

1 COMPENSATORY GROWTH IN DOUBLE MUSCLED BULLS

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4 Different Periods of Feed Restriction Before Compensatory Growth in Belgian Blue Bulls:

5 II. Plasma Metabolites and Hormones¹

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1 ABSTRACT: Plasma metabolites and hormones have been studied in 16 Belgian Blue bulls,
2 double muscled type, maintained at low growth (.5 kg/d) during 4 (G2), 8 (G3) or 14 (G4) mo
3 (low growth period, LGP) before fattening (rapid growth period, RGP). Animals from the
4 control group (CG) were fed a diet high in both energy and protein. The animals from G2, G3,
5 and G4 were fed a restricted amount of a diet low in both energy and protein during LGP and
6 the same diet as CG during RGP. Plasma glucose, alpha-amino nitrogen (AAN), NEFA, urea,
7 creatinine, thyroxine (T4), 3,3',5'-triiodothyronine (T3), and IGF-1 were analysed on blood
8 samples taken fortnightly. Plasma growth hormone (GH) and insulin (I) profiles were
9 analysed on serial blood samples obtained at three moments during growth. RGP was
10 characterized by an initial compensatory growth, by higher plasma glucose, AAN, and urea
11 levels, and by lower plasma NEFA and creatinine levels. Plasma GH concentration decreased
12 after refeeding. Plasma T4 increased linearly during refeeding, as opposed to T3, which
13 showed a different profile in each group. Plasma IGF-1 showed a curvilinear increase during
14 RGP and reached a plateau after 3 mo in each compensating groups. In G4, changes of plasma
15 metabolites and hormones differed often distinctly from G2 or G3. During refeeding, higher
16 nutrient supply improved the functionality of the somatotropic axis and increased the
17 concentration of anabolic hormones, allowing rapid muscle deposition. However, animals
18 underfed the longest period behaved differently than the other groups, possibly because they
19 reached a more complete sexual maturity.

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21 *Key Word:* Belgian Blue Bulls, Compensatory Growth, Metabolites, Growth Hormone,
22 Insulin, Thyroid Hormones, IGF-1

1 Introduction.

2
3 Interactions between hormonal status, metabolites, and environment during growth
4 changes are complex. Feed restriction decreases the concentration of metabolites but
5 increases the concentration of somatotropin (GH) (Blum et al., 1985; Hayden et al., 1993).
6 Age exerts opposite effects and decreases the GH response of bulls to food deprivation
7 (Olbrich-Bludau et al., 1993). Insulin-like Growth Factor I (IGF-1) plays a key role in protein
8 synthesis and its secretion is GH-dependant. However, the IGF-1 concentration, as opposed to
9 GH, is well correlated to growth rate (Van Eenaeme et al., 1989; Dawson et al., 1993). Other
10 hormones also interact with the somatotropic axis. For example, elevation of plasma insulin
11 (I) is associated with a decrease of plasma GH level (Oshibe et al., 1994) whereas thyroid
12 hormones have a synergistic action with somatotropin on metabolism (Burstein et al., 1979).

13 Body development may be physiologically enhanced by compensatory growth (Wilson
14 and Osborne, 1960) when an animal is refed after a period of underfeeding. The effect of
15 compensatory growth on hormones and metabolites has never been reported in double
16 muscled type breeds. The aim of this experiment was to study, in Belgian blue bulls, double
17 muscled type, plasma concentration of metabolites and hormones during the growing and
18 fattening periods as affected by feed restriction lasting for three different time periods.

Material and Methods

The Animal Care and Use Council of our institute approved the use and treatment of animals in this study. A total of 16 Belgian Blue bulls, double muscled type, were used as experimental animals. They were penned in metabolic stalls and were the same animals from whom nitrogen balance were previously reported by Hornick et al. (unpublished results). The animals of the control group (CG) were fed a diet high in both energy and protein. The animals of groups 2, 3, and 4 (G2, G3, G4) were fed initially a restricted amount of a diet low in both energy and protein, calculated to allow a growth rate of .5 kg/d. This low growth period (LGP) lasted for 114, 243, and 419 d, respectively in G2, G3, and G4. At the end of this period, animals were offered, on an ad libitum basis, the same fattening diet as CG, a transition period being managed over 15 d. Feed was offered twice daily, at 0800 and 1400. Feed intake was recorded daily and live weights were measured twice a month. Jugular blood samples (20 ml) were obtained fortnightly, before the animals were fed in the morning. Blood was equally aliquoted in 10 ml tubes containing either Li-heparin (130 Units/10 ml) or 68 mg of mixture of K-oxalate (40.80 mg) and NaF (27.20 mg) per 10 ml, and centrifuged at 4°C after collection. Plasma was separated and stored at -20°C until analysis for determination of glucose, α -amino nitrogen (AAN), non esterified fatty acids (NEFA), urea, creatinine, thyroxine (T4), 3,3',5'-triiodothyronine (T3), and IGF-1. Serial jugular blood samples (10 ml) were obtained in each group during 24h at 20 min interval on three occasions, in order to determine the profile of GH and I concentration. In CG, serial measures were performed at the beginning, and in the middle of the fattening period and one mo before slaughter. In G2,

1 G3, and G4, corresponding measurements were obtained on the middle of the low growth
2 period, 1 mo after the end of the transition period and 1 mo before slaughter.

3 The Autoanalyser Technicon was used for determination of glucose by o-toluidine
4 method (Henry et al., 1974a), urea by diacetylmonoxime method (Henry et al., 1974b) and
5 AAN by trinitrophenyl derivatisation (Palmer and Peters, 1969). NEFA were determined by
6 fused silica capillary GC (Müller and Binz, 1982). Somatotropin, I, T3, and T4 were
7 measured by radioimmunoassay using commercial kits. For GH, the kit used was developed
8 and commercialised by UCB Bioproducts, Braine l'Alleud, Belgium, using a homologous b-
9 GH antiserum and pituitary bovine GH (MW 22000) for tracer and standards as described by
10 Closset et al. (1986). The intra-assay coefficient of variation (CV) was 5.8% and inter-assay
11 CV was 11.8%. For I, the kit was developed and commercialised by Medgenix, Fleurus,
12 Belgium, using an IRMA procedure. The intra-assay CV was 7.1% while inter-assay CV was
13 11.1%. For T3 and T4, a kit commercialised by Orion Diagnostica, Espoo, Finland, was used,
14 and for IGF-1, a kit developed by Medgenix, Fleurus, Belgium, using acid-ethanol extraction.
15 The intra- and inter-assay CV were respectively 3.5 and 5.6% for T3, 3.6 and 5.9% for T4,
16 and 4.7 and 9.3% for IGF-1.

