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MANIPULATING METABOLIC PARAMETERS TO IMPROVE GROWTH RATE AND MILK SECRETION[1]

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Summary

Several opportunities for improving animal efficiency through manipulation of metabolism are discussed. The first opportunity is through identification and selection of animals achieving close to theoretical efficiencies. Based upon differences between highly efficient and average animals, the estimated opportunity for improvement is 20%. A second opportunity for improvement is through manipulation of apparent maintenance requirements. Several contributors to differences in efficiencies are considered. One is the contribution of differences in relative organ weights to differences in apparent maintenance requirements. A potential benefit in the order of 10 to 20% through selection or manipulation seems possible. Manipulations of ion transport and protein turnover could yield maximum benefits of 30 and 15%, respectively. However, complete elimination of these processes is not feasible. Without ion transport, membrane potentials would not be maintained and, without turnover, many important regulatory processes would be affected. The limit to manipulation of these characteristics is unknown. A third opportunity for improvement of animal efficiency is through improvement of apparent biosynthetic efficiency by manipulation of patterns of nutrient utilization. If we could produce, through hormonal or other types of manipulations, an optimum pattern of nutrient use, decreases in heat increments of production in growing animals in the order of 50% might be achieved.

(**Key Words:** Ruminant Metabolism, Maintenance, Production, Energy Metabolism, Efficiency, Growth.)

Introduction

The topic, manipulation of metabolic parameters to improve efficiency of growth and milk production, can be approached in a number of ways. We chose to emphasize identification of opportunities for manipulating and evaluating constraints and possible benefits. It is well known that gross efficiency of production increases with food intake. Therefore, manipulation of food intake will not be considered. Rather, efficiency at a given feed intake will be the reference state. A brief review of the basic terminology of nutritional energetics will be presented so that terms used are interpreted as intended. Then a discussion of elements of energy expenditure and variations in these will be undertaken. The premise of this discussion will be that when considerable biological variation exists, opportunities for improvement are embedded within the variation. Next, an attempt will be made to identify some basic characteristics or parameters of metabolism which might be manipulated. Along with this, inherent constraints imposed upon manipulation will be considered.

Basic Definitions and Elements of Animal Energy Expenditure

Definitions. Metabolizable energy (ME) is considered to be that portion of food energy which is available to the animal for metabolism (Armsby, 1917). Various modifications directed at obtaining more accurate estimates of energy available to the animal for metabolism have been suggested (NRC, 1966). However, the basic definition of ME remains as it was at the beginning of the century: ME = gross energy

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(GE) - energy in feces, urine and gaseous products of digestion.

ME supplied to animals at the maintenance level divides into net energy for maintenance (NE_m) and the heat increment of maintenance (HI_m), where NE_m is equivalent to the amount of body substance spared by food eaten or the amount of energy required for performance of vital functions; HI_m includes energy expenditures associated with digestion and assimilation of food and $ME = NE_m + HI_m$.

ME provided to animals in excess of maintenance requirements can be partitioned into energy which appears in the product (net energy of production; NE_p) and the heat increment of production (HI_p). The latter is the total cost of synthesis of the product. Gross efficiency is energy in the product divided by total ME intake. Net efficiency is energy in the product divided by the amount of ME supplied above maintenance.

In the following paragraphs, selected elements of fasting metabolism, the HI_m and the HI_p will be discussed. In addition, variation in these and opportunities for manipulation will be identified.

Maintenance. In general, elements of maintenance energy expenditure can be divided into two groups: service functions and functions associated with cell maintenance (table 1). Service functions are those performed by tissues for the benefit of the integrated organism and they include kidney work, heart work, respiration, integrative nerve functions and liver service functions. In total, readily identifiable service functions account for 35 to 50% of the total basal energy expenditures of an animal. Cell maintenance functions include protein resynthesis, lipid resynthesis and ion transport. These are functions essential to the maintenance of individual tissues or cells. Cell maintenance functions account for 40 to 55% of the basal energy expenditures. Since service functions are essential to maintenance of an integrated organism, it is difficult to identify significant opportunities for gaining benefit through manipulation of these functions without postulating increases in work efficiency. In the case of cell maintenance functions, some significant benefit might be obtained by decreasing rates of protein turnover or reducing energy expenditures in ion transport. It has been shown that energy expenditures in ion transport in hypothyroid animals are significantly less than those in normal organisms

