (7)]. Under this assumption, also BCF is independent of the contamination rate and depends on milk production only [equation (8)]. The parameters found for one study (Frobish *et al.*) indicate that BCF varies only slightly in the range between low and high milk production, corroborating the observation that BCF is independent of milk production.

Given a limit AFM₁-level in milk, equation (5) may help in deriving the corresponding limit for AFB₁- intake, or, indirect, for AFB₁-level in total feed. Likewise, equation (8) directly relates AFM₁-levels in milk to AFB₁-levels in total feed. Note that the

293 limit for AFB₁-intake depends on the milk production level. When feed intake rate is
294 linearly related to milk production, then under the condition that BCF is only slightly
295 dependent on milk production, the limit for AFB₁-level in feed is independent of milk
296 production.

297
298 In conclusion, it seems that limits for AFB₁ contamination (rate or concentration
299 level) related to a given limit for AFM₁-level in milk depend on the cows race, the
300 source of contamination and total feed composition. Different authors conclude to dif-
301 ferent recommendations. Veldman *et al.* (1992) compare their recommendation of
302 concentrate contamination level not to exceed 3 – 4 µg/kg with the (still) current EU-
303 limit of 5 µg, and conclude that the latter does not guarantee the enforcement of the
304 EU AFM₁-limit in milk of 0.05 µg/kg. Also the recommendation of Frobish *et al.*
305 (1986) of 33 µg AFB₁/kg concentrate, based on the former limit in milk of 0.5 µg
306 AFM₁/kg milk when scaled to the current limit in milk, i.e. 3.3 µg AFB₁/kg concen-
307 trate (well within the range of 3 – 4 µg/kg) is below this limit. Nevertheless, in daily
308 practice, it seems that the EU-limit for AFB₁ in concentrate (5 µg AFB₁/kg) prevents
309 AFM₁-levels to exceed the EU-limit of 0.05 µg AFM₁/kg.

310

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315 **References**

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316 Applebaum, R.S., Brackett, R.E., Wiseman, D.W. and E.H. Marth. (1982), Responses
317 of dairy cows to dietary aflatoxin: feed intake and yield, toxic content and quality of
318 milk cows treated with pure and impure aflatoxin; *J. Dairy Sci.* **65**:1503-1508
319
320 Chopra, R.C., Chhabra, A., Prasad, K.S.N., Dudhe, A., Murthy, T.N. and T. Prasad.
321 (1999) Carry-over of aflatoxin M₁ in milk of cows fed aflatoxin B₁ contaminated ra-
322 tion; *Indian J. Anim. Nutr.*, **16**:103-106
323
324 Frobish, R.A., Bradley, B.D., Wagner, D.D., Long-Bradley, P.E. and H. Hairston.
325 (1986). Aflatoxin residues in milk of dairy cows after ingestion of naturally contami-
326 nated grain; *J. Food Protection*, **49**:781-785
327
328 Van Egmond, H.P. ed.; (1989) *Mycotoxins in dairy products*; Elsevier Science Pub-
329 lishers LTD, Essex, UK,.
330
331 Munksgaard, L., Larsen, J., Werner, H. and B.T. Viuf. (1987) Carry over of aflatoxin
332 from cows' feed to milk and milk products; *Milchwissenschaft*, **42**: 165-167
333
334 Veldman, A., Meijst, J.A.C., Borggreve, G.J. and J.J. Heeres-van der Tol; Carry-over
335 of aflatoxin from cows' food to milk. (1992) *Anim. Prod.*, **55**, 163-168

Table 1. Milk levels of AFM₁ observed, estimated with the model in equation (5)
 ($\alpha = 0.032, \beta = 17$) and the model in equation (8) .

Production level kg/day	Daily AFB ₁ intake μg	AFM ₁ milk level $\mu\text{g/L}$		
44 μg cottonseed /kg total feed		observed	model (5)	model (8)
30.4 (n ^a = 4)	966	0.62	0.65	0.69
18.5 (n = 3)	742	0.59	0.67	0.71
49 μg corn / kg total feed		observed	model (5)	model (8)
31.2 (n = 4)	1116	0.51	0.74	0.76
20.0 (n = 4)	885	0.55	0.77	0.79

a: n is number of animals

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Legends

Figure 1. Kinetic model of the carry-over of AFB₁ to AFM₁. A fraction F of the daily dose $\dot{D}$ enters the system over the gut wall. AFB₁ is cleared by excretion and by bio-transformation to toxicologically non-interesting metabolites (clearance CL_B) and to AFM₁ (clearance $CL_{B:M}$). AFM₁ is cleared by biotransformation to non-interesting metabolites or by excretion through toxicologically non-interesting ways (clearance CL_M) or by excretion through milk ($P_m \dot{M}$), that has a milk:plasma partition coefficient P_m and a daily production of $\dot{M}$. Plasma concentrations of AFB₁ (C_B) and AFM₁ (C_M) are the amounts of AFB₁ and AFM₁ divided by their distribution volume (V_B and V_M , respectively)

Figure 2. Fit of model equation (5) to the data from Frobish et al. (1986), table 3. Upper lines (experimental points: o) show the model for the three different low milk production levels and lower lines (experimental points: *) the model for the three different high milk production levels. Fitted parameter values: $\alpha = 0.032$, $\beta = 17$.

Figure 3. Fit of intake versus milk production model of equation (7) to the data of Frobish et al. (1986), table 3. The symbols denote experimentally determined values and the straight line ($A = 0.43$, $\dot{B} = 10$) shows the model fit. Note the clustering of data at the low and high production levels.

Figure 1.

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365 **Figure 2.**

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