17 Data relative to GH profile were analysed with the Munro algorithm and compared
18 using the Student's t-test and the paired t-test. In order to describe the evolution of plasma
19 metabolite concentrations, values obtained twice a month were averaged per group; profiles
20 during LGP and RGP were calculated, assuming a quadratic evolution with time. Insulin, T3,
21 T4, and IGF-1 concentrations were analysed using a dynamic linear model allowing the
22 inclusion of an autoregression and a random effect in the model. This model took into account
23 the fact that each animal was observed several times, that observations made more closely in

1 time were more closely related and that some observations might be missing (Lindsay et al.,
2 1994). The explanatory variables used to fit the model for I profile were diet, length of the
3 low growth period, days elapse since the beginning of the experiment and accounting for any
4 seasonal component that might affect the mean I profile, age and live weight of the bulls, and
5 sampling time. The IGF-1, T3, and T4 profiles under the low energy and protein diet were
6 assumed to be similar for G2, G3, and G4. A quadratic equation was used to model the
7 evolution in LGP. Another quadratic equation was assumed to describe IGF I, T3, and T4
8 evolution in CG. Data relative to fattening period in G2, G3, and G4 were hypothesized to
9 have different evolutions. A degree two polynomial equation was fitted with a continuous
10 junction at the diet change time, ensured by adding power $t' = (t_i - t_{iC})$ to the reference profile
11 where i indexed the groups and t_{iC} denoted the switch time to the fattening diet for group i . In
12 models relative to IGF-1, T3, and T4 profiles, the effect of weight was included or discarded
13 according to its significance. The average concentrations of each metabolite during LGP and
14 RGP were calculated and compared using Student's t-test.

Results

The ADG during the LGP was close to .5 kg/d in G2, G3, and G4 with values respectively of .57, .54, and .44 kg/d. During the fattening period, the ADG was 1.32 kg/d in CG while in the compensating groups, values reached respectively 1.53, 1.43, and 1.53 kg/d. Only G2 showed a higher ADG during the fattening period than CG ($P < .05$).

The average plasma concentrations of metabolites during LGP and RGP are given in Table 1. Figure 1 depicts the modeled evolution of metabolite concentrations during the experiment. The level of glucose was high in CG and decreased linearly with time. In G2, plasma glucose did not vary substantially during LGP, and raised after realimentation before gradual decline. Therefore, mean values over the two periods were not different (824 vs 815 mg/L). Initial levels of glucose were close in G3 and G4 and decreased in a similar way during LGP. After realimentation, glucose increased rapidly but to a greater extent in G4 where a maximum close to 1000 mg/L was observed about 3 mo after the beginning of realimentation. Only G4 had a lower glucose concentration during LGP than during RGP (720 vs 868 mg/L, $P < .01$). Glucose level was the lowest in G4 during LGP (719 mg/L, $P < .01$) and the lowest in G3 during RGP (762 mg/L, $P < .01$).

The level of AAN showed an increase with time in CG and during LGP for the three restricted groups so that mean values increased with the length of the LGP (40.3, 45.8, and 51.1 mg/L in G2, G3, and G4 respectively, $P < .01$). The level of AAN increased also during the RGP for G2 and G3 (52.8 and 65.6 mg/L). However, the pattern of variation of AAN during RGP of G4 was quite different from the other groups. Whereas in G2 and G3 the increase after the transition period was in the line of preceding values, in G4 RGP was

1 characterised by an initial sharp decrease followed by an increase . All overall mean
2 concentrations were lower during LGP than during RGP.

3 Plasma urea concentration remained high during the whole fattening period in CG.
4 During LGP in the restricted groups, values were low compared to CG, but similar among
5 groups. Animals from G4 had however higher values (92.4 vs 72.7 and 77.1 mg N/L in G4,
6 G2, and G3 respectively). After realimentation, urea level increased. The pattern of
7 concentration change was different in the three groups. In G2, the increase was continuous, in
8 G3 a plateau was reached rapidly and in G4 the concentration reached a maximum and
9 decreased afterwards. Animals from G2 showed the highest urea level (170.1 mg N/L) and G4
10 the lowest (124 mg N/L) during RGP ($P < .01$).

11 Levels of NEFA were low during fattening in CG and during RGP in the restricted
12 groups, especially in G4 (129.9 vs about 250 $\mu\text{mol/L}$ in others groups, $P < .001$), but values
13 were high and close to 330 $\mu\text{mol/L}$ during LGP. In G2 and G4, a sharp decrease of NEFA
14 concentration was observed following the transition period.

15 In CG, the concentration of creatinine was initially low, increased progressively to
16 reach a maximum, and decreased afterwards. During LGP in G2, G3, and G4, plasma
17 creatinine concentration showed a progressive increase (23.9, 26.6, and 27.1 mg N/L in G2,
18 G3, and G4, $P < .05$) but after realimentation, values decreased rapidly, especially in G4.

19 Table 2 shows the average values of GH plasma parameters calculated by the Munro
20 algorithm and of I concentration over a period of 24h. Individual GH profiles for the different
21 groups are given in Figure 2.

22 During the first period of serial blood sampling, the animals from CG had a profile of
23 GH secretion characterized by a lower pulse number than during periods II and III ($P < .001$

1 and $P < .05$), and a higher pulse interval than during period II ($P < .001$). The most significant
2 differences appeared in period III: pulse amplitude as well as pulse surface, nadir and overall
3 mean decreased when compared to period II whereas between period I and II, no differences
4 were observed for these parameters.

5 The GH profile during the low growth period in G2 was characterized by many, close
6 and large pulses with high amplitude and a high nadir, resulting in a higher mean
7 concentration than in periods II and III ($P < .05$). The number, amplitude and area of the
8 pulses, as well as nadir, were numerically higher during period II than during period III, and
9 mean concentration was higher ($P < .01$). Few differences appeared between periods in G3,
10 number, interval and surface of the pulses being similar. The nadir and mean concentration
11 were however higher during period I than during period II ($P < .1$) while the amplitude was
12 lower in period II than in period III ($P < .05$). Although a large variability of response
13 appeared in G4, period III was paradoxically characterized by a greater number of pulses.
14 However, the nadir and the overall mean remained higher in period I than in period II ($P <$
15 $.1$).