TABLE 1. ENERGY EXPENDITURES IN SEVERAL MAJOR MAINTENANCE FUNCTIONS[a]

Function	% basal energy expenditure
Service functions	
Kidney work	6 to 7
Heart work	9 to 11
Respiration	6 to 7
Nervous functions	10 to 15
Liver functions	5 to 10
Total	36 to 50
Cell maintenance	
Protein resynthesis	9 to 12
Lipid resynthesis	2 to 4
Ion transport	30 to 40
Total	40 to 56

[a]*Derivation* of these estimates was discussed in detail by Baldwin (1968), Milligan (1971) and Baldwin and Smith (1974).

(Ismail-Beigi and Edelman, 1970). Whether a reduction in energy expenditures in ion transport could be accomplished without encountering the undesirable effects of hypothyroidism is not known. In a later section, constraints and possible limitations upon attempts to gain benefits in efficiency through manipulation of maintenance functions will be discussed further.

The estimates presented in table 1 are those for an animal in the fasting condition in which fatty acids derived from adipose tissue are the primary energy source. Animal energy expenditures at maintenance can vary significantly depending upon energy source because of differences in the efficiencies with which energy is trapped as ~P in different metabolic pathways. The magnitude of this variation is depicted in table 2, where values of nutrients for maintenance are expressed in relation to stearate. Relative values vary from lows of 80 to 83% for proteins to a high of 105% for glucose. These estimates imply that actual energy expenditures for maintenance in an animal can vary by as much as 20 to 25%, depending upon the nutrients available.

Another source of variation in apparent maintenance requirements is illustrated in figure 1 and table 3. The data shown in figure 1 indicate that maintenance requirements might vary considerably as a function of feed intake. Real estimates of variations in maintenance

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TABLE 2. RELATIVE VALUES OF SEVERAL NUTRIENTS FOR MAINTENANCE[a]

Energy source	Heat loss/~P, kcal	Relative value, %
Stearate	18.6	100
Glucose	17.7	105
Acetate	20.9	89
Propionate	20.4	91
Butyrate	19.4	96
Proteins	22.4 to 23.3	80 to 83

[a]Bases for estimates were discussed by Baldwin (1968), Milligan (1971) and Baldwin and Smith (1974).

energy requirements per unit of metabolic body size ($BW^{\cdot 75}$) range from 40 to 140 kcal (Reid, 1974). Variation in feed intake is not the only cause of differences in maintenance requirements, but it can make a significant contribution. Changes in weights of intestine and liver with feed intake are shown in figure 1. Energy expenditures per unit of mass of liver and intestine are significantly in excess of average body energy expenditure per unit of mass (table 3). Therefore, increases in the relative weights of these tissues increase average body energy expenditure. This effect is shown in table 3, where differences in organ weights are related to differences in maintenance requirements of nonlactating and lactating cows. Relative weights of the digestive tract, liver and heart, all high energy expenditure tissues, increase significantly during lactation. This, presumably, reflects the higher feed intake and work loads imposed upon these tissues in lactating animals. As a result of these tissue changes, energy expenditure per unit of metabolic body weight increases from 110 to 121 kilocalories. These observations suggest that identification of animals that could handle high nutrient intakes without experiencing increases in relative weights of high energy-requiring tissues could reduce apparent maintenance requirements by 10 to 30%. On the basis of available data, it is not possible to assess the potential for gaining improvements in energetic efficiency through selection of animals with this goal in mind. However, as emphasized by Reid (1974), considerable variations in maintenance requirements of producing animals do exist. We are suggesting that a contributor to this variation could be that the liver, heart and gastrointestinal tissues can handle the higher work loads of production in some animals without undergoing hypertrophy.

