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A model for the efficient use of new information within Physiology, Nutrition and Breeding of dairy cows

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A MODEL FOR THE EFFICIENT USE OF NEW INFORMATION WITHIN PHYSIOLOGY, NUTRITION AND BREEDING OF DAIRY COWS.

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PREFACE

The present report represents the conclusion of some years activity in a working group established by a research committee at the National Institute of Animal Science. The group consisted of members from departments of physiology and departments of cattle research at The National Institute of Animal Science and at The Royal Veterinary- & Agricultural University. The task of the group work was to collect and make use of the rapid accumulation of data and observations within the physiology, nutrition and breeding of dairy animals. In May 1986 the group conducted a seminar about the work. The seminar was held at The National Institute of Animal Science, Foulum and was well attended. The theme for the seminar was establishment and evaluation of a model for efficient utilization and continued evaluation of research results in the field of dairy production. The discussions were very enthusiastic and the participants urged the group to publish the results of the group work. The group has made effort to update some of the data and it is believed that the results as well as the principles applied are valuable for research workers in any of the related disciplines several years ahead.

Foulum, November 1989

A. Neimann-Sørensen and Arnold Just

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1 Introduction

What do we know and what do we need to know about physiology, nutrition and breeding of dairy animals?

By Poul Martin Riis

1.1 An interdisciplinary approach to problem solution

One of the problems in the field of physiology, nutrition and breeding of dairy animals as well as in other areas of science is an efficient utilization of the rapidly accumulating information. Progress in the field depends upon this utilization. Moreover, identification and specification of unsolved questions which would be fruitful for future research are continous challenges.

Some years ago workers in the field of physiology, nutrition and breeding at The National Institute of Animal Science (NIAS), Foulum and The Royal Veterinary and Agricultural University (RVAU), Copenhagen decided to attempt an interdisciplinary approach to meet these challenges and formed a working group of the following members from the involved departments:

Agergaard, Niels	Dep. Physiol. Biochem.	NIAS
Danfær, Allan	Dep. Physiol. Biochem.	NIAS
Hvelplund, Torben	Dep. Cattle Res.	NIAS
Madsen, Annemarie	Dep. Animal Physiol.	RVAU
Madsen, Jørgen	Inst. Animal Science	RVAU
Nielsen, Mette O.	Dep. Animal Physiol.	RVAU
Petersen, Poul Henning	Inst. Animal Science	RVAU
Riis, Poul Martin	Dep. Animal Physiol.	RVAU
Sejrsen, Kristen	Dep. Cattle Res.	NIAS
Thilsted, Shakuntala H.	Dep. Animal Physiol.	RVAU

The general objective for the group work was mutual information about development in the interrelated disciplines. Evidently, this information had to include mutual explanation and education regarding the specific background and the specific terminology which develops within each specific discipline and which may limit interdisciplinary understanding and communication.

1.2 The aim of the group work

One of the objectives in physiological, nutritional and breeding research is to improve our possibilities to predict production and to estimate the requirement

for a certain production. Another important objective is to identify factors limiting the productional efficiency with regard to world food supply and to herd economy.

After some time of discussions on items of high actuality, the group found that the most important goal for its future work was to:

Establish an objective method for following four purposes:

1. For evaluation of present available knowledge and theories in the field.
2. For identification of factors limiting the productional efficiency of dairy cows.
3. For improvement of our capability to utilize the continuous stream of new information in the field.
4. For specification of areas and questions which need elucidation and would be fruitful for future research.

Table 1.1 Feed intake, body weight, daily weight gain and milk yield by cows on complete ration (group F) week 15–21 of lactation (From Krohn & Konggaard, 1987).

	Cow no.				
	680	343	394	308	Ave.
Concenrates, kg	7.5	8.1	7.5	6.9	7.5
Beets, kg	7.7	8.5	7.9	7.2	7.8
Beet top silage, kg	2.0	2.1	2.0	1.8	2.0
Straw, kg	2.4	2.6	2.4	2.2	2.4
Dry matter, kg	19.6	21.3	19.8	18.1	19.7
Scand. feed units	19.6	21.5	20.0	18.3	19.8
Crude protein, g	3904	4222	3920	3594	3910
Crude fat, g	965	1041	966	887	965
Starch, g	1323	1432	1327	1219	1325
Sugar, g	5073	5582	5187	4732	5144
Ash, g	1441	1579	1453	1324	1450
Crude fiber, g	2344	2536	2356	2152	2347
Milk, kg	28.3	32.6	27.8	23.7	28.1
Fat, %	3.79	4.39	3.64	4.49	4.07
Butter fat, g	1070	1428	1009	1064	1143
Protein, %	3.23	3.01	3.09	3.43	3.17
Milk protein, g	915	983	857	814	892
Body weight, kg	515	599	634	572	580
Daily gain, g	+171	+629	+400	+114	+329

1.3 The methods and the working hypothesis

In order to pursue this aim it was decided to use available knowledge in the different disciplines to predict the productional performance of cows in a specific feeding experiment, where the production was recorded and to try to specify the factors that determined the production level of these cows in detail. Two groups of cows from a feeding experiment described by Krohn & Konggaard (1987) were chosen for this work.

The cows were Black and White Danish Milk Breed. Both groups had free access to feed. The cows in group F were offered a (complete) ration containing concentrates, sugar beets and silage in a premixed ratio. The cows in the other group, group S, were allowed to select freely between concentrates, sugar beets, silage and straw, that is to make their own ration. Feed intake, chemical composition of the feed, milk production, body weights and weight gains are shown in tables 1.1 and 1.2 for group F and group S, respectively. It should be emphasized

Table 1.2 Feed intake, body weight, daily weight gain and milk yield by 4 cows on complete ration (group S) week 15-21. (From Krohn & Konggaard, 1987).

	Cow no.				
	385	310	383	497	Ave.
Concentrates, kg	4.7	4.4	6.2	6.0	5.3
Beets, kg	14.3	13.2	6.7	9.3	10.9
Beet top silage, kg	1.2	1.5	3.4	2.1	2.0
Straw, kg	0.2	0.8	1.9	1.4	1.1
Dry matter, kg	20.3	19.9	18.2	18.8	19.3
Scand. feed units	20.4	19.4	18.0	18.8	19.2
Crude protein, g	3117	2996	3551	3430	3274
Crude fat, g	582	570	866	785	700
Starch, g	1005	947	1117	1121	1048
Sugar, g	8565	7930	4436	5858	6697
Ash, g	1418	1407	1514	1409	1437
Crude fibre, g	1417	1664	2221	1907	1802
Milk, kg	23.7	19.1	26.9	24.9	23.7
Fat, %	5.00	3.84	3.38	2.87	3.74
Butter fat, g	1181	735	909	714	885
Protein, %	3.60	3.49	3.30	3.40	3.43
Milk protein, g	854	668	890	845	814
Body weight, kg	643	744	586	534	622
Daily gain, g	+1000	+457	+543	+514	+629

that milk production and gains were not known when the predictions were made as the experiments were not finished at that time.

It was decided to try to predict production and body balance in these cows by estimation of nutrient and metabolite flow through the processes involved in digestion, absorption, metabolic turnover and product formation. A diagram of the interrelationship between these processes are shown in figure 1.1.

The model in figure 1.1 is discussed in a review by Riis and Madsen (1983).

In the following chapters the use of the model in figure 1 is divided in following five steps:

A. The rates of digestion and nutrient absorption.
B. The concentration of nutrients and hormones in the circulating pools.
C. Uptake, metabolism and release of nutrients by the liver.
D. Uptake, metabolism and release of nutrients by extrahepatic, non-mammary body tissues.
E. Uptake and metabolism of nutrients in mammary tissues and milk formation.

For each step details in the model are discussed and available data in the literature are used to estimate the rates of the involved processes and the concentrations in the pools of the two groups of cows. Thus, we start with estimation of rates of nutrient absorption and end up with rates of production processes and balances in the turnover of body constituents. For each step unclear areas are discussed and important unsolved problems formulated. Attempts are made to identify the critical limiting factors.

The hypothesis at the start of the present work was that such an analysis was the objective method to obtain answers to the questions: What do we know? and what do we need to know within physiology and nutrition of the dairy cow?

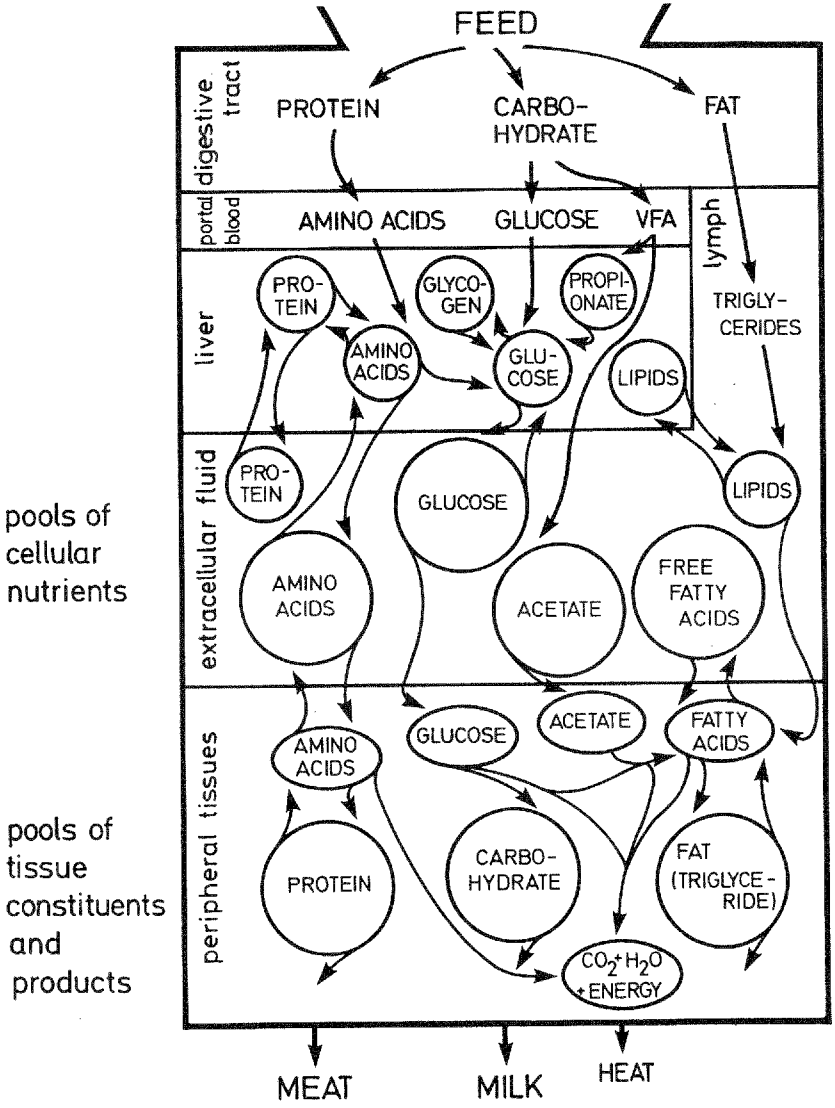

Figure 1.1 A diagram of the interrelationship between the pathways and pools involved in digestion, absorption and utilization of nutrients and in product formation. (Adapted from Riis and Madsen, 1983, by permission from Elsevier Publish Co.)

2. The amount of absorbed nutrients from the gastro-intestinal tract of dairy cows

By Torben Hvelplund and Jørgen Madsen

The position of the reticulo-rumen and the considerable size of the microbial fermentation of the feed in the rumen make the absorption of nutrients from the rumen and the lower gut highly influenced by the microbial metabolism in the rumen. The majority of the absorbed nutrients will thus be endproducts from the microbial metabolism and unfermented nutrients from the feed will only contribute with a small proportion of the total absorbed nutrients from the gastro-intestinal tract. This is an important point to consider in the evaluation of the feeding value of different feedstuffs and thus the ruminants' supply with nutrients.

To estimate the amount of nutrients absorbed from the gastro-intestinal tract of a cow on a specified diet it is necessary to know the amount of nutrients in the feed given, and to have models which can predict the rumen metabolism on that particular diet.

In the following the absorption of nutrients is calculated for two groups of cows. One group fed a complete diet (diet F) and one group fed a diet where the cows had free access to the separate feedstuffs and thus composed the diet by themselves (diet S). The intake of total feed and the different nutrients in the diet for the two groups of cows are shown in table 1.1 and table 1.2. In the succeeding calculations the average intake for the two groups of cows is applied.

2.1 Absorption of nutrients from the gastro-intestinal tract

The absorption of nutrients from separate sections of the gastro-intestinal tract and the total absorption are shown in table 2.1 for the two different diets. Figure 2.1 and 2.2 show in detail the passage of nutrients along the gastro-intestinal tract and the amount of absorbed nutrients supplied from either microbial fermentation or supplied from unfermented feed. The models used for the calculations are the same as used by Hvelplund (1983).

2.2 Calculation of VFA-absorption

The calculation of the VFA-production in the rumen and the large intestine is based on a model, where the production of the separate acids is calculated from the amount of carbohydrates fermented by stoichiometric equations (Baldwin et al. 1970), where the production of VFAs is directly related to the

Table 2.1 The absorption of nutrients from the gastro intestinal tract (kg/day).

	Reticulo-rumen	Small intestine	Large intestine	Total
Ration S (free access)				
Acetic acid	3.58		0.40	3.98
Propionic acid	1.64		0.32	1.96
Butyric acid	1.15		0.05	1.20
Total VFA	6.37		0.77	7.14
Glucose		0.27		0.27
Amino acids		1.87		1.87
Fatty acids		0.81	0.01	0.82
Ammonia-N	0.01	0.09	0.03	0.13
Ration F (complete diet)				
Acetic acid	3.39		0.42	3.81
Propionic acid	1.65		0.36	2.01
Butyric acid	0.99		0.06	1.05
Total VFA	6.03		0.84	6.87
Glucose		0.23		0.23
Amino acids		1.95		1.95
Fatty acids		0.94	0.02	0.96
Ammonia-N	0.09	0.09	0.03	0.21

amount of carbohydrate fermented. Models using the same principles have also been used by Ørskov et al. (1968) and Black et al. (1981). As both the total VFA production and the proportion between the individual acids are determined by the fermentation of the separate carbohydrates in the feed, a correct estimate of the amount fermented of the different substrates (starch, soluble sugars and cell wall carbohydrates) is of great importance. The major errors in predicting the VFA production by these models lie presumably in the prediction of the individual VFAs rather than the total production, as the models ignore the complex interactions between the substrate fermented and the major types of micro-organisms. They assume that a single pathway of fermentation exists for each substrate considered, independently of e.g. structure in the diet or feeding level and the influence of these factors on the pH in the rumen. An example, where the same substrate gave rise to marked differences in the proportion between the individual VFAs, is clearly demonstrated by Ørskov & Reid (1979) in an experiment where 80% of the feed was barley either rolled or NaOH-treated. With the same starch content in the diet, feeding with rolled barley gave rise to a C_2:C_3 molar proportion of 50:38 whereas feeding with NaOH-treated barley resulted in a C_2:C_3 molar proportion of 61:19.

Isotope dilution techniques for measuring the VFA production in the rumen has also been used (Candaravitoon & Riis 1971; Mercer et al. 1973, 1977; Hvelplund et al. 1978). This method requires that the concentration of the rumen VFAs is constant throughout the experiment, which is difficult to achieve under practical conditions. Another technique to those mentioned is to measure the VFA flow through the portal vein and thus estimate the absorption of the individual VFAs by the arteriovenous difference technique. Application of this technique may improve the precision for estimation of VFA production, and thereby improve the models used for calculation of total and individual VFAs produced. The amount of VFA's absorbed on the two diets is shown in table 2.1.

2.3 Calculation of carbohydrate absorption

The amount of potential digestible carbohydrates leaving the rumen is limited as only small amounts normally will escape rumen fermentation. However, a small amount will always pass to the small intestine as microbial carbohydrates and in situations where the feed contains slowly degradable starch, e.g. maize starch, appreciable amounts of starch escape rumen fermentation and pass to the small intestine. The amount of glucose absorbed on the two different diets is shown in table 2.1 and is limited to the amount absorbed from microbial carbohydrates as digestion of both the starch and soluble carbohydrates in these diets is virtually complete within the rumen.