16 Large variability was associated with measurements of I concentration and the model
17 used to characterise I profile retained only the diet effect among the explanatory variables,
18 together with three harmonics to describe the I daily rhythm (Table 4). Insulin concentration
19 was close to 6 mU/L during LGP and raised from 10 to 20 mU/L when the fattening diet was
20 offered. The length of the period of restricted diet, the season, the weight or the age had no
21 detectable effects on mean I concentration. The modeled profile of I concentration over a 24h
22 period is given in Figure 3. Mean I concentration increased from around 05h00 until 09h00
23 and then declined, a maximum being observed about 3 h after the first meal. A second

1 increase occurred from 13h00, reaching the maximum at 18h00. From that time, a continuous
2 decrease was observed till 05h00.

3 The mean concentrations of T3, T4, and IGF-1 during fattening or during LGP are
4 given in Table 3. The modeled profiles of IGF I, T3, and T4 are given in Figure 4. The IGF-1
5 concentration was low and close to 140 ng/mL during LGP in G2, G3, and G4. The CG
6 showed high levels of IGF-1 during the whole fattening (mean value: 262 ng/mL). In
7 compensating groups the fattening period was characterized by a continuous increase with the
8 highest levels observed at the end of the period, mean values being close to 280 ng/mL. A
9 quadratic effect with time was observed for the IGF-1 profile in all groups and during both
10 periods when live weight was discarded from the model (Table 4), the response being similar
11 for all compensating groups. When weight was included in the model, the IGF I profile during
12 LGP and during fattening of CG was linear in time, while in G2, G3, and G4 it remained
13 quadratic and similar in all groups.

14 The T4 concentration was constant during LGP and during fattening in CG, but was
15 higher in the latter case. When switching to the fattening diet, T4 increased linearly and
16 independantly from the time spent on the poorer diet (figure 4). The T3 evolution was
17 different. The initial concentration was low and similar in each group. The equations
18 estimating profiles of T3 were quadratic in all groups both during LGP and fattening period.
19 There were no changes in the profile of T3 from LGP to RGP in G4 as opposed to G2, and
20 G3: G2 showed an increase during about 3 mo, reached a maximum and then decreased. G3
21 showed a progressive and continuous increase until slaughter.

Discussion

Average daily gain was close to .5 kg/d during LGP and a recovery index of 62% was observed in G2. The growth rate increased until about 2 mo after the beginning of RGP, reached a maximum at about 1.8 kg/d and then decreased rapidly (Hornick et al., unpublished results).

Metabolites.

The decrease of plasma glucose with age has been reported in cattle (Bide et al., 1973; Blum et al., 1985). In G2, unlike in G3 and G4, the glucose level did not decrease with time during LGP but this may be due to the short length of restriction. The increase of the glucose concentration after realimentation was probably the result of a higher ruminal production of its precursor propionic acid, associated with a larger concentrate intake (Journet et al., 1995). In G4, the large increase of glucose level after refeeding, when compared to G2 and G3, remains unclear.

The increasing level of AAN in plasma during LGP and during RGP may result from a higher tissue release or a decrease of tissue catch-up of amino acids from plasma because the muscle protein degradation/muscle protein synthesis ratio varies with age (Simon, 1989). Except in G4, plasma AAN did not vary substantially immediately after refeeding, confirming previous results from Hornick et al. (1996) with Belgian Blue bulls maintained at low growth before refeeding. In G4, the sudden decrease of plasma AAN immediately after the beginning of the RGP suggests a catabolic activity of liver, but this hypothesis does not match with the

1 corresponding evolution of plasma urea. Amino acid could also be used for protein
2 deposition. However, this statement is speculative because it does not take into account the
3 interconversion of individual amino acids.

4 The increase in plasma urea concentration when turning from LGP to RGP reflected a
5 higher hepatic synthesis resulting from enhanced microbial ammonia production in the rumen
6 or greater amino acid degradation in the liver. Ellenberger et al. (1989) reported an initial
7 decrease in plasma urea after realimentation in steers and postulated that it was due to high
8 nutrient demand for increasing visceral growth. This effect was not observed in the present
9 experiment, possibly because a longer transition period was managed between LGP and RGP.
10 The longer period was necessary because the diets offered during the two periods were quite
11 different, in contrast to the experiment reported by Ellenberger et al. (1989). The slower
12 overall increase of plasma urea during RGP in G4 provided another support to protein
13 deposition, as the G4 animals had the highest nitrogen balance during RGP (Hornick et al.,
14 unpublished results). This high nitrogen deposition could result from an increase of sexual
15 steroids status associated with the age of the animals.

16 The marked higher plasma NEFA concentration during LGP, compared to fattening,
17 indicated a greater fat mobilisation, as reported by Blum et al. (1985) and Ellenberger et al.
18 (1989). This mobilisation resulted probably from endocrine status, especially the low I/GH
19 ratio (Vernon, 1992). Also thyroid hormones are known to be lipolytic, especially in cold
20 exposure (Sasaki and Weekes, 1986). However, in our experiment, T3 and T4 levels were low
21 during LGP, so their contribution to high NEFA levels was presumably not important.

22 Plasma creatinine concentration is known to be weight dependent (Seashore et al, 1981;
23 Schroeder et al., 1990). Surprisingly, it decreased when animals were catching-up weight. The

1 sudden decrease in the concentration of creatinine after realimentation has been observed
2 previously in our laboratory (unpublished results). Keenan and Allardyce (1986) reported also
3 changes in creatinine levels in sheep under different nutritional status, and ascribed it to
4 changes in creatinine clearance.