2.4 Calculation of amino acid absorption

The amount of amino acids absorbed from the small intestine is partly of microbial origin and partly from feed protein, which has escaped degradation in the rumen. The degradability of feed protein was estimated to 67% for diet S and to 64% for diet F, respectively. The degradability in the two diets was calculated from estimated nylon bag degradabilities on the separate feedstuffs used (Madsen & Hvelplund 1985). The microbial protein production was calculated from the amount of ATP produced during fermentation in the rumen using a production of 20.4 g microbial dry matter for each mol ATP produced during fermentation (Kennedy & Milligan 1972; Harrison & McAllan 1980). The ATP production was calculated according to Baldwin et al. (1970). The amount of absorbed amino acids shown in table 2.1 deviates only slightly from the amount supplied if the amino acid absorption has been calculated on the principles outlined in the AAT-PBV protein evaluation system (Madsen 1985), where the amount of absorbed amino acids (AAT) on diet S is calculated to 1785 g and on diet F to 1907 g respectively. This is only 4 and 2% lower than the values shown in table 2.1.

2.5 Calculation of fatty acid absorption

The fatty acids absorbed from the small intestine are a mixture of fatty acids from the feed and acids synthezised by the microbes in the rumen. The calculated amount of microbial fatty acids assumes that 10% of the microbial fatty acids are directly incorporated from fatty acids in the feed and that 90% are de novo synthezised in the rumen. The calculation also assumes a fat content of 10.8% in the microbial dry matter. As the main proportion of the fatty acids in the feed is unaffected by rumen metabolism and fatty acids are de novo synthezised in the rumen, this means that the flow of total fatty acids to the small intestine is in excess of the quantities of fatty acids consumed. The amount of fatty acids absorbed on the two diets is shown in table 2.1.

2.6 Discussion

A comparison of the nutrient intake with those nutrients absorbed from the gastro-intestinal tract shows that the fermentation in the rumen has a marked influence.

The most obvious change is the amount of carbohydrates absorbed from the gastro-intestinal tract which is negligible compared to the quantity consumed, but the amount of absorbed acetic-, propionic- and butyric acid produced during fermentation in the rumen is considerable. The calculations also show, that the microbial fermentation in the rumen has a marked influence on both the amount of absorbed amino acids and fatty acids on the two different diets considered.

The amount of absorbed nutrients as shown for the two diets in table 2.1 demonstrates the importance of evaluating the feedstuffs in a new way, where the value is expressed in the amount of actually absorbed nutrients. As shown in figures 2.1 and 2.2 there is a marked difference between the amount and type of the apparent digested nutrients and the quantity of actually absorbed nutrients. An important task is therefore to gain new knowledge in this field in order to improve the precision of predicting animal response to nutrient and energy intake.

Introduction of the proposed AAT-PBV protein evaluation system (Madsen 1985) where the protein value of the feed is expressed as the amount of amino acids, which can be absorbed from the small intestine is a step in this direction, and the system has reached a development where it can be introduced into practice within a few years.

A precise quantitative estimate of the amount of fatty acids absorbed from the intestine requires that the microbial fatty acid synthesis can be estimated in different diets. An important question to be solved is how much microbial fat is de novo synthezised and how much is directly incorporated from fatty acids in the feed and the factors that influence this proportion.

The major amount of nutrients absorbed from the gastro intestinal tract is

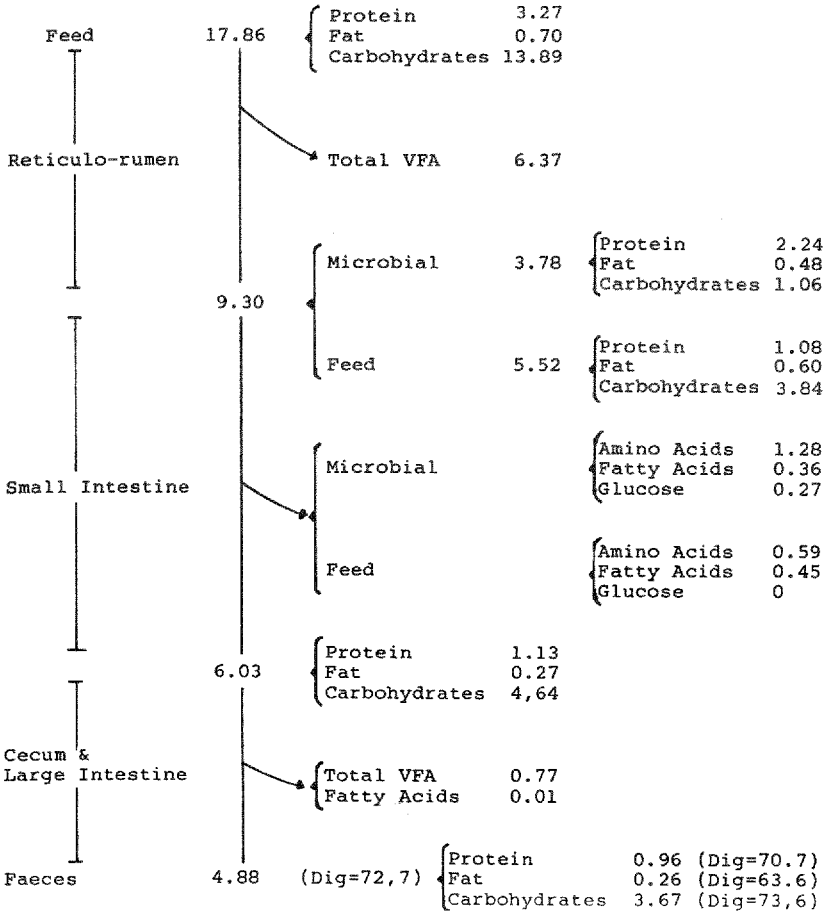

Figure 2.1 The amount of organic matter passing through the gastro-intestinal tract and the absorption of nutrients from different sections of the gut on ration S (kg/day). Shown is also the apparent digestibility (Dig) of organic matter, protein, fat and carbohydrates (crude fibre + NFE).

VFAs and although the total amount of VFA can be estimated with reasonable accuracy from the total amount of fermented carbohydrates, there is a considerable uncertainty on the estimation of the contribution of the individual acids to the total production. The influence of different carbohydrates and also the structure of the diet on the production of the different VFAs in the rumen and by this on the amount absorbed, is an area, where much knowledge still needs to be gained, and research in this field will be a valuable contribution to a better description of the amount of nutrients absorbed on a particular diet.

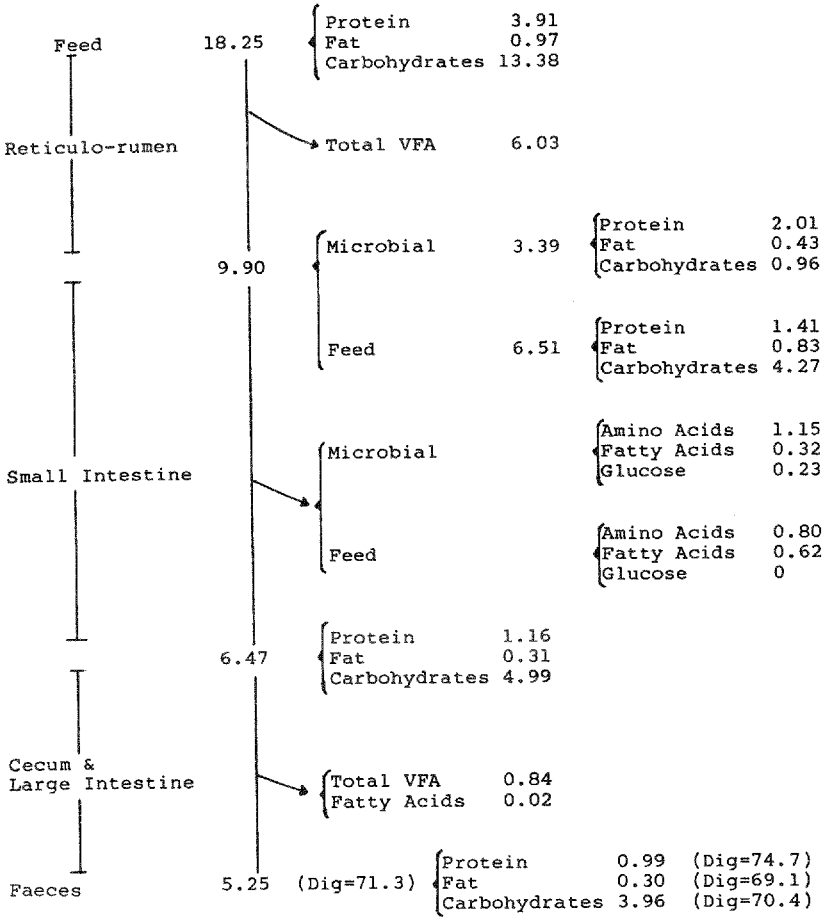

Figure 2.2 The amount of organic matter passing through the gastro-intestinal tract and the absorption of nutrients from different sections of the gut on ration F (kg/day). Shown is also the apparent digestibility (Dig) of organic matter, protein, fat and carbohydrates (crude fibre + NFE).

Calculations based on the amount of absorbed nutrients from the gastro-intestinal tract, may in the future be a more precise system for evaluation of energy content in the feed than the system used today. Such a system which can predict the actual amounts of nutrients absorbed from the diet, will also be a more direct and precise tool in the description of animal response to nutrient intake than the present system with big differences between digested nutrients and nutrients available for production.

3 The concentrations of nutrients and hormones in the extracellular fluid

By Shakuntala Haraksingh Thilsted and Kristen Sejrsen

The nutrients glucose, amino acids, acetate, ketone bodies, free fatty acids, total lipids and triglycerides reach the various tissues through circulation in the extracellular fluid (figure 1.1).

The concentrations of these nutrients in the extracellular fluid affect the secretion of several hormones, which in turn regulate the flow of nutrients to different productive tissues. The extracellular nutrient concentrations are therefore important parameters in predicting milk production in cows.

The concentrations of nutrients and hormones in the extracellular fluid are normally determined by analysis of blood plasma. The term plasma concentration is therefore used instead of the longer concentration in extracellular fluid.

The expected plasma concentrations of the above nutrients found in the cows in group S and F are shown in table 3.1. The values presented are means over a 24 hour period. These values have been predicted taking into consideration the amount and composition of the rations in both groups of cows, the amounts of absorbed nutrients (table 1.1) and values found in the literature.

Table 3.1 Plasma concentrations of nutrients and hormones.

Nutrient/ hormone	Plasma concentrations (mean for a 24 hour period)		
	Group S	Group F	Units
Glucose	3.5 – 4.5	3.0 – 4.0	mM
Amino acids	1.5 – 3.0	1.5 – 3.0	mM
Acetate	1.2 – 1.8	1.2 – 1.8	mM
Ketone bodies	0.8 – 1.0	0.8 – 1.0	mM
Free fatty acids	0.3 – 0.5	0.3 – 0.5	mM
Total lipids	3 – 4	3 – 4	mg/ml
Triglyceride	0.08 – 0.14	0.08 – 0.14	mg/ml
Insulin	1.0 – 1.5	0.8 – 1.3	ng/ml
Total glucagon	0.3 – 0.5	0.3 – 0.5	ng/ml
Thyroxine (T_4)	50 – 60	40 – 50	ng/ml
Somatomedin	1.0 – 1.2	0.8 – 1.0	U/ml
Growth hormone	2 – 10	2 – 10	ng/ml

3.1 Glucose

Plasma glucose concentration was predicted as 3.5–4.5 mM in group S and 3.0–4.0 mM in group F. Values in this range have been found in dairy cows in mid-lactation (Hart et al., 1975).

The lower range of plasma glucose concentration predicted in group F as compared to group S was based on the differences in ration composition and feeding regime. In group F, the proportion of roughage (beet top silage and straw) in the ration was 22% of dry matter as compared to 16% of dry matter in group S. It is well established that plasma glucose concentration is greater in cows fed low roughage rations than in cows fed high roughage rations (Jenny & Polan, 1975; Evans et al., 1975). Even though propionate production was nearly the same in both groups of cows, 26.4 mol in group S and 27.1 mol in group F (table 2.1), it was assumed that the rate of absorption was more uniform in the cows of group F, which were fed a complete ration, than in the cows of group S, which were offered each ration component separately and at the same time, therefore having free choise. A more uniform absorption of propionate could lead to a more uniform and lower plasma glucose concentration.

The ranges of plasma concentrations of the other nutrients shown in table 3.1 were predicted as being the same for both group S and F. Based on the information presented in the foregoing chapters and the values from the literature, there seemed to be no basis for choosing different ranges for group S and F.

3.2 Amino acids

Plasma amino acids concentration was predicted as 1.5–3.0 mM in both group S and F. These values fall within the range found by Bickerstaffe et al. (1974) in Friesian cows in mid-lactation.

3.3 Acetate and ketone bodies, free fatty acids and total lipids

The plasma concentration of acetate was predicted as 1.2–1.8 mM and ketone bodies as 0.8–1.0 mM. These values are comparable to those found by Annison et al. (1974) in Friesian lactating cows.

Plasma free fatty acids concentration was predicted as 0.3–0.5 mM. Thilsted (1980) found that plasma free fatty acids concentration was 0.55 mM in a lactating cow in the first 6 weeks postpartum, fed a ration similar to that in group S. The range chosen was lower than 0.55 mM based on the findings of Hart et al., (1978) that plasma free fatty acids concentration decreases with progressing lactation. The range presented is comparable to values found by Annison et al. (1974). Even though the same range was chosen for both group S and F, it was felt that there may be a tendency for the cows in group F, with lower plasma glucose concentration, to have a higher plasma free fatty acids concentration (Kunz & Blum, 1981; Rulquin, 1983).

Plasma total lipids concentration was predicted as 3–4 mg/ml in both groups of cows. This range falls within the values of 3–6 mg/ml plasma found in lactating cows in early lactation (Dale et al., 1979; Herdt et al., 1983). Plasma triglyceride concentration was predicted as 0.08–0.14 mg/ml. Annison et al. (1974) found a mean plasma triglyceride concentration of 0.09 mg/ml in two Friesian cows in mid-lactation.

3.4 Insulin, glucagon, thyroxine, somatomedin and growth hormone

The plasma concentrations of the hormones insulin, total glucagon, thyroxine, somatomedin and growth hormone were predicted. The ranges chosen for mean concentrations over a 24 hour period are shown in table 3.1.

Plasma insulin concentration was predicted as 1.0–1.5 ng/ml in group S and 0.8–1.3 ng/ml in group F. The basis for predicting plasma insulin concentration was the values chosen for plasma glucose concentration in group S and F. A higher range for plasma insulin concentration was chosen for group S as compared to group F relating to the higher glucose concentration in group S than in group F. It has been found that there is a tendency in lactating dairy cows with low plasma glucose concentrations to also have low plasma insulin concentrations (Hart et al., 1978; Thilsted, 1985).

The plasma concentration of total glucagon (pancreatic and gut glucagon) was predicted as 0.3–0.5 ng/ml in both groups of cows. The above range seems feasible for dairy cows in mid-lactation based on the results obtained by Manns (1972) and Thilsted (1985).

Plasma thyroxine (T_4) concentration was predicted as 50–60 ng/ml in group S and 40–50 ng/ml in group F. There seems to be a tendency for cows with low plasma insulin concentrations to also have low plasma thyroxine concentrations (Hart et al., 1978; Thilsted, 1985). Hence, based on the higher range of plasma glucose concentration in group S, a higher plasma thyroxine concentration was predicted in group S than in group F.

Plasma somatomedin concentration was predicted as 1.0–1.2 U/ml in group S and 0.8–1.0 U/ml in group F. As is the case for plasma thyroxine concentration, there seems to be a tendency for plasma somatomedin concentration to follow plasma insulin concentration (Falconer et al., 1980). Hence the different ranges for groups S and F.

Plasma growth hormone concentration was predicted as 2–10 ng/ml in both group S and F. The range chosen is comparable to the values found by Hart et al. (1978) but higher than those found by Thilsted (1985) in early lactation.

3.5 Diurnal variations in nutrient and hormone concentrations

The values shown in table 3.1 are predicted means of plasma concentrations over a 24 hour period. It is well-known that plasma concentrations of, for exam-

ple, glucose and insulin are related to time of feeding (Thilsted, 1980; Hart, 1983; Riis, 1983c).

Especially for insulin, there can be immense variations between values found around feeding times and values found many hours post-prandial in cows fed twice daily (Thilsted, 1980). However, both groups of cows had free access to feed throughout the day and most probably ate more frequently than twice daily, and therefore daily variations in plasma glucose and insulin concentrations related to time of feeding may not have been so large. Hart (1983) has shown that plasma insulin concentrations were less variable and lower in dairy cows fed six times daily compared to cows fed twice daily.

The mean values predicted for plasma somatomedin and growth hormone concentrations also cover very large diurnal variations (Hart et al., 1980; Thilsted, 1980; Nielsen, 1986). Daily variations in plasma total glucagon concentration are not so large and plasma thyroxine concentrations are fairly stable over a 24 hour period (Thilsted, 1985).

3.6 Reliability of the predicted concentrations

For many of the nutrients and hormones presented in table 3.1, the ranges of values chosen for both group S and F are the same. It was difficult to predict values since there are not many values that can be found in the literature for dairy cows in mid-lactation and for cows fed as those in group S and F. Also, there are large variations in the values found in the literature.

Nevertheless, it was considered worthwhile to establish plasma concentrations of the hormones insulin, total glucagon, thyroxine, somatomedin and growth hormone since changes in plasma concentrations seem to reflect alterations in secretion rates (Trenkle, 1978; Lomax et al., 1979; Hart et al., 1980). It is important to have some knowledge of secretion rates of the above hormones, since they all, to some extent play a role in the partitioning between and utilisation of nutrients in the mammary gland and nonmammary tissues in lactating dairy cows (Thilsted, 1980; Nielsen, 1986).

The lower levels of plasma concentrations predicted for insulin and thyroxine in group F as compared to group S already point towards a partitioning and utilisation of nutrients that favour the mammary gland more in group F than in group S. If this holds true, then milk production in group F should be higher than in group S. It must be borne in mind, however, that the above differences in plasma hormone concentrations between group S and F are based on the difference in plasma glucose concentration between the two groups, and this difference is presumably very small.

4 Nutrient metabolism in the liver

By Allan Danfær

4.1 Introduction

The liver is a central organ for the adjustment of the absorbed nutrients to the requirements of the body. The organ receives blood from two sources, the portal vein transporting absorbed nutrients from the gastrointestinal tract and the hepatic artery supplying nutrients and metabolites from the general circulation. Nutrients from the liver to extra-hepatic tissues are transported by the hepatic veins and by hepatic lymph vessels.

In ruminants absorbed nutrients taken up by the liver from the portal blood are volatile fatty acids (VFA), short-chain fatty acids ($C \leq 10$), amino acids, NH_3/NH_4^+, nucleotides and normally small amounts of glucose. Long-chain fatty acids ($C > 10$) are absorbed as triglycerides in chylomicrons via the intestinal lymph vessels to the general circulation. Major nutrients taken up by the liver via the hepatic artery are amino acids, free fatty acids, glycerol and lactate.

The most important metabolic processes which these nutrients undergo in the liver are gluconeogenesis, glycogenesis, glycogenolysis, protein turnover, urea synthesis, lipid synthesis and synthesis of endogenous acetate and ketone bodies. To maintain this metabolically active organ and to fuel the synthetic processes the rates of oxidation and heat production are very high in the liver.

Products from liver processes removed by hepatic veins and lymph vessels for utilization in extra-hepatic tissues or excretion are glucose, plasma proteins, amino acids, urea, triglycerides (in very low and low density lipoproteins), acetate and ketone bodies. An outline of nutrient metabolism in the liver is depicted in figure 4.1.

In the following sections of this chapter the estimated quantities of nutrients taken up, metabolized and secreted by the liver of cows from group F (complete diet) and group S (free choice diet) are presented and discussed.

4.2 Nutrient uptake by the liver

The estimated daily quantities of absorbed nutrients for group S and group F are summarized in table 4.1. The values are those presented in chapter 2, table 2.1, with the addition that the amounts of triglycerides formed from fatty acids during absorption are shown along with the corresponding amounts of glycerol.

The nutrients taken up by the liver are shown in figure 4.2 (group S) and figure 4.3 (group F) and the flow rates (in moles/d) are estimated as follows below:

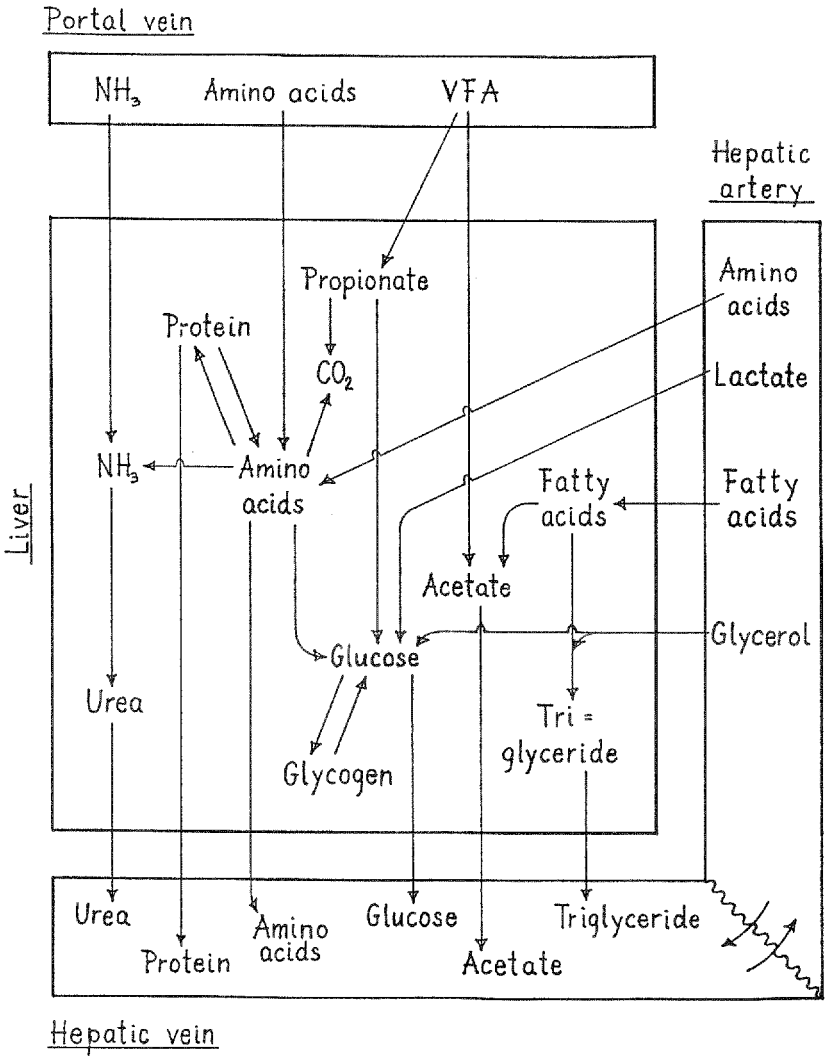

Figure 4.1 Outline of liver metabolism.

Acetate, propionate, glucose, amino acids and NH_3/NH_4^+ are derived directly from table 4.1.

During absorption most of the butyrate is oxidized to ketone bodies (Annison & Armstrong, 1970; Stevens, 1970). According to a review by Madsen (1983c) 3–5 moles/d of butyrate are taken up by the liver of lactating fed cows, this

Table 4.1 Nutrients absorbed from the gastro-intestinal tract.

Nutrient	Mol. weight	Group S		Group F	
		kg/d	moles/d	kg/d	moles/d
Acetate	60	3.98	66	3.81	63
Propionate	74	1.96	26	2.01	27
Butyrate	88	1.20	14	1.05	12
Glucose	180	0.27	1.5	0.23	1.3
Amino acids	115	1.87	16	1.95	17
Fatty acids	270	0.82	3.0	0.96	3.5
(Triglycerides[1]	848	0.86	1.0	1.00	1.2)
(Glycerol[1]	92	0.09	1.0	0.11	1.2)
NH_3–N	14	0.13	9.0	0.20	15

[1] Calculated from fatty acids on a molar basis.

amount being approximately 30% of the butyrate produced by rumen fermentation (table 4.1). The amounts of *butyrate* are therefore 14 × 0.30 = 4.2 moles/d (group S) and 12 × 0.30 = 3.6 moles/d (group F). The uptake of *beta-OH-butyrate* is calculated by difference: 14–4.2 = 9.8 moles/d (group S) and 12–3.6 = 8.4 moles /d (group F).

Fractional turnover rate of body proteins in adult cows is in the order of 1% per day (Lobley et al., 1980). This means that at protein equilibrium 1% of the body protein mass is degraded and resynthesized each day. Assuming total body protein to be 15% of live weight (Riis, 1983a) the rate of protein breakdown in a 600 kg cow can be calculated as: 600 × 0.15 × 0.01 = 0.90 kg protein or 7.8 moles of amino acids per day.

Amino acids from degraded body protein taken up by the liver are then estimated as 8.0 moles/d in group S and a little lower, 7.5 moles/d, in group F because of the lower concentrations of insulin and thyroxine in the cows from this group (see chapter 3).

Free fatty acids (FFA) in the extracellular fluid originate from lipolysis in adipose tissue. According to Danfær (1983) the total flux rate of FFA through the extracellular pool is in the order of 2 moles/d equivalent to 0.50 kg/d. In chapter 5 the FFA flux rate is assumed to be 0.50 kg/d in group F and 0.45 kg/d in group S, the difference being based on the higher plasma concentration of insulin in the latter group. The major proportion of the FFA flux is taken up by muscle tissues and it is suggested here that in cows in mid-lactation the muscles utilize 80% and the liver 20% of total FFA flux rate. Therefore the uptake of FFA by the liver is 0.20 × 0.45 = 0.09 kg equivalent to 0.33 moles/d in group S and 0.20 × 0.50 = 0.10 kg equivalent to 0.37 moles/d in group F.

Lactate is mainly produced in muscles by anaerobic metabolism of glucose (glycolysis). From experiments with sheep (Jarrett et al., 1976) reviewed by

Madsen (1983a) the release of lactate from muscle tissue of cows can be roughly estimated at 0.25 kg/d. Assuming that this is exclusively utilized in the liver, the uptake of lactate is 0.25 kg equivalent to 2.8 moles/d in both group S and group F.

Glycerol is made available by 2 routes: 1) hydrolysis by lipoprotein lipase during tissue uptake of fatty acids from triglycerides in the blood and 2) lipolysis of depot fat in adipose tissue. Utilization of glycerol only takes place in tissues like the liver and the mammary gland where glycerol can be activated to glycerol-P by glycerol kinase (Lindsay, 1970; Bauman & Davis, 1974). It is assumed here that glycerol released from triglycerides taken up by the mammary gland is utilized in the gland itself, and the liver uptake is then calculated as glycerol from triglycerides taken up by adipose tissue plus glycerol from lipolysis in adipose tissue (see chapter 5). According to this the uptake of glycerol by the liver is 1.3 moles/d in group S as well as in group F.

4.3 Nutrient metabolism in the liver

It follows from the scarce absorption of glucose due to ruminal fermentation of carbohydrates that the gluconeogenic processes in the liver play a very dominant role in supplying nutrients to the ruminant. Glucose flux through the extracellular fluid is a measure of total available glucose to the extra-hepatic tissues both from exogenous and endogenous sources. The rate of glucose flux has been measured by Thilsted (1980) who found 14 moles of glucose/d for a cow in early lactation with a similar feed intake (19 kg dry matter/d) of a similar ration (see chapter 1) as cows in group F.

In chapter 3 it is concluded that plasma glucose concentration – often used as a parameter of glucose metabolism—is higher in group S than in group F. But as there seems to be no clear relationship between glucose concentration in blood plasma and glucose flux rate (Thilsted, 1980), the rate of glucose flux is assumed to be the same in both groups, 14 moles/d.

The rate of *gluconeogenesis* is then calculated as the difference between glucose flux and glucose absorption: 14 – 1.5 = 12.5 moles/d in group S (figure 4.2) and 14 – 1.3 = 12.7 moles/d in group F (figure 4.3).

The substrates for glucose synthesis in the liver are propionate, amino acids, lactate and glycerol (Lindsay, 1970), and the contributions of these substrates to gluconeogenesis are estimated as follows:

Propionate and amino acids are quantitatively the most important sources for glucose synthesis, and it is assumed that for gluconeogenesis and oxidation these substrates, taken together, are utilized in the same amount in the 2 groups. Amino acid catabolism in the liver is in the order of 10 moles/d in high-producing cows as judged from a review by Riis (1983b). As 26 and 27 moles of propionate/d are available in groups S and F, respectively, the catabolism of

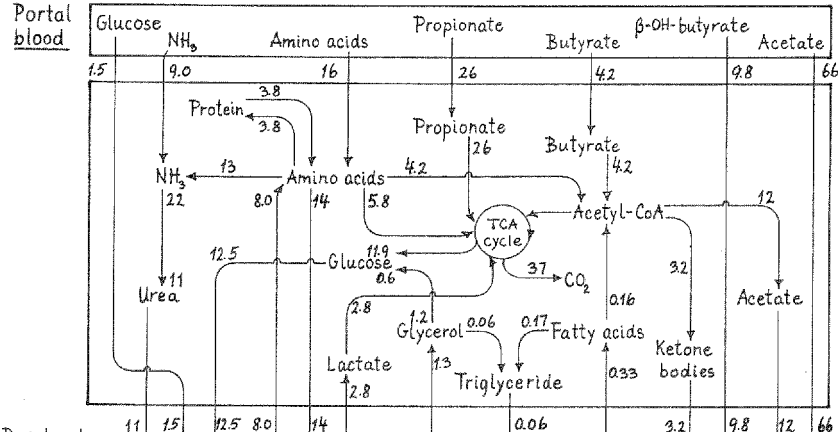

Figure 4.2 Liver uptake, metabolism and secretion of nutrients. Group S, moles/d.

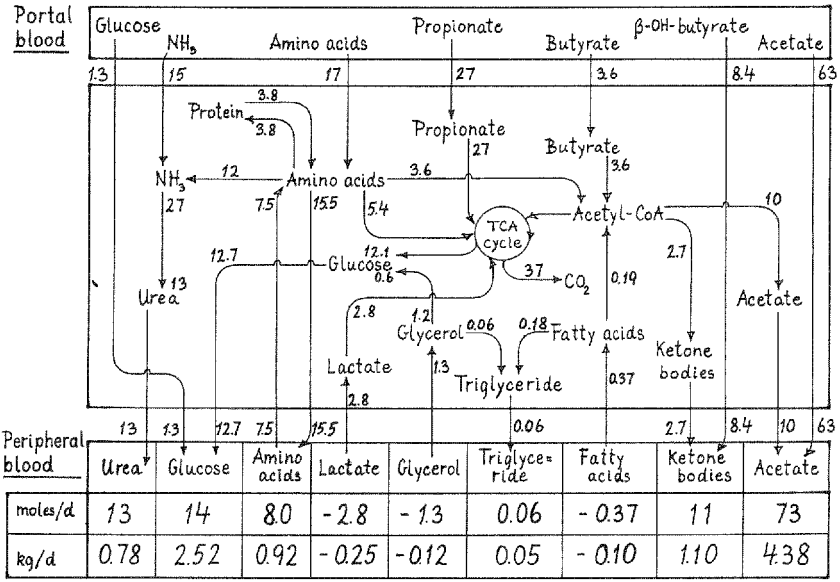

Figure 4.3 Liver uptake, metabolism and secretion of nutrients. Group F, moles/d.

amino acids is 10 and 9.0 moles/d, so that the sum of propionate and amino acids is 36 moles/d in both groups.

The contribution of lactate and glycerol to gluconeogenesis is calculated as the sum of lactate and glycerol taken up by the liver less the amount of glycerol used in lipid synthesis which is 0.06 moles/d in both groups, as discussed later in this chapter.

Group S and F: 2.8 moles of lactate/d and 1.3 – 0.06 = 1.2 moles of glycerol/d.

The contribution to gluconeogenesis of propionate and amino acids is then calculated by subtraction from total gluconeogenesis multiplied by 2 (2 moles of substrate are used per mole of glucose synthesized):

Group S: $12.5 \times 2 - (2.8 + 1.2) = 21.0$ moles/d of propionate + amino acids.
Group F: $12.7 \times 2 - (2.8 + 1.2) = 21.4$ moles/d of propionate + amino acids.

The partition between gluconeogenesis and oxidation is assumed to be the same for both these substrates. Therefore, the proportion of propionate and amino acids used for glucose synthesis can be estimated as 21.0/36 = 0.58 for group S and 21.4/36 = 0.59 for group F. Now the numerical contributions to the rate of gluconeogenesis are easily derived:

Group S: $26 \times 0.58 = 15$ moles of propionate/d
$10 \times 0.58 = 5.8$ moles of amino acids/d.
Group F: $27 \times 0.59 = 16$ moles of propionate/d
$9 \times 0.59 = 5.4$ moles of amino acids/d.

Fractional protein turnover rate is 15% per day of the liver protein pool in a non-lactating cow (Lobley et al., 1980), but is here estimated as 20%/d as liver weight and metabolic activity increase about 25% from the non-lactating to the lactating state (Smith & Baldwin, 1974). Liver weight is approximately 11 kg in a lactating cow (Smith & Baldwin, 1974) and the protein content is 20% of liver weight (Lobley et al., 1980). *Protein turnover* rate in the liver is then calculated for both groups as:

$11 \times 0.20 \times 0.20 =$ 0.44 kg protein or 3.8 moles of amino acids/d – the rates of synthesis and breakdown being equal.