5

6 Hormones.

7

8 Considerable variation among GH profiles appeared between animals. The meaning of
9 such differences is not known (Wheaton et al., 1986; Gluckman et al., 1987). Several authors
10 reported that the secretion of GH was increased during a period of nutritional restriction
11 (Breier et al, 1986; Wheaton et al., 1986; Breier et al., 1988b; Ellenberger et al., 1989), or
12 during a period of low growth rate (Wheaton et al., 1986; Dawson et al, 1993). Similar results
13 have been observed in this experiment. The plasma concentration of GH is the balance
14 between pituitary secretion and clearance from the circulation (Van der Walt, 1994). Thus,
15 the lower nadir and mean concentration of GH during the beginning of RGP than during LGP
16 came from either a decrease of the secretion by the pituitary gland or by a higher clearance
17 from the plasma. If a stimulation of the secretion of GH was implicated in the higher mean
18 GH levels, this should be reflected by higher pulse number or higher pulse amplitude in LGP
19 when compared to RGP. This was not observed in our experiment, suggesting that lower
20 clearance was responsible of high mean GH levels during LGP. Lower clearance during LGP
21 could be associated with the low synthesis of high affinity hepatic GH receptor in feed
22 restricted animals (Breier et al., 1988a, 1988b). The decrease of GH levels during RGP could
23 also be explained by the inhibition of GH release following the distension of the rumen

1 (Tindal et al., 1985), because during RGP, the animals were fed on an ad libitum basis, as
2 opposed to LGP.

3 The high GH levels during LGP could also explain the high NEFA concentration during
4 this period, because GH has a lipolytic activity on adipose tissue (Grichting et al., 1983; Hart
5 et al., 1984), while GH receptor are not negatively regulated by feed restriction, in contrast to
6 liver receptor (Gluckman et al., 1987). This allowed the use of fat as energy source during
7 feed restriction.

8 Feeding conditions and growth rates were similar during LGP in the restricted groups
9 and also during fattening in all groups. However, there were, to some extent, significant
10 decreases in the concentration of GH with live weight and age in both periods (Table 3). Age
11 or live weight alter the sensitivity of the pituitary gland to hypothalamic hormones (Della-
12 Fera et al, 1986; Dubreuil et al, 1987; Schwartz et al., 1992). Plouzek and Trenkle (1991b)
13 and Mears and Schaalje (1993) observed that, as body weight increased, secretion, clearance,
14 and half-life of GH decreased. Similarly, Olbrich-Bludau et al (1993) reported that young
15 bulls responded to a greater extent to feed restriction than mature bulls, by increasing
16 frequency and amplitude of GH peaks. More surprising was the high pulse frequency
17 observed in G4 and the overall higher pulse interval, amplitude, area, nadir, and GH average
18 concentration at the end of the fattening period in compensating groups when compared to
19 CG. This may be due to an effect of the compensatory growth or to the different feeding
20 behaviour at this stage of fattening as animals tended to delay feeding at the end of the RGP,
21 possibly altering their GH secretion profile. The onset of progressive sexual maturity during
22 RGP could also enhance GH secretion (Plouzek and Trenkle, 1991a), especially in G4.

1 Numerous factors, such as nervous stimulation, plasma glucose, volatile fatty acids and
2 amino acids trigger the secretion of I by the pancreas (Brockman, 1984; Weekes, 1986).
3 Nervous induced stimulation occurred in our experiment because I concentration began to
4 increase before feeding (Figure 3). This phenomenon has been also reported by Ndibualonji et
5 al. (1995) in cows. Concentrates are known to increase the production of propionic and
6 butyric acids in the rumen (Journet et al., 1995) and propionate is particularly efficient in
7 inducing secretion of I (Istasse et al., 1987). The larger intake of protein during fattening
8 when compared to LGP could also enhance the secretion of I as a result of a higher portal
9 plasma amino acids. Insulin is implicated in post-prandial protein synthesis (Preedy and
10 Garlick, 1986) but is mainly lipogenic (Gregory et al., 1982). Thus, the low concentration of I
11 during LGP resulted in lower anabolic processes and higher lipolysis, enhancing lipid
12 mobilisation induced by high GH levels (Blum et al., 1985; Hayden, 1993). Furthermore, the
13 increase in plasma I concentration during the fattening period could have reduced GH levels
14 (Pecile et al., 1971; Oshibe et al., 1994).

15 Higher plasma IGF-1 during RGP was related to nutritional status, especially dietary
16 protein intake (Elsasser et al., 1989), and also to growth rate (Breier et al., 1986; Gluckman et
17 al., 1987; Ellenberger et al., 1989). Our results supported thus the somatomedin hypothesis of
18 Daughaday et al. (1972). Indeed, the opposite change in IGF-1 concentration as compared to
19 GH production is explained by a "receptor blocking system" during LGP, preventing GH to
20 attach to high affinity hepatic receptors, thus breaking off the mediation of GH action by IGF-
21 1. The lower IGF-1 concentration during LGP may also be related to alterations in ratio of
22 high and low affinity IGF-1 binding protein (IGFBP) (Breier and Gluckman, 1991). In
23 addition, Massart et al. (1995) reported that plasma from our bulls contained less high affinity

1 IGFBP-3 and more low affinity IGFBP-2 during the LGP. These observations suggest that the
2 onset of GH-dependent IGF-1 action would be possible only when feeding conditions are
3 sufficiently favourable (Breier et al., 1988b). The IGF-I concentration increased also with live
4 weight or age. This has been reported several times in bulls (Breier et al., 1988b; Ronge and
5 Blum, 1989; Schwartz et al., 1992). However, plasma IGF-1 increased more rapidly and
6 reached higher maximum values in G2, G3 and G4 than in CG, suggesting an effect of
7 compensatory growth. Both profiles -growth curve and IGF-1 concentration- were similar
8 during the first part of RGP. Afterwards, the IGF-1 concentration remained high at the end of
9 the RGP in G2, G3, and G4, whereas ADG decreased rapidly as animals reached their mature
10 live weight. This decrease ADG should be associated to higher fat deposition. Although the
11 relationship between ADG and the corresponding IGF-1 concentration is weak (Davis et al.,
12 1989; Ronge and Blum, 1989; McKinnon et al, 1993), these observations suggest that other
13 hormonal alterations were responsible for fat deposition during fattening. The ratio I to GH is
14 among the most important of these alterations (Vernon, 1992).

15 According to Kühn et al., 1986 and Cabello and Wrutniak (1989), the synergistic
16 relationship between activities of thyroid and somatotropic axes also has a decisive role in
17 growth control. In hypothyroidic rats, the circulating GH and IGF-1 concentrations are
18 decreased and neither Growth Hormone Releasing Factor (GRF) nor GH are able to restore
19 GH or IGF-1 concentration (Burstein et al., 1979; Dieguez et al., 1986). Hyperthyroidism also
20 affect the function of the somatotropic axis and growth response because it blunts the GH
21 response to GRF (Dieguez et al, 1986) and increases basal metabolism, although results are
22 less clear in cattle (Elsasser et al., 1992). However, in the present experiment, it could be
23 assumed that the animals were euthyroidic, at least during the fattening period.