Total *urea synthesis* is derived from NH_3/NH_4^+ taken up by the liver and NH_2-groups from catabolized amino acids. If the average amino acid has 1.3 moles of N per mole, then the urea production will be $(9.0 + 10 \times 1.3)/2 = 11$ moles/d in group S and $(15 + 9.0 \times 1.3)/2 = 13$ moles/d in group F.

The free fatty acids taken up by the liver are either esterified with glycerol to triglycerides or oxidized to acetyl-CoA and it is assumed here that each of these pathways uses 50% of the available FFA. Hence, *lipid synthesis* in the liver can

be taken as $0.5 \times 0.33/3 = 0.06$ moles of triglycerides/d in group S and $0.5 \times 0.37/3 = 0.06$ moles of triglycerides/d in group F. The substrates used for this synthesis are 0.06 moles of glycerol plus 0.17 moles of FFA (group S) and 0.06 moles of glycerol plus 0.18 moles of FFA (group F).

All the substrates not yet accounted for are either oxidized to CO_2 or converted into acetate and ketone bodies. These include propionate and amino acids not used in gluconeogenesis, all the butyrate and the FFA not used in lipid synthesis (see figures 4.2 and 4.3). Assuming that the average amino acid molecule contains 5 C-atoms and that the chain length of the average fatty acid molecule is 17 C-atoms, the total amount of available carbon can be derived:

Group S			
From propionate:	$(26 - 15) \times 3 = 33$	moles/d	
From amino acids:	$(10 - 5.8) \times 5 = 21$	»	
From butyrate:	$4.2 \times 4 = 17$	»	
From FFA:	$(0.33 - 0.17) \times 17 = 2.7$	»	
Total carbon:	74	moles/d	
Group F			
From propionate:	$(27 - 16) \times 3 = 33$	moles/d	
From amino acids:	$(9.0 - 5.4) \times 5 = 18$	»	
From butyrate:	$3.6 \times 4 = 14$	»	
From FFA:	$(0.37 - 0.18) \times 17 = 3.2$	»	
Total carbon	68	moles/d	

According to a review of liver cell metabolism by Madsen (1983c) the *syntheses of acetate* and *ketone bodies* in lactating, fed cows are 1.5 and 0.8 μmol carbon per min per g liver or 12 moles/d of acetate and 3.2 moles/d of ketone bodies, when the liver weight is assumed to be 11 kg (Smith & Baldwin, 1974). These figures are used directly for group S, but are estimated to be a little lower in group F, 10 moles/d and 2.7 moles/d for acetate and ketone bodies, respectively. The remaining carbon is *oxidized to CO_2:*

$74 - (12 \times 2 + 3.2 \times 4) = 37$ moles of CO_2/d in group S
and
$68 - (10 \times 2 + 2.7 \times 4) = 37$ moles of CO_2/d in group F.

The production of acetate and ketone bodies in group F is estimated according to the following principles:

First, the production and consumption of ATP are calculated for group S. The production, 254 moles/d, is derived from propionate and amino acid oxida-

tion to CO_2, and oxidation of ketogenic amino acids, butyrate and FFA to acetyl-CoA, which in turn is converted to acetate and ketone bodies. The use of ATP for protein synthesis, urea synthesis, gluconeogenesis, lipogenesis and ketogenesis amounts to 142 moles/d according to standard biochemical pathways. The difference between the ATP production and ATP consumption in synthetic processes is 112 moles/d and can be regarded as a »maintenance« requirement for the liver.

Then, two conditions are assumed to be valid: 1) that the "maintenance" re-

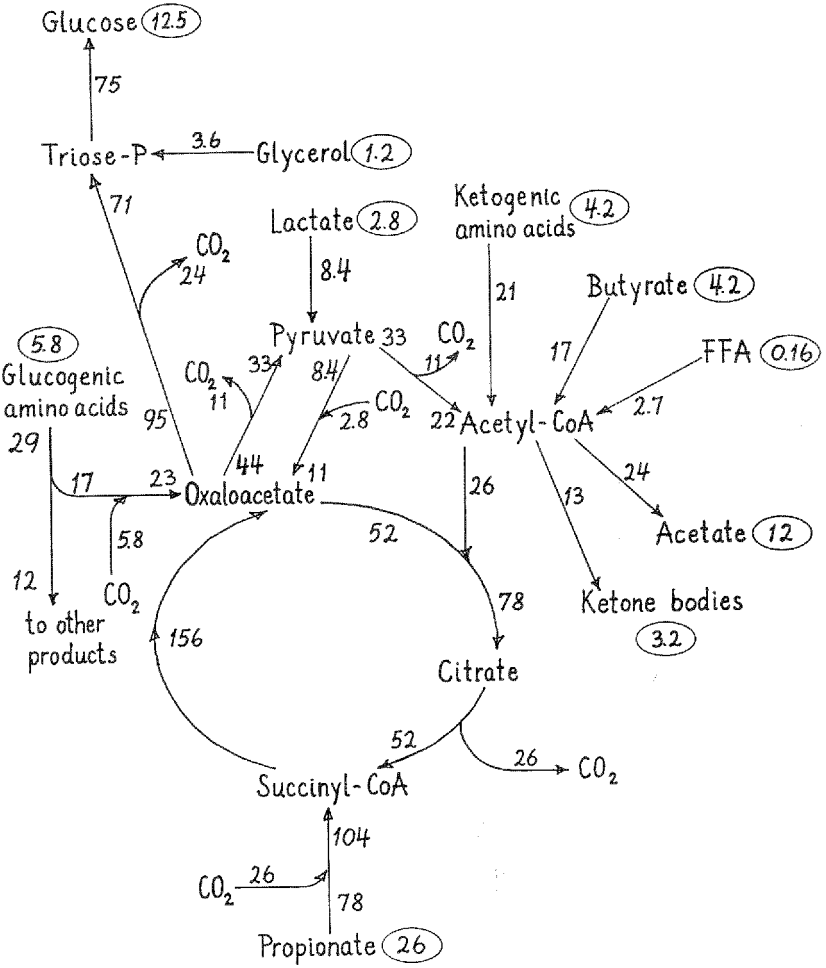

Figure 4.4 Distribution of carbon between gluconeogenesis, acetate production, ketogenesis and oxidation, mol C/d and mol substrate or product/d. Group S.

quirement in group F is the same as in group S, 112 moles of ATP/d and 2) that the ratio between acetate and ketone bodies produced is the same in group F as in group S, 12/3.2 = 3.75. These two assumptions make it possible to calculate the absolute amounts (moles/d) of acetate and ketone bodies synthesized in group F.

Figures 4.4 and 4.5 show in detail the contribution of carbon from propionate, butyrate, amino acids, lactate, glycerol and FFA to glucose, acetate, ketone bodies and CO_2 in group S and group F, respectively. For convenience it is as-

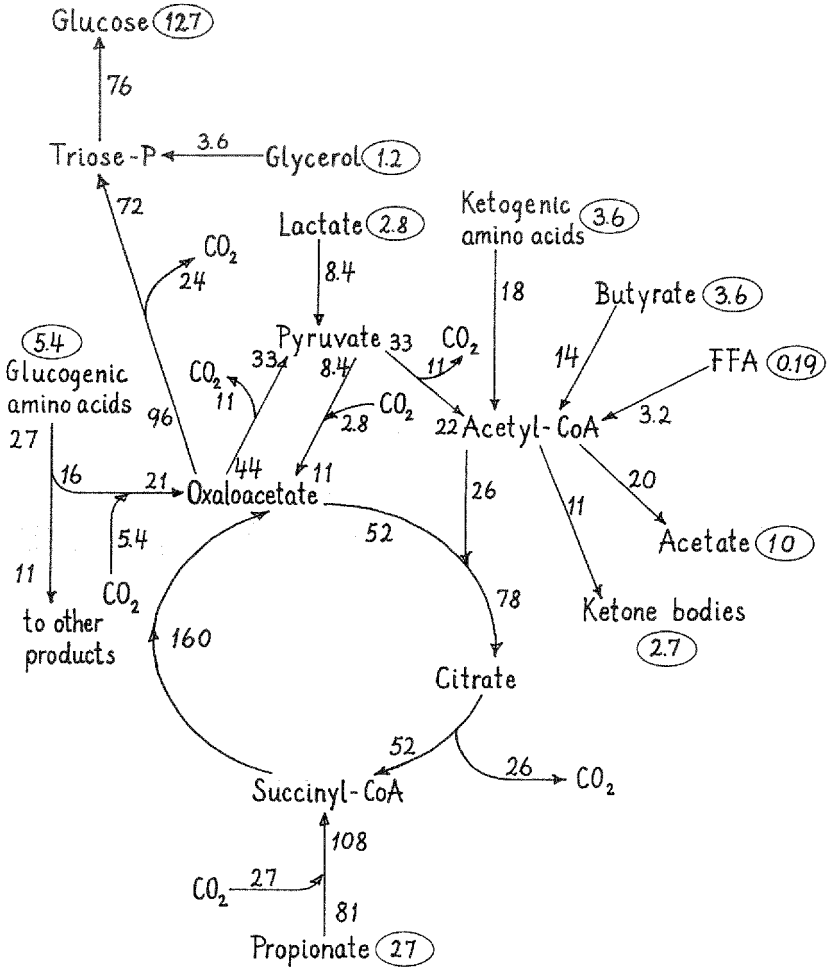

Figure 4.5 Distribution of carbon between gluconeogenesis, acetate production, ketogenesis and oxidation, mol C/d and mol substrate or product/d. Group F.

sumed that all the glucogenic amino acids are used in gluconeogenesis and that amino acid oxidation takes place via acetyl-CoA. It is further assumed that only 3 of the 5 carbon atoms in the average amino acid molecule are used in gluconeogenesis while the remaining 2 carbon atoms are converted into other products and excreted in the urine.

The net production of CO_2 is found as the overall balance:

$26+11+11+24-(26+5.8+2.8) = 37$ moles/d in group S and
$26+11+11+24-(27+5.4+2.8) = 37$ moles/d in group F.

4.4 Nutrient secretion from the liver

The net outputs of nutrients from the liver are shown at the bottom of figures 4.2 and 4.3. Negative values mean net uptake from arterial blood. Absorbed acetate, beta-OH-butyrate and glucose are assumed not to be metabolized in the liver because of low activity of the activating enzymes, acetyl CoA synthetase, beta-OH-butyryl CoA synthetase and hexokinase. Therefore, these nutrients pass from the portal blood through the hepatic veins into the peripheral circulation.

The total amounts of acetate, ketone bodies and glucose available for extrahepatic tissues are the sums of dietary (absorbed) and endogenous sources: $66 + 12 = 78$ and $63 + 10 = 73$ moles of acetate/d, $9.8 + 3.2 = 13$ and $8.4 + 2.7 = 11$ moles of ketone bodies/d and $1.5 + 12.5 = 14$ and $1.3 + 12.7 = 14$ moles of glucose/d in group S and group F, respectively. Amino acids available for net protein synthesis in extra-hepatic tissues are $16 - (5.8 + 4.2) = 6.0$ moles/d in group S and $17 - (5.4 + 3.6) = 8.0$ moles/d in group F.

Assuming that no energy is retained in the liver, heat production can be estimated as the difference between energy in nutrients taken up and energy in nutrients secreted. Using values for heat of combustion for propionate, butyrate, amino acids, lactate, glycerol, FFA, urea, glucose, triglyceride, acetate and ketone bodies (Handbook of Chemistry and Physics, 1973; Livesey, 1984) the heat output is 19 MJ/d in group S and 18 MJ/d in group F.

4.5 Discussion

Evaluation of the estimated nutrient fluxes across and within the liver shown in figure 4.2 and figure 4.3 is difficult because experimental data on liver metabolism in lactating cows are very limited as pointed out by Baldwin & Smith (1983). Therefore, the following discussion cannot be comprehensive or conclusive but will only stress some important questions.

Lomax and Baird (1983) have measured nutrient exchange across the liver and the digestive tract of lactating and non-lactating cows. They found that in lactating animals the portal exchanges of acetate, propionate, butyrate, and

beta-OH-butyrate were 31, 11, 4.4 and 4.4 moles/d, respectively. The present estimates in figures 4.2 and 4.3 comparable to these data are 63–66 (acetate), 26–27 (propionate), 3.6–4.2 (butyrate) and 8.4–9.8 moles/d (beta-OH-butyrate). Except for butyrate, it seems that the calculated amounts of absorbed nutrients arriving to the liver are overestimated by more than 100%. The reason for this could be that substantial proportions of the absorbed nutrients are metabolized in gut tissues before reaching the liver. From similar studies with sheep, it has been concluded that only 70% of acetate, 50% of propionate and 10% of butyrate produced in the digestive tract actually reach the portal blood (Bergman, 1975 c.f. Sutton, 1985). This is not taken into account in the model calculations presented here. However, if the data of Lomax & Baird (1983) are adjusted to a similar feed intake as that of the model cows, i.e. 19.3–19.7 kg dry matter/d (see chapter 1), using linear regression equations given by Lomax & Baird (1983), the portal exchanges of acetate, propionate and beta-OH-butyrate increase to 60, 21 and 7.7 moles/d, respectively. These adjusted values are in a much better agreement with the values estimated in this chapter.

Gluconeogenesis is a key process in the liver and it is extremely important to whole animal metabolism. In an excellent study, Wiltrout & Satter (1972) measured propionate production rate, glucose flux rate and the contribution of propionate to glucose flux rate in 2 cows. The average feed intake was 17 kg dry matter/d and the average milk yield was 29 kg/d. Propionate production, glucose flux and propionate contribution to glucose flux were 25 moles/d, 14 moles/d and 61%, respectively. These figures are very close to the corresponding averages for group S and group F (26.5 moles/d, 14 moles/d and 56%).

The estimates of amino acid contribution to glucose flux rate are 21% and 19% in group S and F, respectively. These values are in the middle of a range of estimates from different authors. According to Bruckental et al. (1980) no more than 2% of glucose flux rate was contributed by amino acids in high-yielding dairy cows, while Black et al. (1968) in isotope studies with lactating cows estimated that as much as 50% of glucose-C could be synthesized from amino acid-C. Lomax & Baird (1983) calculated that the maximum possible contribution to gluconeogenesis from nutrients taken up by the liver were as follows: 46% for propionate, 16% for lactate, 0.6% for pyruvate, 8.6% for 4 amino acids and 0.8% for glycerol—making a total of 72% of glucose production. If it is assumed that the deficit (28%) is made up of amino acids other than the 4 actually measured, the total contribution of amino acids would have been 37% as a minimum, unless hepatic glycogenolysis had contributed significantly to glucose production.

Based on these estimates and a glucose flux rate of 14 moles/d the requirement for glucogenic amino acids would range from $0.02 \times 14 \times 2 = 0.6$ moles/d to $0.50 \times 14 \times 2 = 14$ moles/d. It seems hard to believe that a range of this order

can exist for lactating cows fed normal rations. It is also clear, however, that it is very critical to the total amino acid requirement in high-yielding cows whether the amino acid contribution to glucose flux rate is 2% or for instance 20% as found in the present model, as suggested by Elliot (1976) and as calculated by Danfær (1983).

The low estimate of Bruckental et al. (1980) is based on a measured rate of urea formation and the following assumptions: 1) that only 35% of the synthesized urea-N can be accounted for by catabolized amino acid-N and 2) that only 20% of catabolized amino acid-C is synthesized into glucose. The corresponding percentages in the present models are 44–59% and 35–36%, respectively. If we accept that the estimate of a 2% contribution of amino acids is valid, then 98% of glucose flux rate must be synthesized from substrates other than amino acids or must be absorbed from the digestive tract. The consequences of this would be that in group S $(14 \times 0.98 - 1.5) \times 2 = 24.4$ moles/d, and in group F $(14 \times 0.98 - 1.3) \times 2 = 24.8$ moles/d of 3-carbon precursors (propionate, lactate and glycerol) are required for gluconeogenesis—or 80% of the total available amounts of these substrates. This figure is very high compared to the value of 20% of amino acids assumed by Bruckental et al. (1980), especially when it is considered that carbon from the major substrate, propionate, and carbon from glucogenic amino acids mix in the citric acid cycle and pass through the same regulatory steps in the gluconeogenic pathway (Lindsay, 1970).

This discussion demonstrates a need for more experimental evidence within the quantitative and regulatory aspects of gluconeogenesis and leads to the identification of some crucial questions:

1) How much glucose, propionate and amino acids are absorbed from the digestive tract?
2) In which proportions do the glucogenic substrates contribute to glucose synthesis?
3) How are 1) and 2) affected by genetic factors, nutrition and stage of lactation?

The present estimates of urea synthesis amount to 11–13 moles/d. This is rather high compared to the value of 8 moles/d found by Bruckental et al. (1980) in cows 8–9 weeks post-partum. However, these cows were fed 900 g crude protein less than group S and 1500 g crude protein less than group F per cow per day.

The feed nitrogen intake, the faecal nitrogen excretion and the urea nitrogen recycling to the digestive tract in the two groups of cows are calculated in chapter 2. Using these figures and assuming that body nitrogen balance is zero in both groups the rate of nitrogen excretion in milk can be estimated to 128 g N/d in group S and 155 g N/d in group F. If the nitrogen content in milk is 34.2/6.38 = 5.4 g/kg (Jenness, 1974) the calculated milk yield will be 24 kg/d in group S and 29 kg/d in group F.

Finally, the oxidation of substrates will be briefly discussed. The heat production calculated as the energy balance across the liver is 18-19 MJ/d. A more direct estimate is the heat combustion value of the oxidized propionate and amino acids which is 18 MJ/d in group S and 19 MJ/d in group F, when heat combustion values of 1.53 MJ/mole propionate (Handbook of Chemistry and Physics, 1973) and 2.23 MJ/mole amino acid (Livesey, 1984) are used. These figures are very close to the 17.6 MJ of heat production in the liver from lactating cows estimated by Smith & Baldwin (1974).

During oxidation 254 moles/d and 260 moles/d of ATP are produced in group S and group F, respectively. The use of ATP for synthetic purposes is 142 moles/d and 148 moles/d in the 2 groups—equivalent to 56-57% of the total ATP production.

5 Consumption of nutrients in extrahepatic, non-mammary body tissues

By Annemarie Madsen and Poul Martin Riis

Non-mammary body tissues compete with the mammary gland for nutrients from the common extracellular pool. The consumption of nutrients and the storage or mobilization of protein and fat are therefore important factors in the regulation of nutrient supply to the mammary gland. The uptake and release of nutrients by the liver were discussed in the preceeding chapter of this report. The major consumption of nutrients in extrahepatic, non-mammary tissues takes place in adipose tissue and in muscle and connective tissues. This chapter deals with the metabolism in these two groups of tissues.

It is the purpose of the present chapter to elucidate the following questions:

1. To what extent can we predict the nutrient consumption and metabolic output by extrahepatic, non-mammary tissues, when we know the rates of nutrient absorption and the nutrient balance of liver metabolism?
2. Which are the major deficiencies in our knowledge limiting our ability to fulfil the purpose expressed in item 1?

The purpose is pursued by the use of data from the cows in group S and F (table 1.1 and 1.2) as a case study. The estimates of nutrient and hormone concentrations presented in chapter 3 and those for nutrient consumption in the liver presented in chapter 4 are applied. The metabolism in adipose tissue is treated first, because adipose tissue supplies the free fatty acids (FFA), which is a major fuel in muscle tissue.

5.1 Metabolism in adipose tissue

The following gives a selected outline of adipose metabolism. More comprehensive descriptions are found in recent reviews by Madsen (1983b) and by Vernon and Clegg (1985). The metabolism in adipose tissue is dominated by the lipid cycle, comprising continuous synthesis and breakdown of triglycerides (figures 5.1 and 5.2). During the turn of the cycle, FFA is released to the extracellular fluid. The synthesis of fat as well as the maintenance of cell structures require a continuous generation of ATP, which is derived from the oxidative processes shown to the left in figures 5.1 and 5.2. The major fuel is acetate but some oxidation of glucose is necessary for the generation of NADPH in the glucose-6-phosphate pathway. Glucose is also required for the generation of glycerol-phosphate and for activation of mitochondrial oxidation.

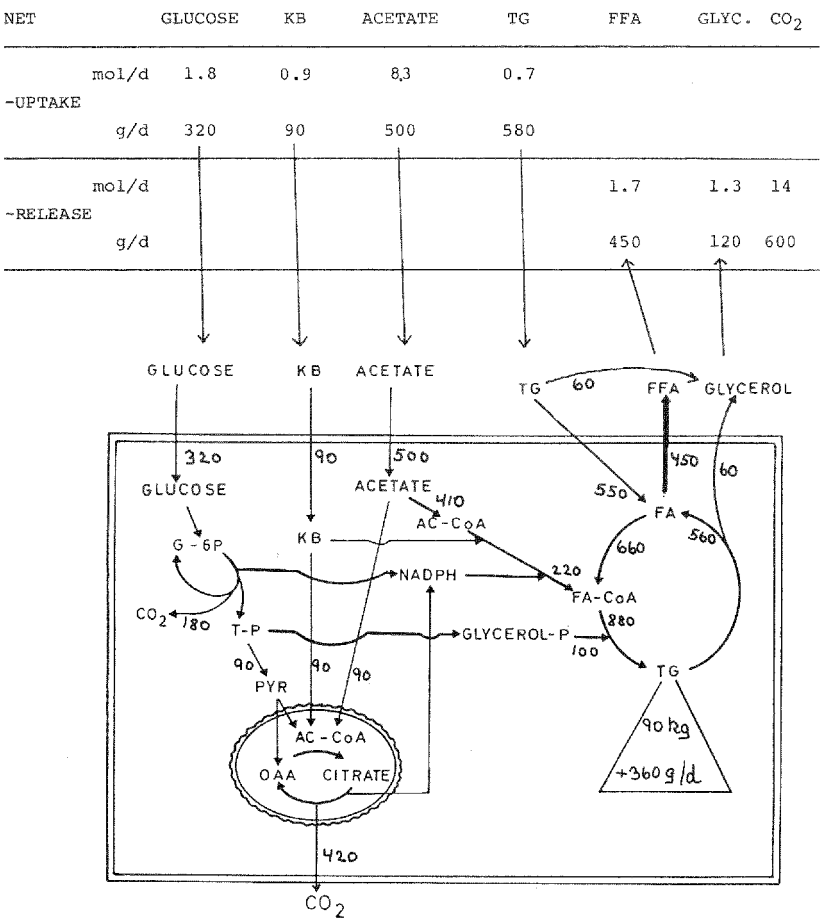

Figure 5.1 Uptake and metabolism of nutrients in adipose tissue of cows on ration S.

Figures 5.1 and 5.2 also show the flow rates of nutrients and metabolites through the various metabolic pathways in the two groups of cows, S and F. The estimation of these flow rates is discussed below.

5.1.1 Rates of FFA-release

Flux rates of FFA in lactating goats and cows have been determined in experiments with continuous infusion of isotope labelled long chain fatty acids (Annison et al., 1967, Annison et al., 1974, Madsen, 1985 & 1988). The results of these experiments indicate an average flux rate about 4g FFA day^{-1} kg body $wt^{-0.75}$. This gives about 500 g/day for a 600 kg cow ($600^{0.75} = 121$). In several experi-

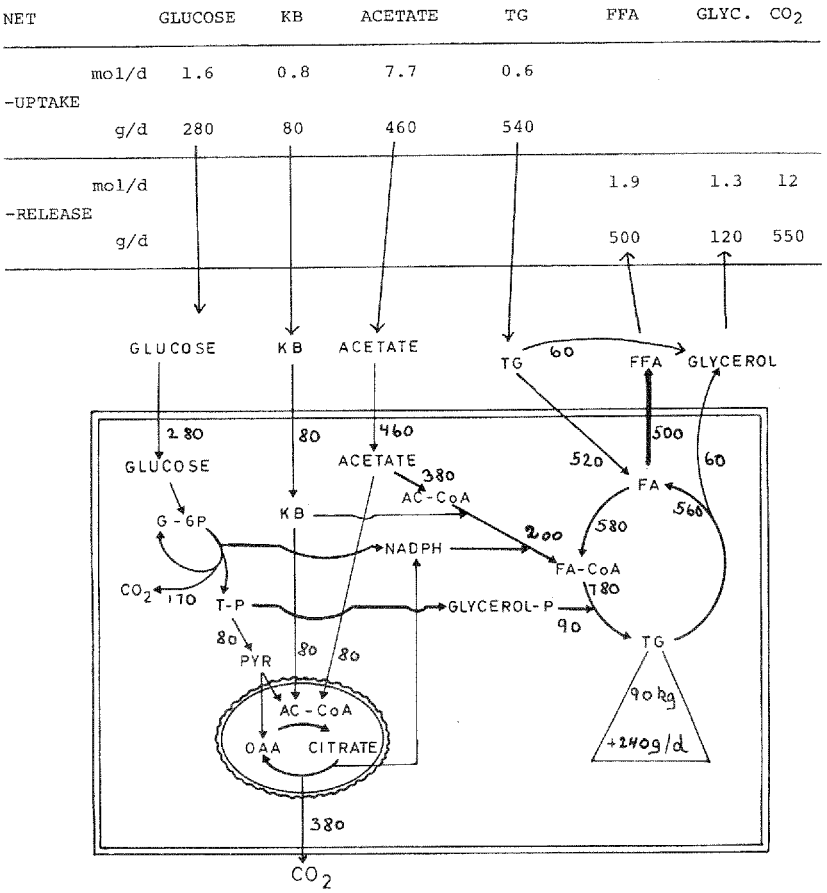

Figure 5.2 Uptake and metabolism of nutrients in adipose tissue of cows on ration F

ments it has been found that FFA-flux rates vary linearly with FFA-concentrations, at least within a moderate concentration range (Baldwin & Smith, 1983, Madsen, unpublished). In chapter 3, it was concluded that cows in group S had slightly lower FFA concentrations than cows in group F. Thus FFA flux rate should be lower in group S than in group F. On this basis it was assumed that release of FFA from adipose tissue in group S was 450 g/day and in group F 500 g/day.

5.1.2 Rates of lipolysis and reesterification

Some of the fatty acids liberated from triglycerides by lipolysis in adipose tis-

sues are reesterified. The rate of lipolysis will then be higher than the release of FFA. The degree of reesterification varies from negligible to 50% or more of the rate of lipolysis (Vernon & Clegg, 1985). Rates of esterification are stimulated by high concentrations of insulin, glucose and thyroxine. Lipolysis is stimulated by adrenalin and noradrenalin which is released from the sympathetic nerves in adipose tissue. The sympatico-adrenal activity also affects the blood flow which is necessary for the transport of FFA from the adipose tissue.

There is no reason to assume any difference between the two groups with regard to sympathetico-adrenal activity. Glucose, insulin and thyroxine concentrations were estimated a little higher in group S than in group F which means that capacity for esterification should be a little higher in the former than in the latter group. The rate of lipolysis may be calculated from the rate of FFA-release assuming 10% of reesterification in group F and 20% in group S. This gives the same rate of lipolysis for both groups, namely 560 g/day. The rate is expressed as the amount of fatty acid liberated in the process. The amount of glycerol, liberated by hydrolysis of intracellular triglycerides and plasma lipids, is about 120 g/day in both groups (figures 5.1 & 5.2). The glycerol is released from the tissue, since it cannot be reutilized due to lack of the activating enzyme, glycerokinase.

5.1.3 Fat balance

The balance in the turnover of triglycerides in the lipid cycle may be estimated from the weight change. Well fed dairy cows will usually be in positive balance during the 15th–24th week of lactation. At this stage the average weight gain is about half a kilogram body weight per day for a 600 kg cow (Andersen, 1983). Body tissue balances correlates positively with plasma concentrations of insulin and thyroxine (Kunz and Blum, 1985). It must therefore be assumed that the gain is a little higher in group S than in group F. A gain of 600 g/day is adopted for group S and a gain of 400 g/day for group F. One kilogram of body weight gain contains about 600 g of fat (Sørensen, 1984). The fat balances are thus 360 g and 240 g per day in group S and group F, respectively.

5.1.4 Rates of fat synthesis

Rates of fat synthesis, i.e. the rates of fatty acid esterification may be calculated as the sum of the rate of fat deposition and lipolysis. The fat balance estimated above corresponds to 320 and 220 g fatty acids, respectively. The rate of lipolysis was 560 g/day in both groups. Total esterification should then be 880 and 780 g/day in group S and F, respectively. The fatty acid entering esterification originates in de novo synthesis, uptake of fatty acids from plasma lipids and fatty acid released by lipolysis in the adipose tissue. The relative contributions of de novo synthesis and fatty acid uptake to the input of fatty acids in the lipid

cycle depend on the relative availability of substrates and the activity of key enzymes in the two pathways. Both pathways are stimulated by high levels of insulin, glucose and thyroxine. High levels of these compounds give high levels of ATP in the cells which promote synthetic processes generally. Moreover, insulin activates the lipoprotein lipase which is responsible for the uptake of fatty acids from plasma lipids. De novo synthesis of fatty acids from acetate is also enhanced by insulin through its stimulatory effect on the fatty acid synthetase complex. Increased glucose availability leads to increased rate of formation of reduced coenzyme NADPH that is required for fatty acid synthesis.

A comparison of results from numerous studies in vitro and two studies in vivo (Madsen, 1983b & 1988) indicates that the de novo synthesis of fatty acid usually accounts for 20–30% of the total fatty acids esterified. The rates of de novo fatty acid synthesis are therefore calculated as 25% of the total esterification rates. That gives 220 and 200 g of fatty acid for group S and F, respectively (figures 5.1 & 5.2). The input from uptake of plasma lipid fatty acid is then calculated as difference between total esterification and the sum of reesterification and de novo synthesis, giving 550 and 520 g of fatty acid for group S and F, respectively.

5.1.5 Turnover of the fat pool

The total amount of fat in the cows of group S and F may be calculated as 15% of the body weight. This gives a fat pool of 90 kg. The rates of fat synthesis and of lipolysis estimated above mean therefore that the fat pool is turned over by about 1% per day.

In vivo studies with rats and mice reviewed by Vernon and Clegg (1985) have shown rates of fat synthesis corresponding to 0.1–1% of the total fat pool. Prior (1978) found values of 0.1–0.2% per day by in vivo studies with dry ewes. In recent studies with goats at different stages of lactation Madsen (1985 and 1988) found rates between 0.1 and 0.6% per day. The estimates for the cows in group S and F are thus well within the ranges found in experiments with animals in similar situations. They are also in accordance with values found by in vitro studies as reviewed by Madsen (1983b). Baldwin et al. (1976) applied a turnover rate of 2% per day in their theoretical model of fat metabolism in lactating cows.

5.1.6 Rates of oxidative processes

The rates of oxidative processes shown in figure 5.1 and 5.2 were calculated from a theoretical model for lactating cows (Baldwin et al., 1976) by assuming a constant relation between the rates of oxidation and the rates of fat synthesis.

5.2 Metabolism in muscle and connective tissue

The main metabolic processes in muscle and connective tissues are illustrated in the diagrams figure 5.3 and 5.4. The diagrams may apply to other body tissues as well. The metabolism is dominated by the oxidative processes. Energy in the form of ATP is constantly needed to pull the anabolic processes in protein turnover, for transport processes and for contraction of muscle fibers. The contraction of muscle fibers which gives the tonic tension in striated skeletal muscle is the major energy consuming proces. The processes of muscle contractions are not illustrated in the diagrams, which focus on the oxidations and on the protein turnover.

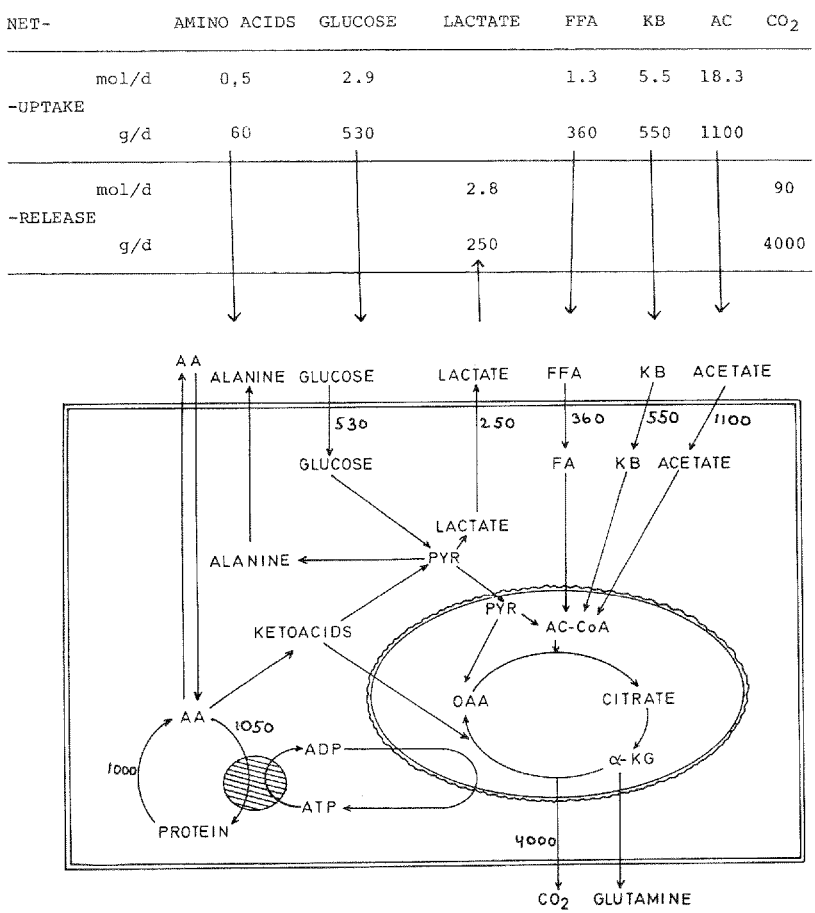

Figure 5.3 Uptake and metabolism of nutrients in muscle tissue of cows on ration S.