1 The lower T3 and T4 concentration during LGP may be ascribed to different
2 phenomena, such as reduced thyroidic stimulating hormone secretion, higher degradation rate,
3 lower conversion of T4 into T3 or a shift in conversion from T3 to inactive reverse T3
4 (Balsam and Ingbar, 1979; Tveit and Almlid, 1980; Wrutniak and Cabello, 1987). These
5 lower levels had probably a role in the uncoupling of GH and IGF-1 concentration during
6 feed restriction (Blum et al., 1980; Blum and Kunz, 1981; Tveit and Larsen, 1983; Hayden et
7 al., 1993).

8 The T3 evolution was quadratic and similar to that of IGF-I in CG and during RGP in
9 G2. By contrast, T4 evolution was stable in CG and increased linearly during RGP of
10 compensating groups. These results suggest that T3 is a better indicator of changes in growth
11 rates and growth composition. However, Ellenberger et al. (1989) observed that T3 levels was
12 unaltered after refeeding. It was possible that their period of blood sampling, about 1 mo, was
13 too short to observe such an increase in T3 levels. The sensibility of T3 to environmental
14 factors is also suggested by the response of animals from G3 which showed the greatest
15 increase in T3 concentration, as they were fattened during winter. Indeed, T3 is known to be
16 involved in thermogenesis (Scott and Christopherson, 1993). In G4, the lack of a detectable
17 increase of T3 levels after realimentation, associated with the other metabolic alterations
18 reported previously, indicates that in this group, the mechanism of compensatory growth was
19 probably different with respect to G2 or G3.

Implications

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3 Compensatory growth was characterized by alterations of several hormone
4 concentrations. Presumably, the onset of compensatory growth in Belgian Blue double
5 muscled bulls may be ascribed to large protein deposition associated with a more functional
6 somatotrophic axis and with increased levels of anabolic hormones such as insulin, IGF-I and
7 thyroid hormones. Afterwards, fat deposition occurs rapidly as a consequence of increase
8 insulin to GH ratio. After a very long period of restricted feeding, the mechanism of
9 compensatory growth seemed different on a metabolic or endocrinologic point of view. Further
10 experiments are needed to study the effects of severe feed restriction before compensatory
11 growth on plasma metabolites and hormones in double muscled cattle.

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Table 1. Mean concentration of α -amino nitrogen, urea nitrogen, non esterified fatty acids and creatinine during fattening (CG) or during low growth periods (LGP) lasting for 4, 8, or 14 mo (G2, G3, G4) before a fattening period (RGP) in Belgian Blue double muscled bulls.

| Items | Group | | | | Levels | SEM |
|--------------------|--------------------|---------------------------------|---------------------------------|---------------------------------|--------|------|
| | CG | G2 | G3 | G4 | | |
| Glucose, mg/L | | | | | | |
| LGP | | 824.3 ^a | 774.2 ^{ab} | 719.7 ^b _x | + | 15.6 |
| RGP | 845.9 ^a | 815.4 ^a | 762.3 ^b | 867.5 ^a _y | + | 17.8 |
| AAN, mg N/L | | | | | | |
| LGP | | 40.3 ^a _x | 45.8 ^b _x | 51.1 ^a _x | + | 1.5 |
| RGP | 49.3 ^c | 52.8 ^{bc} _y | 65.6 ^a _y | 53.7 ^b _y | + | 1.7 |
| Urea, mg N/L | | | | | | |
| LGP | | 72.7 _x | 77.1 _x | 92.4 _x | NS | 5.7 |
| RGP | 161.7 ^a | 170.1 ^a _y | 151.1 ^a _y | 124.0 ^b _y | + | 6.3 |
| NEFA, μ mol/L | | | | | | |
| LGP | | 342.4 _x | 335.8 | 318.7 _x | NS | 23.8 |
| RGP | 261.7 ^a | 294.4 ^a _y | 254.9 ^a | 129.9 ^b _y | * | 20.7 |
| Creatinine, mg N/L | | | | | | |
| LGP | | 23.9 | 26.6 _x | 27.1 _x | NS | 0.8 |
| RGP | 21.6 ^a | 22.9 ^b | 24.3 ^{ab} _y | 23.6 ^b _y | + | 0.7 |

^{a,b,c} Effect of group. Means with different superscript within a row differed at $P < .1$ (+) or $.05$

(*). NS: not significant.

_{x,y,z} Effect of period. Means within a column for each metabolite and with different lowerscript differed at $P < .05$

Table 2: Characteristics of GH profiles calculated by the Munro algorithm and mean insulin concentration, at the beginning, in the middle and at the end of the fattening period (CG), in the middle of the low growth period lasting for 4, 8 or 14 mo (G2, G3, G4) and at the beginning and the end of the subsequent fattening period in Belgian Blue double muscled bulls.