The fuel requirement in the oxidative processes is covered by uptake of glucose, FFA, acetate and ketone bodies. No significant net oxidation of amino acids takes places in muscle or other extrahepatic tissues.

The flux rates estimated in the following also include uptake and utilization of nutrients in kidneys, nervous tissues, blood cells and other small groups of extrahepatic, non-mammary tissues. Nutrient consumption in these tissues is small in relation to that in muscle and connective tissue. The error introduced by including these tissue under the term: muscle and connective tissues is therefore small in quantitative terms. It is important, however, to remember that nutrient uptake and metabolism may be differently regulated in different tissues.

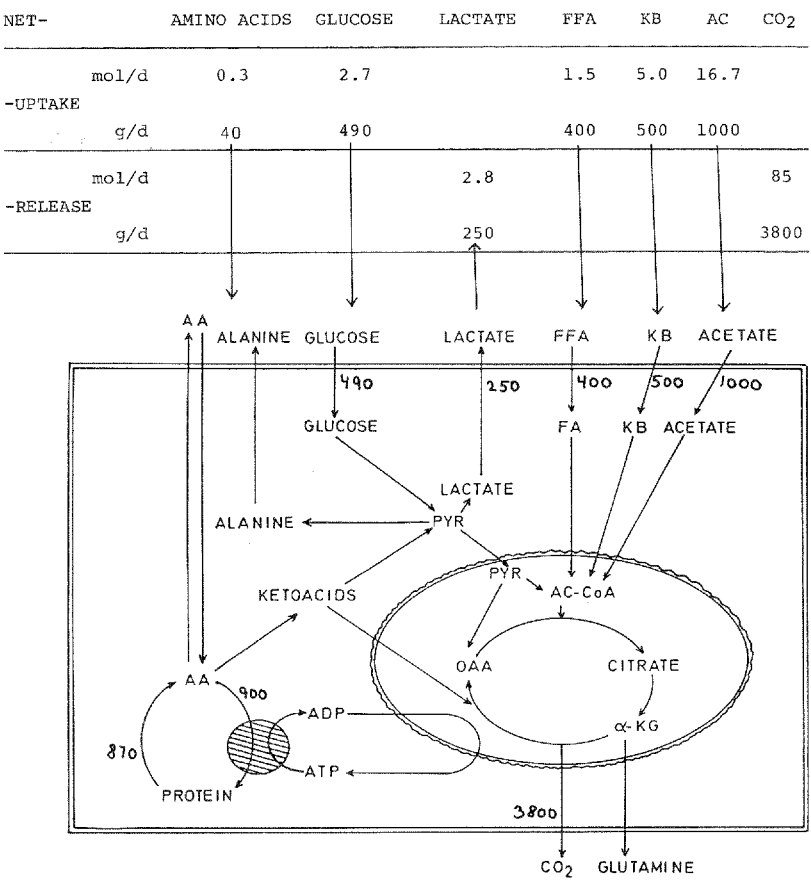

Figure 5.4 Uptake and metabolism of nutrients in muscle tissue of cows on ration F.

Thus glucose uptake and utilization in muscle, adipose and connective tissue is sensitive to variations in insulin concentration whereas in nervous tissue and in erythrocytes it seems independent of insulin.

5.2.1 Glucose uptake and oxidation

Measurements of glucose flux rates in lactating cows with body weights between 550 and 600 kg show that the total glucose consumption by non-mammary body tissues is 4–4.5 moles per day (Thilsted, 1980 & 1985a). The lowest values apply to early lactation. The cows in the present example have passed the most early phases of lactation and it seems therefore reasonable to assume an average utilization rate of 4.5 mole or 810 g glucose for the body tissues in the cows of group F and S.

Group S had higher insulin levels than had group F (chapter 3) and the rate of glucose utilization must therefore also be higher in group S than in group F. The difference is assumed to be 10% or 80 g. Available information about relation between insulin levels and glucose utilization rates in insulin sensitive tissues does not allow accurate estimations of the difference between the two groups of cows. Since 810 g was the average for the two groups the value for group S becomes 850 g and that for group F 770 g. The values in figure 5.3 and 5.4, i.e. 530 and 490 g respectively are obtained by subtracting the glucose consumption in adipose tissues from the total consumption in non-mammary tissues.

5.2.2 Lactate production

Values referred in a recent review (Madsen, 1983a) indicate that the release of lactate from muscle amounts to from 40% to 60% of the glucose consumption. The 250 g chosen in the present cases (figure 5.3 & 5.4) is thus in the upper range. There is no basis for differentiation between the two groups in this regard.

5.2.3 FFA-uptake and utilization

The transport of FFA from adipose tissue to muscles for oxidation accounts for the major part of the FFA net flux. The liver is the only other tissue which utilizes significant parts of the FFA. Oxidative processes in the muscles of the cows in group S and F (figure 5.3 & 5.4) were obtained by subtracting the estimates for FFA utilization in the liver (chapter 4) from the FFA released from adipose tissue (figure 5.1 & 5.2).

5.2.4 Acetate and ketone bodies

Data presented in a review (Madsen, 1983a) indicate that the amounts of acetate taken up and oxidized in the muscles are twice to three times the amounts

of FFA metabolized. The flow of ketone bodies is about half of that of acetate. For group F the acetate flow is estimated to be 1000 g/day that is 2½ times the FFA flow. The flow rate of ketone bodies is made to half of that, 500 g/day. The metabolic activity in the muscle and connective tissues of group S must be higher than that in group F, because the concentration of insulin and thyroxine is highest in the former group (chapter 3). Total fuel consumption must therefore be highest in group S. To compensate for that the acetate and ketone body consumption is assumed to be higher, namely 1100 g and 550 g respectively (figure 5.3).

5.2.5 Amino acid and protein turnover

Investigations with cows and goats (Lobley et al., 1980, Oldham et al., 1980, Reeds et al., 1981, Fenster and Pfeffer, 1982 and Riis, 1988) indicate that turnover rate of whole body proteins varies between 1 and 2%/day in lactating ruminants. The lowest values apply to early lactation.

Since whole body protein accounts for about 15% of the body weight, the cows in the present example had a protein pool of 90 kg. The fat pool and the protein pool are thus of the same size. If we assume a turnover rate of 1% per day, then the rate of protein synthesis and proteolysis would be 900 g/day. Whole body protein synthesis includes the protein synthesis in the liver which accounts for about 12% of total whole body synthesis (Riis, 1983a). Because both groups of cows were in positive balance it is reasonable to assume that whole body protein synthesis is 10–20% higher than the rate in very early lactation. The rate of protein synthesis in muscle and connective tissues is therefore assumed to be 900 g/day in group F. Rate of protein synthesis correlates positively with plasma concentrations of insulin and thyroxine and it must therefore be higher in group S than in group F. A rate of 1050 g/day is adopted for the protein synthesis in muscle and connective tissues of cows in group S.

It was assumed (see discussion on fat balance above) that cows in group S gained 600 g/day and those in group F gained 400 g/day. The protein content of the weight gain is 10% (Sørensen, 1984). Thus, cows of group S had a positive balance of 60 g and cows of group F a positive balance of 40 g in the protein turnover. Rate of proteolysis becomes then 990 and 860 g/day in group S and F, respectively.

The flow of amino acids in and out of the cells in muscle and connective tissues is of the same order as the rate of protein synthesis and proteolysis. This gives a net consumption of 60 and 40 g amino acids in group S and F respectively (figure 5.3 & 5.4). There is no net catabolism of amino acids in extrahepatic tissues (Riis, 1983b). Because of transamination processes whereby amino groups are transferred from entering amino acids to keto acids formed by metabolism in the cells, the pattern of amino acids entering the cells may be very different

from that of amino acids leaving the cells. It is evident that the turnover of proteins gives a considerable flow associated with a significant energy consumption. The energy is required to pull the synthetic processes.

5.3 Discussion and conclusion

5.3.1 Reliability of the estimated flux rates

The first of the two main questions which this chapter attempted to answer, was to which extent we can predict nutrient consumption and metabolic output by extrahepatic, non-mammary tissues. The answer requires evaluation of the estimated flux rates in figures 5.1–5.4. The evaluation is carried out below by calculating the heat losses from the flux rates in figures 5.1–5.4 and comparing the result with estimates of heat losses obtained from measurement of heat production in ruminants. The calculation of heat loss from the estimates in figure 5.1–5.4 is shown in table 5.1. The net uptake of each nutrient is converted to metabolizable energy and total heat losses appear as the sum in each column. Net release and deposition of metabolizable energy is in table 5.1 counted as output.

Flatt et al. (1969) found by respiration experiments with dairy cows that the total heat production was about 90 MJ in a non-lactating cow with a body weight between 500 and 600 kg. Of these 90 MJ, 15–20%, or about 15 MJ is heat loss

Table 5.1 Balance in energy flow through metabolic pathways in non-mammary, extrahepatic tissues in two groups of cows. The balance for each nutrient is given in metabolizable energy which is calculated from the fluxes shown in figures 5.1–5.4.

	Balance of energy flow*, MJ/day					
	Adipose tissue		Muscle and connective tissues		Total	
Nutrient/ metabolite	group S	group F	group S	group F	group S	group F
Glucose	5.12	4.48	8.48	7.84	13.6	12.32
Acetate	7.50	6.90	16.5	15.0	24.0	21.9
Ketone bodies	1.8	1.6	11.1	10.0	12.9	11.6
FFA	–17.1	–19.0	13.68	15.2	–3.42	–3.8
Amino acids	–	–	1.02	0.68	1.02	0.68
Lactate	–	–	–4.0	–4.0	–4.0	–4.0
Glycerol	–2.04	–2.04	–	–	–2.04	–2.04
Triglyceride	8.36	11.4	–	–	8.36	11.4
Protein	–	–	–1.02	–0.68	–1.02	–0.68
Heat production	3.6	3.3	45.8	44.0	49.4	47.4

*) Calculated as input – (output + deposition)

of digestion. Liver metabolism accounts for another 15–20 MJ (chapter 4). This leaves 60 MJ to come from metabolism in extrahepatic tissues. Heat production in extrahepatic, non-mammary tissues of a lactating cow may be a little lower, because lactation is associated with decrease in thyroxine secretion (Riis & Madsen 1985). However, the estimates of 47 and 49 MJ for cows of group F and S respectively represent presumably underestimations although the order may be correct.

Heat production in muscle and connective tissues accounts for 90% of the total heat production in extrahepatic, non-mammary body tissues (table 5.1). This is in accordance with the idea that muscle tone and heart work are the major contributors to basal heat production. Measurements of arterio-venous differences over the hind leg of sheep yielded estimates of heat productions on 0.18 MJ day^{-1} kg $muscle^{-1}$ for resting muscles (Madsen, 1983a). This gives 45 MJ for 250 kg muscle which would be the amount of muscle tissues in the cows of group S and F. Since the measurements were made on resting muscles the 45 MJ must be considered a minimum value. It supports the conclusion that the estimate in table 5.1 is of the correct order, but a little too low.

The amount of cytoplasma in adipose tissue is less than 1/10 of that in the muscle and connective tissues. Muscle tissue comprises 50% of the body weight and around 80% of the tissue mass is cytoplasma. The fat pool was calculated as 15% of the body weight and the ratio of fat to cytoplasma in adipose tissue is around 9:1 which means that cytoplasma in adipose tissue will account for only 2–4% of the body weight. It seems therefore reasonable that heat production in adipose tissue is less than 10% of that in muscle and connective tissues. The low heat production indicates a high metabolic efficiency of adipose tissue. The deposition of fat has an energy equivalent of 9–14 MJ and the FFA-output an energy equivalent of 17–19 MJ. However, there is no possibilities for more exact evaluation of the estimates for nutrient flow and heat production in adipose tissue.

The most likely causes of an underestimation of total heat production are errors in the estimates of acetate and ketone body consumption. These estimates are based on relative flux rates found in theoretical models. The flux rates of the other major fuels, glucose and FFA, were estimated from results of measurements of these flux rates in animals kept under conditions which could be related to the situations for the cows in group S and F. It is therefore justified to conclude that these latter estimates give the correct order for true flux rates. There is no possibility for evaluation of the estimates for the partition of glucose between different groups of non-mammary body tissues. Flux rates of lactate and glycerol were also estimated from theoretical models. However, these flux rates are relatively small and errors in the estimates have little influence on the total energy flow and heat production.

5.3.2 Correction of estimated flux rates and nutrients available for the mammary gland

The estimates of nutrient consumption are used to calculate the amounts of nutrients available for the mammary metabolism and milk formation, which is treated in the following chapter. The calculation is shown in table 5.2 & 5.3. In order to avoid that the apparent underestimation of acetate and ketone body consumption causes a biased prediction of milk production an extra 11 and 10 moles of acetate plus extra 3.3 and 3 moles of ketone bodies have been added to the estimates of nutrient consumption for group S and F respectively. Thus, the estimates in the middle parts of tables 5.2 & 5.3 are the sum of the consumptions shown in figures 5.1 to 5.4 plus these extra additions.

Table 5.2 Nutrient availability and consumption by non-mammary, extrahepatic tissues and amounts available for the mammary gland in group S.

	Total amounts available for extrahepatic tissues[1])		Amounts consumed by extrahepatic non-mammary tissues[2])		Amounts available for mammary gland	
Nutrient	(kg/day)	(moles/day)	(kg/day)	(moles/day)	(kg/day)	(moles/day)
Acetate	4.68	78	2.26	38	2.42	40
Ketone bodies	1.30	13	0.97	9.7	0.33	3.3
Glucose	2.52	14	0.85	4.7	1.67	9.3
Amino acids	0.69	6.0	0.06	0.05	0.63	5.5
Triglycerides	0.91	1.1	0.58	0.71	0.33	0.39

[1]) Estimations from chapter 2 and 4.

[2]) The sum of net uptakes in fig. 5.1 and 5.3, plus 11 moles of acetate and 3.3 moles of ketone bodies (see text).

Table 5.3 Nutrient availability and consumption by non-mammary, extrahepatic tissues and amounts available for the mammary gland in group F.

	Total amounts available for extrahepatic tissues[1])		Amounts consumed by extrahepatic non-mammary tissues[2])		Amounts available for mammary gland	
Nutrient	(kg/day)	(moles/day)	(kg/day)	(moles/day)	(kg/day)	(moles/day)
Acetate	4.38	73	2.06	36	2.32	39
Ketone bodies	1.10	11	0.88	8.8	0.22	2.2
Glucose	2.52	14	0.77	4.2	1.75	9.7
Amino acids	0.92	8.0	0.04	0.04	0.88	7.7
Triglycerides	1.05	1.2	0.54	0.61	0.51	0.60

[1]) Estimations from chapter 2 and 4.

[2]) The sum of net uptakes in fig. 5.2 and 5.4, plus 11 moles of acetate and 3 moles of ketone bodies (see text).

The added extra amounts of acetate and ketone bodies are estimates of acetate and ketone body oxidations in nervous tissues and the alimentary tract. The estimates of acetate and ketone body consumptions shown in figure 5.3 and 5.4 were based on theoretical models applying to muscle tissues exclusively. Consumption in other extrahepatic tissues was only included to the extent that the consumption of acetate and ketone bodies is related to glucose consumption as in muscles. The relative consumption of acetate and ketone bodies in nervous tissues and the alimentary tract is likely to be considerably higher than in muscles. The estimates for glucose and FFA consumption in figure 5.3 and 5.4 do include consumption in other extrahepatic tissues because these estimates were based on measurements of total flux rates of glucose and FFA in animals.

Annison (1983) reviewed experiments showing values for partition of nutrient fluxes between tissue groups in sheep. It may be concluded from these results that the ratio of acetate consumption in muscles over that in nervous tissues and the alimentary tract is around 8:5. This ratio was used to estimate the above mentioned additions. The addition means an extra heat production of 16.6 and 15 MJ per day for group S and F respectively. Total heat production in extrahepatic, non-mammary body tissues is then 66 MJ in group S and 62 MJ in group F. This may be a little too high. The correction may thus have resulted in slight overestimation, but nevertheless in more correct values. The amount of nutrients available for mammary metabolism appears in the last columns of tables 5.2 & 5.3. The metabolism in the mammary gland and milk formation is discussed in chapter 6.

5.3.3 Issues requiring elucidation

It seems evident that the possibilities for reliable prediction of acetate and ketone body flux rates and partition between groups of tissues ought to be a major concern in future studies on metabolism in lactating cows. It requires studies on relation between flux rates and plasma concentrations of these nutrients under different conditions. Also studies on partition of not only acetate and ketone bodies but also of glucose, FFA and plasma lipids between mammary tissues and different groups of non-mammary tissues are required.

The estimated heat production provided basis for evaluation and correction of the estimated flux rates of individual nutrients. However, the estimates of heat production were based on only a few measurements of heat production in cows. The estimated partition of heat production between groups of tissues was apparently very rough approximations. It would improve possibilities for prediction of animal performance if more data were available on total heat production as well as on heat production arising from metabolism in different groups of tissues.

It is evident that plasma concentrations of insulin and thyroxine are impor-

tant regulatory factors in the partition of nutrients between tissues and in the turnover of fat and protein in body tissues. They play a major role in the determination of body energy balance which is a result of the balance in fat and protein turnover. Provided the predicted differences between the two groups of cows with regard to plasma concentrations of glucose, FFA, insulin and thyroxine (chapter 3) are correct, then the trends in the differences in metabolic flux rates, protein and fat turnover are also correct. However, much more information on the relation between concentration of these regulatory factors and the metabolic flux rates and balances are required. This would allow more reliable predictions of the size of differences in metabolic flux rates at a certain difference in plasma concentrations of regulatory factors.

The balance in protein and fat turnover, i.e. in body energy balance, was predicted from general knowledge about weight changes and body compositions at different stages of lactation in well fed dairy cows. More data on the relation between plasma concentrations of key regulatory factors and the rates of synthetic and catabolic processes in fat and protein turnover would improve the reliability of predicted nutrient consumptions and metabolic balances. However, although insulin and thyroxine are well established as key regulatory factors it is evident that other hormones may play a crucial role in different situations.

It seems evident that a prediction of metabolic rates as carried out in this chapter shows how useful present knowledge is in prediction of animal performance, but it also clearly indicates the weak points in the present knowledge of the field. Thus, the work presented in the present chapter provides a model for specifying areas in which future research is likely to yield progress in the field.

6 Nutrient metabolism in the mammary gland

By Mette O. Nielsen

6.1 Introduction

Milk synthesis occurs in the mammary gland and imposes a great demand on total nutrient turnover in the lactating dairy cow. The major metabolic pathways in the mammary gland involve synthesis of the milk components lactose, protein and fat plus formation of energy (oxidation) to drive the synthetic processes. The quantitatively most important substrates for milk synthesis in the ruminant are glucose, amino acids, acetate, beta-hydroxy-butyrate, and plasma lipids, primarily chylomicrons and low-density lipoproteins (Linzell, 1974). These nutrients are taken up by the mammary gland from the extracellular fluid, and the amount of nutrients taken up will determine milk synthesis and thus total milk yield. Much of the information available on nutrient uptake and nutrient metabolism in the mammary gland is based on isotopic tracer studies and arterio-venous difference investigations. From these investigations it seems clear that an important determining factor for nutrient uptake in the mammary gland is total nutrient supply, which in turn is determined by mammary blood flow and nutrient concentration in plasma. Still, however, much remains to be established concerning the regulation of nutrient uptake and metabolism in mammary tissues, and in this context especially the role of mammary gland synthetic capacity is completely unknown.

In the preceding chapters, nutrient metabolism in extramammary tissues have been dealt with. In tables 5.2 and 5.3 the amount of nutrients available for (and taken up by) the mammary gland has been estimated for cows from group S (free choice diet) and group F (complete diet) respectively. In the following sections of this chapter, metabolism of the available nutrients and milk synthesis will be presented and discussed with reference to actual observed milk yields in the two groups of cows.

6.2 Nutrient metabolism and milk synthesis

The calculated incorporation of nutrients into individual milk components (and the total milk production) are summarized in tables 6.1 and 6.2 for cows from groups S and F respectively.

The passage of the nutrients through various metabolic pathways in the mammary gland are presented in greater details in the figures 6.1 and 6.2.

Table 6.1 Nutrient uptake and milk synthesis in cows from group S.

Mammary uptake		Milk synthesis (kg/day)			
Nutrient	Moles /day*	Lactose	Protein	Fat	Total milk yield
Glucose	9.3	1.11	–	0.06**	–
Amino acids	5.5	–	0.63	–	–
Acetate + ketone bodies	43.3	–	–	0.76+	–
Plasma lipids	0.39	–	–	0.28++	–
Total	–	1.11	0.63	1.10	23.1

* Values taken from table 5.2.
** Glycerol, partly derived from glucose and glyceride-glycerol in plasma lipids.
+ De novo synthesized fatty acids with an average chain length of 12 C-atoms.
++ Preformed fatty acids with a chain length of 18 C-atoms.
For calculations: see text.

Table 6.2 Nutrient uptake and milk synthesis in cows from group F.

Mammary uptake		Milk synthesis (kg/day)			
Nutrient	Moles /day*	Lactose	Protein	Fat	Total milk yield
Glucose	9.7	1.16	–	0.06**	–
Amino acids	7.7	–	0.89	–	–
Acetate + ketone bodies	41.2	–	–	0.73+	–
Plasma lipids	0.60	–	–	0.43++	–
Total	–	1.16	0.89	1.22	24.2

* Values taken from table 5.3.
** +, ++: See legend to table 6.1.

6.2.1 Calculation of lactose synthesis

Lactose is synthesized in the mammary gland from glucose extracted from the extracellular fluid. Two moles of glucose are spent in the synthesis of one mole of lactose with an efficiency (on weight basis) of 95%. The synthesis of lactose imposes a great demand for glucose by the mammary gland. It has been seen in experiments with lactating goats and cows that 60–98% of total glucose flux, i.e. glucose consumption, is utilized in this relatively small organ (Annison and Linzell, 1964; Bickerstaffe et al., 1974).

The calculated distribution of glucose between mammary and non-mammary tissues in tables 5.2 and 5.3 is in fairly good agreement with these observations. Most of the glucose metabolized by the mammary gland is incorporated into lac-

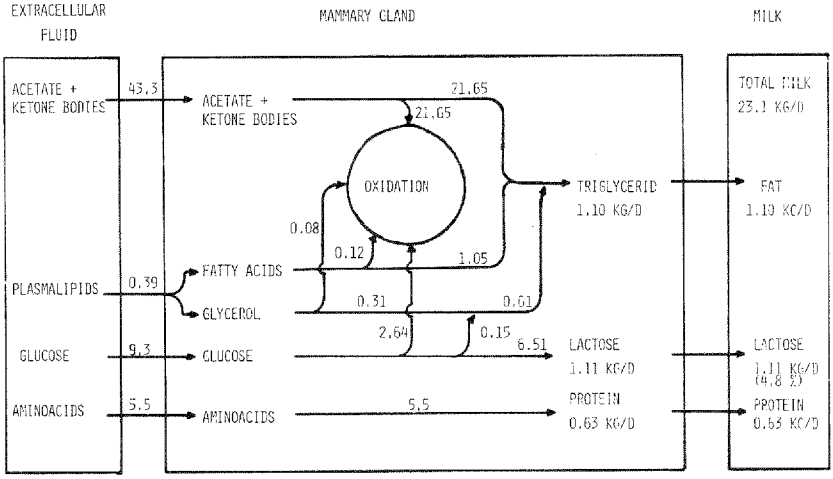

Figure 6.1 Nutrient metabolism and milk synthesis in the mammary gland in cows group S. All values in moles/d unless otherwise stated. For calculations see text.

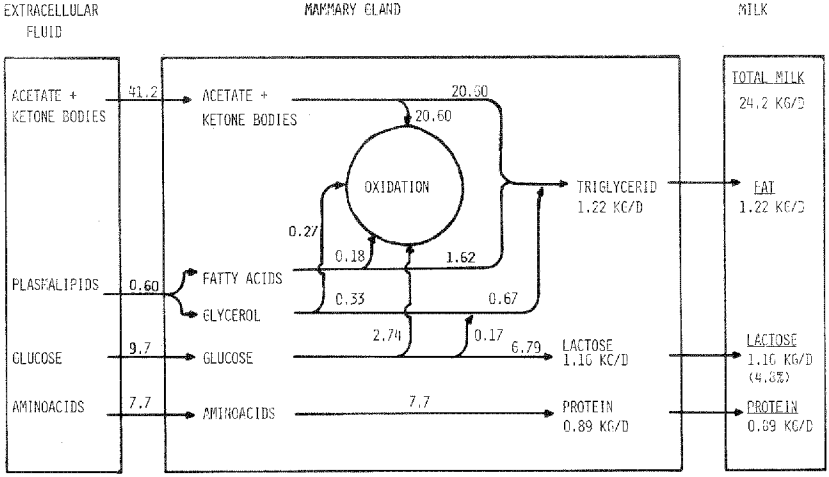

Figure 6.2 Nutrient metabolism and milk synthesis in the mammary gland in cows group F. All values in moles/d unless otherwise stated. For calculations see text.

tose. In goats and cows lactose synthesis accounts for approximately 70% of mammary glucose consumption (Annison and Linzell, 1964; Annison et al., 1974). Mammary uptakes of glucose of 9.3 and 9.7 moles/day in cows from group S and F thus give rise to a lactose production of 1.11 and 1.16 kg/day respectively.

6.2.2 Calculation of total milk yield

Lactose is the major osmotic factor in milk. Lactose concentration in milk is therefore fairly constant and not liable to change due to alterations in feeding regime. In cows of the breed in question (Black and White Danish Milk Breed), lactose content in milk is approximately 4.8%, and this figur has been used to calculate total daily milk yields in tables 6.1 and 6.2.

6.2.3 Calculation of protein synthesis

In established lactation more than 92% of the nitrogenous compounds in cows' milk are synthesized in the mammary gland and secreted in the form of proteins. As in other tissues, proteins are synthesized from amino acids extracted from the extracellular fluid. In arterio-venous difference investigations, it has been found that the proportion of amino acid uptake in the mammary gland to amino acid secretion in milk proteins varies rather much between individual amino acids. A number of amino acids are extracted in greater quantities than secreted. This is the case for the essential amino acid arginine and the branch-chained amino acids valine, isoleucine and lysine (Peeters et al., 1979). For the other essential amino acids, there is a close relation between uptake and secretion in milk proteins. Non-essential amino acids generally show deficit in uptake compared to the secretion in milk and are thus synthesized from other (essential) amino acids in the gland itself (Clark et al., 1978; Peeters et al., 1979; Mepham, 1982). Overall, however, total uptake of alfa-amino-N from the extracellular fluid is of the same magnitude as total alfa-amino-N secretion in milk (Bickerstaffe et al., 1974; Linzell, 1974; Peeters et al., 1979). The milk protein synthesis in tables 6.1 and 6.2 has thus been calculated directly from the mammary uptake of amino acids.

6.2.4 Calculation of fat synthesis

Triglycerides constitute approximately 98% of the total amount of lipids secreted into milk in cows (Davies et al., 1983). Synthesis and secretion of other lipid fractions are thus of minor quantitative importance. Triglycerides in milk fat differ significantly from triglycerides synthesized in other tissues by having a large content of short and medium-chained fatty acids (C4–C14). These fatty acids and part of palmitic acid (C16) are synthesized de novo in the mammary gland, primarily from acetate and beta-hydroxybutyrate. In goats, Annison and Linzell (1964) found that about half the amount of the acetate taken up by the mammary gland is used for de novo fatty acid synthesis, and the other half is oxidized. Long-chained (part of C16 and larger) fatty acids are derived from triglycerides in the plasma lipids, mainly low-density lipoproteins and chylomicrons. These fatty acids are incorporated into milk triglycerides virtually unal-

tered, and oxidation of long-chained fatty acids in the mammary gland normally seems to be very limited (Annison et al., 1967; Annison, 1983).

In calculating the milk fat synthesis in the tables and figures 6.1 and 6.2, it has been assumed that 50% of the acetate and ketone bodies extracted by the mammary gland are used for synthesis of de novo fatty acids with an average chain length of 12 C-atoms (MW=192). It has further been assumed that 90% of the long-chained fatty acids (C18) from plasma lipids are incorporated into milk triglycerides. The remaining 10% are oxidized in agreement with a model developed and described by Baldwin and Smith (1983). Glycerol on a weight basis accounts for about 5% of the triglycerides, and is derived partly from glucose and partly from glyceride-glycerol in plasma lipids.

Normally half (or more) of the fatty acids in milk fat from cows are long-chained and thus originates from extracted plasma lipids (Bauman and Davis, 1974; Bickerstaffe et al., 1974; Peeters et al., 1979). According to the calculations in tables 6.1 and 6.2, however, only 28% and 38% of the fatty acids in milk fat are long-chained. The uptake and contribution of plasma lipids to milk fat synthesis thus seems to have been underestimated especially in group S, while de novo synthesis from acetate and ketone bodies has been overestimated.

Milk fat yield could alternatively have been calculated assuming that 50% of the fatty acids in milk fat are derived from plasma lipids and the other 50% synthesized de novo. This would, on the other hand, have resulted in an unrealistically high oxidation of acetate (81% and 70% in groups S and F respectively).

The quantities of triglycerides available for and taken up by the mammary glands of cows from groups S and F were calculated to be 0.33 and 0. 51 kg/d respectively (tables 5.2 and 5.3). These values are in good agreement with measured triglyceride uptakes of 230–525 g/d in the mammary gland of lactating cows (Bickerstaffe et al., 1974; McNamara et al., 1983) with a daily milk fat yield of 0.35–1.3 kg/d. Acetate uptake in the mammary glands of cows from groups S and F was calculated to be 2.42 kg/d respectively (tables 5.2 and 5.3) which is equivalent to over 50% of the total amount of acetate available. These figures are extraordinarily high in comparison with results obtained in isotopic tracer experiments. Annison et al. (1974) and Bickerstaffe et al. (1974) thus found an acetate uptake in the mammary glands of Jersey and Friesian cows of only 0.230–0.518 kg/d or only 10% of total acetate entry in the whole animal. In these experiments, however, uptake of acetate could only account for a minor fraction of the total amount of fatty acids secreted in milk. Annison and Linzell (1964) also measured a quite low uptake of acetate in the mammary gland of lactating goats (14–15% of total acetate entry) except in one goat where 41% of total acetate entry was utilized by the mammary gland. Only in this goat could acetate account for 45% (by weight) of fatty acids secreted in milk (17–29% in

the other goats) as it is normally seen. It thus seems reasonable to believe that mammary acetate uptake generally has been estimated too low in these experiments. This is supported by the fact that acetate and glucose (the quantitatively far most important substrates in mammary oxidative metabolism) in such isotopic tracer studies only have accounted for around ⅔ of total CO_2 production in the mammary glands of cows (Annison et al., 1974; Bickerstaffe et al., 1974). Low estimates of mammary uptake of acetate could be due to methodological problems involved in isotopic tracer studies of acetate metabolism. Therefore, although the mammary uptake of acetate in tables 5.2 and 5.3 may be overestimated, it is at present impossible to evaluate to what extent.

6.3 Recorded milk yields

Milk yields in the two groups of cows were recorded in a feeding and production experiment (see chapter 1) and are presented in table 6.3.

Table 6.3 Average recorded milk yields in cows from groups S (free choice ration) and F (complete ration).

Yield	Group S		Group F	
	kg/d	% in milk	kg/d	% in milk
Milk	23.7	–	28.1	–
Lactose	1.14	4.8	1.35	4.8
Protein	0.81	3.43	0.89	3.17
Fat	0.89	3.74	1.14	4.07

6.4 Discussion

From the preceding sections, it appears that overall estimated milk yields and yields of individual milk component (tables 6.1 and 6.2) are in the same range as the recorded milk yields in table 6.3. Further, yields were estimated higher in group F that in group S, which is in agreement with table 6.3.

The greatest deviations in estimated from recorded milk yields were seen for protein (–22%) and fat (+24%) in group S, and for lactose (–14%) in group F. There seems to have been an over-estimation of de novo fatty acid synthesis in the mammary gland (see section 6.2.4), and this can at least partly explain the high estimate of fat yield in group S. There are still many unsolved questions concerning nutrient metabolism in the mammary gland and partitioning of nutrients between synthetic and oxidative pathways. Especially acetate metabolism and its regulation is poorly understood. Apparently uptake of acetate in the mammary gland has been underestimated in isotopic tracer studies, and as already mentioned (section 6.2.4) this may be due to methodological difficulties

involved in measuring acetate metabolism. An important task in the future will therefore be to develop new and more reliable methods for measuring nutrient uptake in the mammary gland and especially the roles of acetate and fatty acids in mammary metabolism need to be further elucidated.