| Items | Group | | | | Levels | SEM |
|-----------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|--------|-------|
| | CG | G2 | G3 | G4 | | |
| Period I | | | | | | |
| GH | | | | | | |
| -Pulse number | 7.3 _x | 9.0 _x | 8.5 | 7.3 _x | NS | 1.0 |
| -Pulse interval, min | 186.7 _x | 163.4 _{xy} | 185.7 | 191.2 _x | NS | 23.2 |
| -Pulse amplit., ng/mL | 23.9 _{xy} | 32.6 _x | 19.6 _{xy} | 18.8 | NS | 5.1 |
| -Pulse area, ng.mL | 1191.3 _{xy} | 1581.8 | 917.1 | 918.9 | NS | 293.6 |
| -Nadir, ng/mL | 11.5 _{xy} | 17.1 _x | 13.6 _x | 12.9 _x | NS | 1.7 |
| -Average, ng/mL | 15.8 ^a | 28.3 _x ^b | 21.7 _x ^{ab} | 18.1 _x ^a | + | 2.7 |
| Insulin, mU/L | 10.7 ^a | 5.4 _x ^c | 5.2 _x ^{bc} | 7.1 _x ^b | *** | 0.6 |
| Périod II | | | | | | |
| GH | | | | | | |
| -Pulse number | 10.8 _y | 8.5 _x | 7.8 | 10.0 _x | NS | 1.4 |
| -Pulse interval, min | 126.9 _y | 180.0 _x | 192.0 | 148.3 _x | NS | 26.3 |
| -Pulse amplit., ng/mL | 19.3 _x | 16.5 _{xy} | 15.3 _x | 16.5 | NS | 2.4 |
| -Pulse area, ng.mL | 837.3 _x | 887.1 | 657.1 | 717.7 | NS | 139.1 |
| -Nadir, ng/mL | 11.1 _x ^a | 13.3 _y ^a | 10.6 _y ^{ab} | 7.4 _y ^{bc} | + | 1.5 |
| -Average, ng/mL | 17.9 _x ^a | 19.1 _y ^{ab} | 13.7 _y ^{bc} | 12.4 _y ^c | + | 1.7 |
| Insulin, mU/L | 14.5 | 11.6 _y | 16.1 _y | 11.9 _{xy} | NS | 2.7 |
| Périod III | | | | | | |
| GH | | | | | | |
| -Pulse number | 10.3 _y ^b | 4.7 _y ^c | 8.5 _{bc} | 13.0 _y ^a | * | 0.9 |
| -Pulse interval, min | 133.0 _{xy} ^a | 234.4 _y ^a | 189.5 ^a | 107.6 _y ^b | + | 32.7 |
| -Pulse amplit., ng/mL | 12.2 _y ^a | 14.0 _y ^{ab} | 21.1 _y ^b | 20.8 ^{ab} | + | 3.9 |
| -Pulse area, ng.mL | 542.8 _y ^a | 823.7 ^{ab} | 944.5 ^b | 849.1 ^{ab} | + | 190.4 |
| -Nadir, ng/mL | 6.5 _y ^a | 12.7 _y ^b | 10.1 _{xy} ^{ab} | 8.0 _{xy} ^a | + | 1.4 |
| -Average, ng/mL | 10.4 _y ^{ac} | 16.0 _z ^b | 15.9 _{xy} ^b | 15.9 _{xy} ^{bc} | + | 2.5 |
| Insulin, mU/L | 10.3 ^a | 19.7 _{xy} ^{ab} | 10.0 _y ^a | 19.5 _y ^b | * | 3.2 |

^{a,b,c} Effect of group. Means with different superscript within a row differed at $P < .1$ (+), .05 (*), or .001 (***). NS: not significant.

_{x,y,z} Effect of period. Means referring to similar items and with different lowerscript within a column differed at $P < .1$

Table 3. Mean concentration of T3, T4, and IGF-1 during fattening (CG) or during low growth periods (LGP) lasting for 4, 8, or 14 mo (G2, G3, G4) before a fattening period (RGP) in Belgian Blue double muscled bulls.

| Items | Group | | | | SEM |
|--------------|-------------------|--------------------------------|---------------------------------|---------------------------------|------|
| | CG | G2 | G3 | G4 | |
| T3, nmol/mL | | | | | |
| LGP | | 0.67 _x | 0.80 _x | 0.74 _x | 0.13 |
| RGP | 1.15 | 0.91 _y | 1.02 _y | 1.05 _y | 0.16 |
| T4, nmol/mL | | | | | |
| LGP | | 36.6 _x | 48.1 _x | 42.2 _x | 6.2 |
| RGP | 61.8 ^a | 47.9 _y ^b | 58.5 _y ^{ab} | 52.1 _y ^{ab} | 7.6 |
| IGF-1, ng/mL | | | | | |
| LGP | | 135.3 _x | 158.4 _x | 119.0 _x | 17.1 |
| RGP | 262.3 | 267.4 _y | 306.7 _y | 260.1 _y | 38.5 |

^{a,b} Effect of group. Means with different superscript within a row differed at $P < .1$

_{x,y} Effect of period. Means within a column for each metabolite and with different lowerscript differed significantly at $P < .05$

Table 4. Equations describing the modeled profile of insulin concentration on 24h period and of T3, T4 and IGF-1 concentration on biweekly blood samples.

| Hormone | |
|------------------|---|
| Insulin | SEM: 4.7 |
| LGP (a) | $y = 6.02 + .1437\cos(wt) - 2.014\sin(wt) - .8692\cos(2wt) - .7966\sin(2wt) + .7219\cos(3wt) + .8087\sin(3wt)$ |
| RGP (b) | $y = 13.38 + .1437\cos(wt) - 2.014\sin(wt) - .8692\cos(2wt) - .7966\sin(2wt) + .7219\cos(3wt) + .8087\sin(3wt)$ |
| T4 | SEM: 11.2 |
| CG (c) | $y = 24.92 + .6868.X$ |
| LGP (d) | $y = 16.45 + .6865.X$ |
| RGP (e) | $y = 16.45 + .6865.X + .1470\text{trg}$ |
| T3 | SEM: 0.32 |
| CG (f) | $y = .507 + .00571.t\text{f} + .0000178.t\text{f}^2 + .408.X0$ |
| LGP (G2, G3) (g) | $y = .586 - .00189.t\text{lg} + .0000048.t\text{lg}^2 + .408.X0$ |
| RGP (G2) (h) | $y = .586 - .00189.t\text{lg} + .0000048.t\text{lg}^2 + .408.X0 + .0111.t\text{rg} - .0000622.t\text{rg}^2$ |
| RGP (G3) (i) | $y = .586 - .00189.t\text{lg} + .0000048.t\text{lg}^2 + .408.X0 + .00323.t\text{rg} - .0000757.t\text{rg}^2$ |
| G4 (j) | $y = .586 - .00189.t\text{lg} + .0000048.t\text{lg}^2 + .408.X0$ |
| IGF1 | SEM: 53.5 |
| CG (k) | $y = 18.14 + 1.584\text{trg} - .005225\text{trg}^2 + .6704X0$ |
| LGP (l) | $y = 50.03 + 0.2621\text{tlg} + .0002155\text{tlg}^2 + .6704X0$ |
| RGP (m) | $y = 50.03 + .2621\text{tlg} + .0002155\text{tlg}^2 + .6704X0 + 2.433\text{trg} - .01054\text{trg}^2$ |

$w = 2\pi/24$; t = clock time in hours; tlg and trg denote the time elapse since the beginning of the Low Growth or the

Rapid Growth Period respectively; $X0$ denotes the value at $\text{tlg} = 0$.

Figure 1: Modeled profile of daily concentration of glucose, alpha amino nitrogen, urea, non esterified fatty acids and creatinine during fattening (CG) or during low growth periods lasting for 4, 8, or 14 mo before a fattening period (G2, G3, G4) in Belgian Blue bulls double muscled. Arrows indicate the beginning of the fattening period. The bars indicate the standard error of the mean.

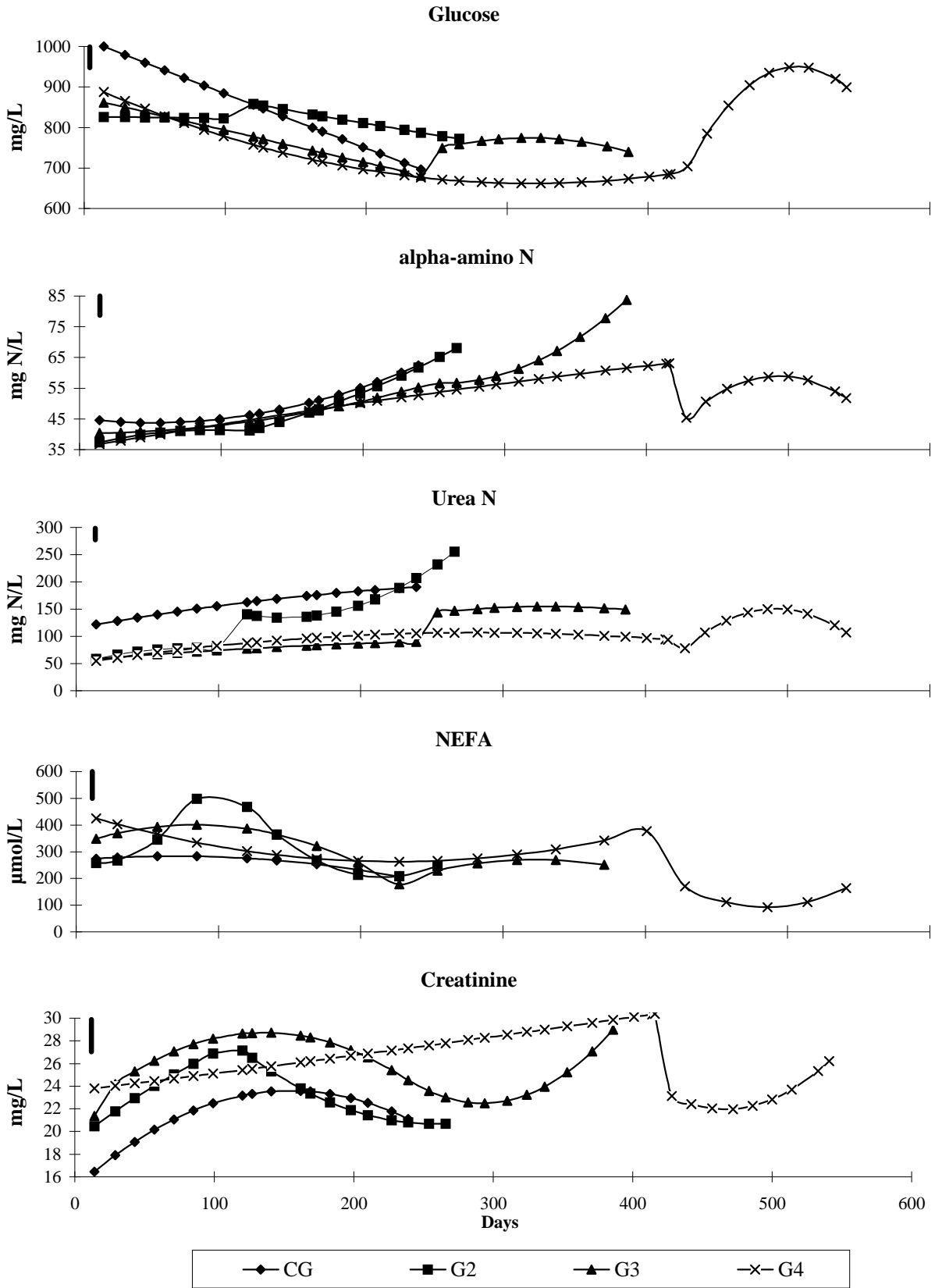


Figure 2: Individual plasma profiles of GH from blood sampled during 24h periods, at the beginning, in the middle and at the end of the fattening period (CG), in the middle of the low growth period lasting for 4, 8 or 14 mo and at the beginning and the end of the subsequent fattening period (G2, G3, G4) in Belgian Blue bulls double muscled.