In tables 6.1 and 6.2 nutrient uptakes in the mammary gland have been estimated as total nutrient flux — nutrient consumption in nonmammary tissues. This may be a backward procedure. Under many conditions, it is more likely the nutrient uptake and synthetic activity in the mammary gland that determine nutrient availability and consumption in other tissues. The precise role of the mammary gland in partitioning of nutrients between mammary and non-mammary tissues and the changes which occur through lactation are, however, only poorly understood. It has been suggested that the synthetic capacity of the mammary gland can be a determining factor for mammary nutrient uptake (Nielsen, 1988) since the stimulating effect of growth hormone on milk yield seems to involve increased activity of some key enzymes in the gland. It has also been suggested that it is the nutrient supply to the mammary gland that determines the rate of nutrient uptake and thus milk synthesis. In agreement with this suggestion, fairly close correlations have been observed between mammary blood flow and milk yield in both lactating cows and goats (Linzell, 1974; Mepham, 1982). But whether it is mammary blood flow that determines mammary metabolism, or mammary metabolism that determines mammary blood flow is still unknown. It will be of great importance to elucidate the role of the mammary gland in nutrient partitioning in order to get a better understanding of what induces changes in milk yield in response to alterations in various conditions such as feeding regime and stage of lactation.

7 Breeding aspects of physiological measurements in dairy cattle

By Poul Henning Petersen

7.1 Introduction

In recent years scientists have showed an increasing interest for the physiology of the domestic animals for various reasons. The increasing intensity of production brings along a higher pressure on the animals and farmers as well as more public concern about health and welfare of animals and the wholesome food products. It is felt that a better understanding of the physiology of production may help not only to improve production efficency but also to prevent some of the objectionable effects of modern production methods on the welfare of animals and the quality of products.

In animal breeding recent developments have improved the traditional statistical-genetic methods and practical breeding measures have been reformed to something close to perfection. In order to find new ways the scientists among other things are looking for physiological predictors of genetic merits of breeding amimals. Challenge test of potential bull calves with intensive measurements of physiological traits with the purpose to predict the breeding values for milk production may well be part of the selection programmes in a near future.

It is the purpose of the present study to focus on the problems and prospects of using physiological traits in the dairy cattle breeding.

7.2 Estimation of genetic parameters for physiological traits

Estimation of genetic parameters for physiological traits, including their associations to production traits, is complicated as rather large family structured data sets are required. Genetic studies on simultaneously measured physiological activities and milk yield would be costly because of the required technology. Furthermore, a certain physiological activity by lactating animals has to be considered a different genetic trait as compared to the same activity by non-lactating relatives of the opposite sex, and therefore genetic parameters for physiological traits of lactating cows might well be useless as tools for prediction of breeding values from similar measurements on male calves.

The most realistic procedure for routinely procuring relevant data for estimation of genetic parameters should include measurements of physiological traits of the bull calves at the performance test stations and measurements of the performance of their half sib of daughter groups in the production herds. The mea-

surements of half sib groups of performance tested bulls would form the basis for estimation of heritabilities and genetic correlations for the physiological traits, and the genetic associations between physiological and production traits would be obtained from correlations relatives at the stations and in the field.

The first attempts to estimate the mentioned genetic parameters for physiological traits were reported by Joakimsen et al. (1971). The genetic correlation between thyroxine degradation in mature breeding bulls and milk yield of the daughter groups was estimated to, r_G=0.42. These investigations were followed up by studies on performance tested bulls and their daughter groups (Sørensen et al., 1981). They obtained an heritability estimate of, h^2=0.19, for thyroxine degradation and a genetic correlation to fat yield of, r_G=0.42.

7.3 Breeding aspects

Modern breeding programmes are based on a solid knowledge about the quantitative genetics of the production traits and on a selection theory which has been proven efficient in practice.

Inclusion of secondary traits, among these workability traits and physiological measurements, in well established and efficient breeding programmes, requires adequate knowledge about the genetics of these traits, including their association to the milk production traits. Furthermore, as each physiological activity is only an element of the process which leads to milk secretion, potential sideeffects have to be considered in case that this element is appointed a selection criteria.

Measuring physiological traits on lactating cows as part of the procedure for evaluation of breeding values for milk production does not seem worth the efforts, as the total index, namely milk yield itself, is easily registrated simultaneously. The additional information from physiological measurements would probably be of negligible value and the generation intervals would be unchanged.

In dairy cattle breeding the major impediment for a rapid genetic improvement of the population is the long generation intervals, especially for the bulls where progeny testing is required before the genetic merit for milk production can be accurately estimated. In case the breeding value could be predicted with even a moderate accuracy from genetically associated physiological traits of the young bull at the performance test subsequent selection might speed up the rate of improvement.

Sørensen et al. (1981) presented heritability estimate, h^2=0.19, for thyroxin-degradation rate in performance tested bulls, and an estimate of the genetic correlation between this trait and butterfat yield registrated from daughter groups in production herds, r_G=0.42. The accuracy of predicting the breeding value of the young bull for fat yield on the basis of hormone measurements becomes,

$r_{IA}=h.r_G=\sqrt{0.19}x0.42=0.18$, and an estimated selection of 50% of tested bulls on the basis of this criteria would result in a genetic superiority of 2.3 kg butterfat for the young bulls.

With no reduction of the generation intervals this selection response would increase the expected anual genetic gain from 1.56% in the conventional selection programme (Petersen et al., 1974) to 1.61%.

Petersen (1973) evaluated a simplified model of the conventional breeding structure, where selection for hormone activity on performance tested bulls was followed by immediate use of these bulls, as the only cow sires, to 95% of the cow population. The 5% best cows were mated to ordinary progeny tested bull sires. For the combination of genetic parameter estimates mentioned above, i.e. $r_{IA}=0.2$, the optimum breeding plan was expected to yield an annual genetic gain of 1.30% in fat yield. In spite of the reduced response as compared to the 1.56% for the conventional plan the net returns were approximate equals for the two breeding plans, which was due to reduced costs of bull maintenance and semen production and storage for the plan with selection on hormone activity.

Christensen & Liboriussen (1985) evaluated the aspects of including physiological predictors in the juvenile MOET scheme outlined by Nicholas & Smith (1983). On the assumption that selection was performed in both sexes on the basis of a physiological trait with a heritability of, $h_2=0.2$, and a genetic correlation to milk yield of $r_G=0.5$, it was estimated that the expected genetic progress could be increased by 31%.

7.4 Concluding remarks

The present knowledge concerning physiological processes as potential predictors in a selection programme is insufficient for practical application. The first results indicate that utilization of a single predictor may not offer great prospects, but it is very likely that an index based on more physiological traits may change the conventional selection programme and increase the improvement rate.

The increasing knowledge of the physiology of the high yielding dairy cow may influence the breeding work in an indirect way. An increasing understanding of the physiological background of the overall productivity of the dairy cow may help to foresee potential unfavourable sideeffects of onesided selection efforts.

8 Conclusion and perspectives

By Poul Martin Riis

According to the introduction the aim of the present work was to establish an objective method or a model for evaluation of knowledge for identification of limiting factors in production, for improved utilization of accumulating information and for specification of fruitful research areas (section 1.2). The model is established and described in the chapters 2–7. The following is an attempt to show to what extent the model serves the purposes aimed at.

8.1 Prediction of production through estimated metabolic flux rates

The value of research information related to dairy production may be estimated by its usefulness in prediction of production under given circumstances and in estimation of requirements for a certain wanted production. Thus a comparison of the predicted performance with the actually recorded milk production and body gains should give an evaluation of our present available knowledge in the field.

Table 8.1 shows that in all cases the predicted values were close to the re-

Table 8.1 Predicted and recorded performance of dairy cows fed ad libitum on a free choice ration (S) and a complete pre-mixed ration (S).

Predicted milk yields are transferred from tables 6.1 and 6.2.
Predicted body gains of protein and fat are transferred from figures 5.1–5.4.
Recorded milk yields are transferred from tables 1.1 and 1.2. The "recorded" gains in body protein and fat are calculated from the recorded body weight gains (tables 1.1 & 1.2 under the assumption that 1 kg body gain contains 100 g of protein and 600 g of fat.

Production component	Yield, kg per day			
	group S		group F	
	prediction	recorded	prediction	recorded
Milk	23.1	23.7	24.2	28.1
Milk protein	0.63	0.81	0.89	0.89
Milk fat	1.10	0.89	1.22	1.17
Milk lactose	1.11	1.14	1.16	1.35
Body weight gain	0.60	0.63	0.40	0.33
Body protein gain	0.06	0.064	0.04	0.033
Body fat gain	0.36	0.38	0.24	0.19

corded productions. The difference between the two groups was predicted to the correct direction although the order of difference in milk yields was considerably underestimated. The predicted difference in body weight gain was close to the observed difference.

The prediction of body weight gain was based on empirical experience from production experiments with cows in similar situations. The difference in weight gain was more or less a guess based on predicted plasma concentrations of insulin, somatomedin and thyroxine (chapter 3). It is known that energy-balance in lactating cows correlates positively with plasma concentrations of insulin, triiodothyronine and tetraiodothyronine (thyroxine), but the order of energy-balance at a certain level of these hormones is not known (Kunz and Blum, 1985). It is apparently a fortunate coincidence that the predicted difference between the weight gains in the two groups was that close to the recorded one.

Predicted as well as "recorded" values for protein and fat gain are calculated on the assumption that 1 kg body gain contains 100 g of protein and 600 g fat (Sørensen, 1984). Protein and energy balances were not measured in the experiment, there were therefore no true recorded values of protein and fat gain.

It appears from the discussion in chapter 6 that the crucial factor in prediction of milk yield was the estimated uptake of glucose in the udder. It was assumed that lactose formation accounted for 70% of the glucose uptake and that lactose concentration in milk was constantly 4.8%. The prediction of milk fat and milk protein secretion was obtained independantly of this figure. The fact that predicted milk yield for group S was very close to the recorded yield (table 8.1) justifies the conclusion that available data form basis for prediction of the correct order of glucose flux rate and partition in lactating cows.

The prediction of lactose secretion in group F was apparently too low. The reason may be an underestimation of total glucose flux rate or error in the predicted partition of total glucose between mammary and non-mammary body tissues (section 5.2.1). A comparison of the recorded and predicted values for protein secretion supports the idea that total gluconeogenesis was higher than predicted in group F.

For group F the predicted milk protein output was equal to the recorded yield whereas for group S the predicted value was considerably lower than the recorded milk yield. This may indicate that the total amino acid entry rate was predicted too low in both groups and the amount used for gluconeogenesis underestimated for group F but correctly estimated for group S.

According to the estimations in chapter 4, amino acids provide ¼ of the total substrate for gluconeogenesis. This value is in accordance with an estimate made in the review by Lindsay (1983). Nevertheless, variations in gluconeogenesis from amino acids may easily give variations in glucose supply which are equivalent to 0.2 kg lactose, 3.5–4 l milk.

It is unlikely that the whole error in predicted glucose supply to the udder in group F cows was on the entry rate of amino acids from the alimentary tract. Errors in the estimated flux rates of amino acids through metabolic pathways in the liver (chapter 4) and in the glucose consumption by non-mammary body tissues (chapter 5) may be important contributing factors.

The possible reasons for the overestimation of milk fat output, especially in group S, were discussed in some detail earlier (section 6.4).

In view of the rather small differences between predicted and recorded performance of the cows, it appears safe to conclude that available research data allow a reasonably correct prediction of flux rates through metabolic pathways in lactating cows. The model used in the present work yields presumably also a better prediction of production than a mere guess based on experience from previous production experiments. It seems likely that the model used from the other end, i.e. from a given production would have yielded a fairly good estimate for the nutrient requirement for this production. The use of the model has thus given an evaluation of the available research information. The above analysis of the crucial factors in prediction of individual parametes indicates the factors limiting productional efficiency.

8.2 Factors limiting productional efficiency

Productional efficiency usually increases when the rate of production increases. With a complete change of system one could imagine that increased efficiency could be associated with lower production rate. A major factor determining rate of production is the level of feed intake. The present model starts with a given feed intake. It does therefore not include discussion of factors affecting level of feed intake. This question was reviewed by Madsen (1983) and possibilities for control of energy intake through variation in feed composition were discussed by Kristensen (1983). When the feed intake is given, the amount of absorbed energy and different nutrients as well as their partition between tissues become the determining factors.

In the model, the amount of glucose uptake in the udder was used as the factor determining the milk production (chapter 6). The glucose uptake reflects the lactose formation which accounts for 75–80% of total glucose consumption by the udder. Lactose concentration in milk is almost constant because it is the major osmotic factor and milk is isoosmotic with blood. It follows, therefore, that the rate of lactose formation determines the rate of milk secretion. The rate of lactose formation is determined by the activity of the lactose synthetase and the glucose supply (Kuhn, 1983; Nielsen, 1988).

The activity of this and other enzymes, which constitute the synthetic capacity of the mammary gland, may be highly controlled by hormones as placental lactogen, pituitary prolactin and growth hormone (Nielsen, 1988). The secre-

tion of these hormones is presumably mainly genetically determined (chapter 7). The glucose supply is a function of gluconeogenesis and the partition of glucose between mammary and non-mammary body tissues.

Regulation of gluconeogenesis has recently been reviewed by Kraus-Friedmann (1984). Supply of gluconeogenic precursors is of course a critical factor. It is also evident from the discussion in section 8.1 that entry rate of the major gluconeogenic precursors, amino acids and propionic acid, may be limiting factors for milk production.

Utilization of the synthetic capacity in the mammary gland is dependant upon an adequate fuel supply. The major fuels in the mammary gland are acetate and long chain fatty acids (chapter 6). Acetate is the dominating fuel. It accounts for up to ¼ of total CO_2 production in the mammary gland (Baldwin and Smith, 1983). It is also an old, general observation that feed composition leading to high proportions of acetate in the total amount of volatile fatty acids entering from the alimentary tract favours milk formation (Riis, 1964).

Fuel is of course not the only factor necessary for efficient utilization of the synthetic capacity, adequate supply of precursors for milk components is also needed. The importance of glucose and amino acid supply was discussed above. Milk fat is formed from acetate and long chain fatty acids. Milk fat formation is thus limited by the same factors as the fuel supply. High synthetic activity strengthens the ability of the udder to drain nutrients from the extracellular nutrient pool. The homeostatic and homeorhetic hormonal adaptation to lactation also favours the mammary gland in the partition of the available nutrients between mammary and non-mammary body tissues (Bauman & Currie, 1980; Collier et al., 1984; Thilsted, 1985b; Riis & Madsen, 1985).

Mobilization of body components may supply a small amount of milk precursors for a period. However, the main part of the precursor supply must come from the absorbed nutrients. The emphasis on glucose and amino acids above supports rather than challenges the old theory that the rate of milk production depends upon the total amont of absorbed nutrients as well as on the relationship between individual absorbed nutrients.

8.3 Utilization of new research information

Publications of original research data concern normally a limited area. The utilization of such information requires the data placed in a wider connection. That is a model covering a complete functional unit. The advantage of the present model is that it is very easy to overlook the consequences of incorporation of new data. The simplicity of the model gives an advantage with respect to its use for identification and specification of fruitful research areas, whereas more complicated computerized models may give larger improvement with regard to prediction, when new data are incorporated.

8.4 Fruitful areas for future research

Some of the most critical questions emerging from the discussion in chapters 2–7 are:

1. What is the pattern and rate of nutrient absorption on different rations?
2. How does change in entry rate of amino acids and propionic acid from the digestive tract affect the rate of gluconeogenesis?
3. What is the partition ratio of total glucose entry between mammary and non-mammary body tissues on different conditions of feeding and hormonal balance?
4. What is the entry rate of acetate from the digestive tract and its partition between mammary and non-mammary body tissues?
5. How is total heat production divided between mammary and non-mammary body tissues and how is it related to the hormonal balance?
6. What is the relative importance of placental lactogen, pituitary prolactin in the build up and maintenance of synthetic capacity of the mammary gland?
7. What is the role of placental lactogen, pituitary prolactin and growth hormone in the homeorhetic adaptation to lactation?

It appears from the discussion in previous sections that these questions and others that could be derived from the discussions are all critical for the performance of lactating ruminants. The answers to these questions will add to our ability to control and thus increase productional efficiency. We may therefore conclude that the model established in the chapters 2–7 represents a useful tool for identification and specification of fruitful areas for future research.

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