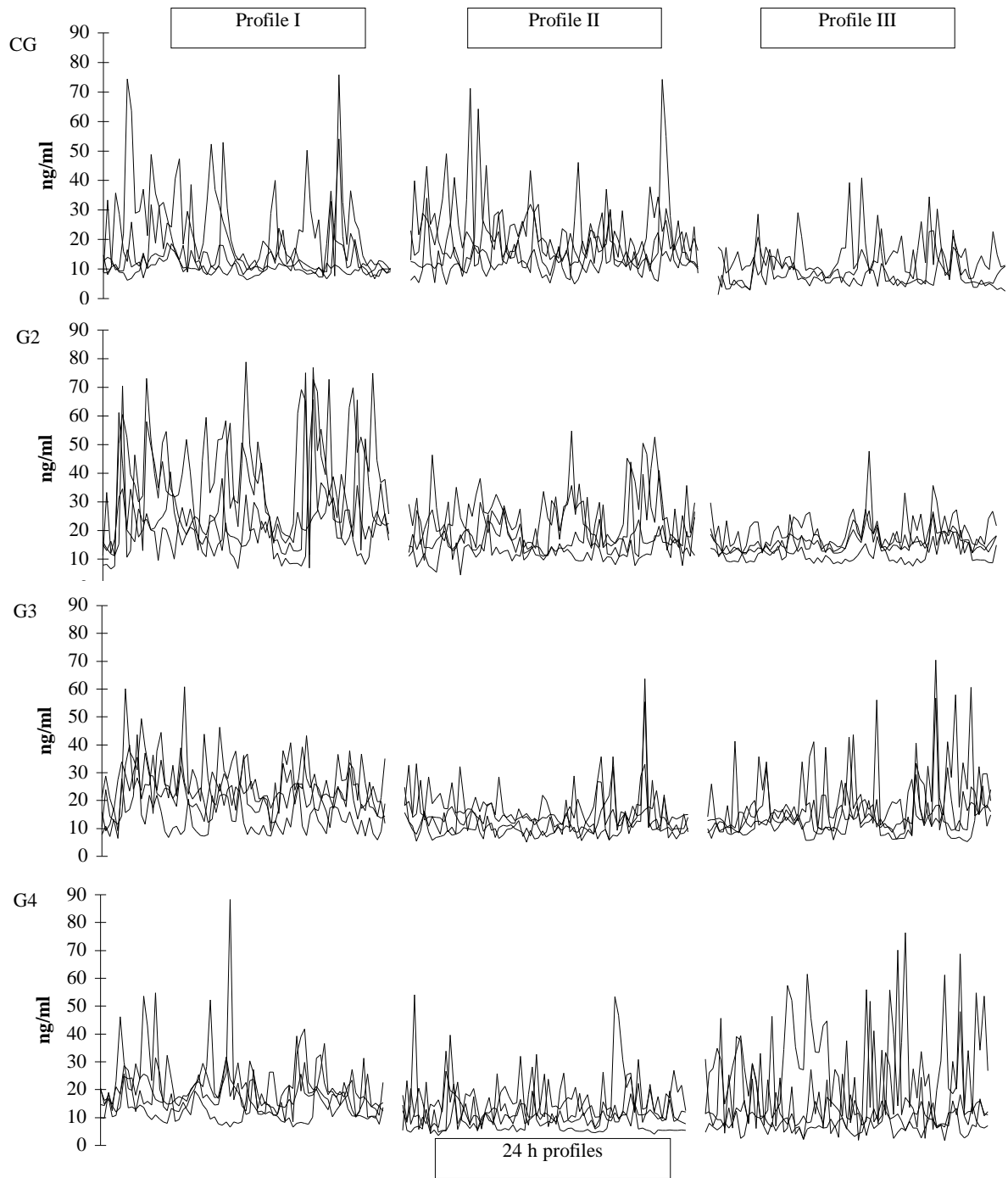


Figure 3: Modeled profile of insulin secretion during a 24h period in fattening bulls or in bulls maintained at low growth rate for periods lasting 4, 8 or 14 mo. Arrows indicate feeding time. The bar indicates the standard error of the mean.

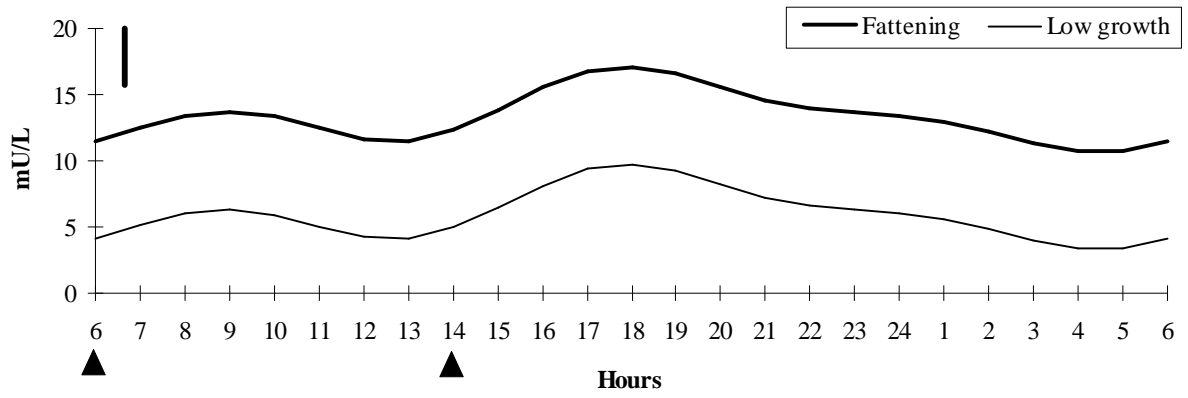
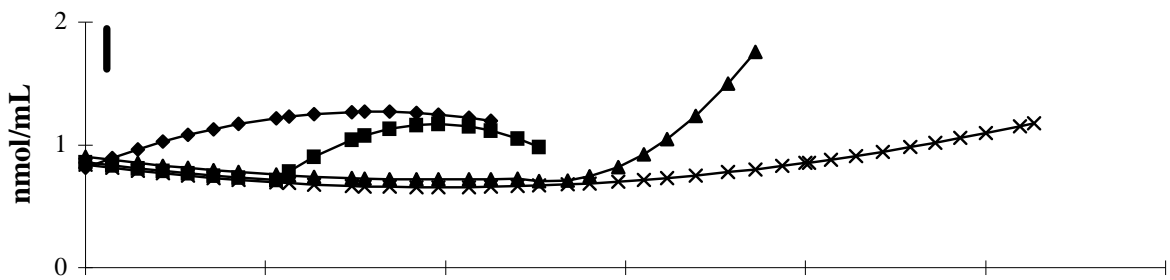
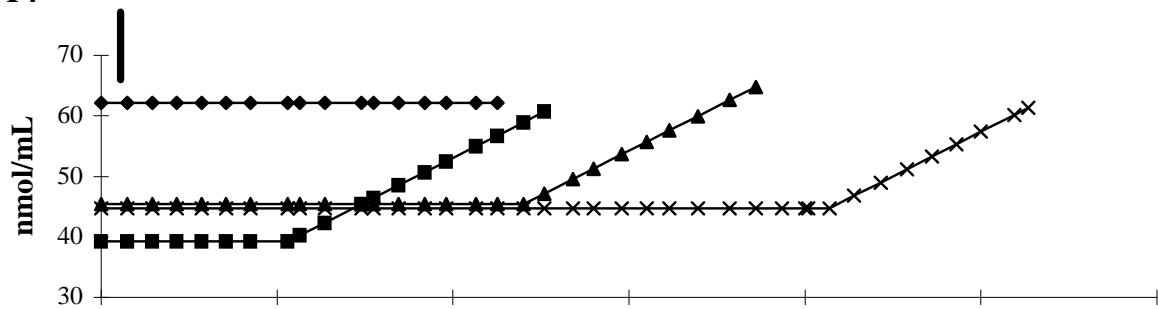


Figure 4: Modeled profile of daily concentration of T3, T4, and IGF-1 during fattening (CG) or during low growth periods lasting for 4, 8, or 14 mo before a fattening period (G2, G3, G4) in Belgian Blue bulls double muscled. Arrows indicate the beginning of the fattening period. The bars indicate the standard error of the mean.

T3



T4



IGF-1