HIM. The HI_m represents costs of digestion, absorption and assimilation of a meal. A quantitative assessment of these elements is presented in table 4. These calculations assume consumption of one or two meals a day. Two sources of variation in HI_m are identified. The first is composition of diet. Two diets are considered: (1) high carbohydrate and (2) one-half carbohydrate and one-half fat. The heat increment associated with the mixed diet is less than one-half that associated with the high carbohydrate diet. A greater effect of diet composition is seen when protein is used to a significant extent as a source of energy. In the case of high protein diets, as discussed by Krebs (1964) and Baldwin and Smith (1971a), theoretical and observed heat increments of HI_m are in the order of 25 to 30% of ME. Current technology makes possible the formulation of diets that produce minimum energy expendi-

TABLE 3. EFFECTS OF RELATIVE ORGAN SIZE ON HEAT PRODUCTION AT MAINTENANCE[a]

Tissue	Nonlactating		Lactating	
	% BW	kcal/day	% BW	kcal/day
Carcass	58.0	3,892	53.6	3,602
Digestive tract	3.75	1,078	4.85	1,383
Liver	1.3	3,369	1.65	4,220
Heart	.35	1,497	.45	1,843
All tissues	92.9	14,971	92.9	16,476
$Kcal/kg^{\cdot 75}$		110		121

[a]Adapted from Smith (1970).

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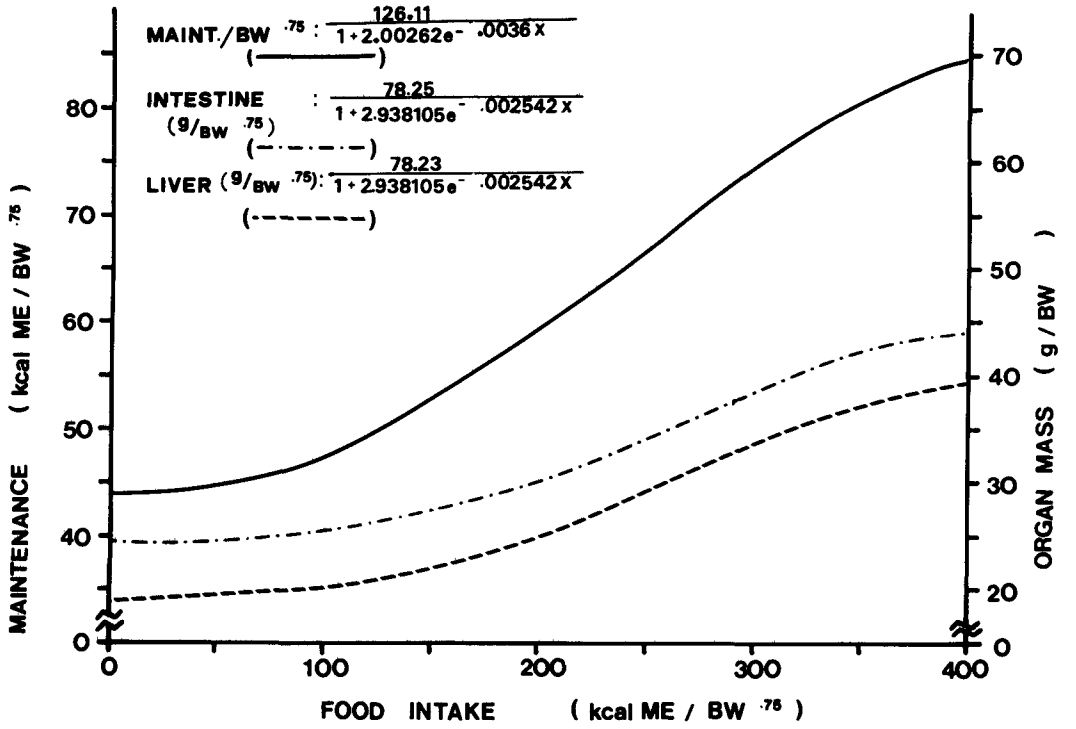

Figure 1. Relationship between food energy intake and maintenance energy requirement (——). Also shown are changes in weights of intestine (- • - •) and liver (- - - -) as a function of energy intake (R. Cänas, *unpublished data*).

tures in digestion, absorption and assimilation, even for ruminants (Lofgreen, 1965).

Another source of variation in HI_m is to be considered. Nearly 65% of the energy expenditures associated with HI_m are for storage of carbohydrate as glycogen or fat. Frequent feeding would be expected to reduce storage costs and, as a result, HI_m. An extreme example of this was continuous infusion of glucose at the maintenance rate throughout the day (Blaxter, 1962). In that case, energy expenditures in digestion and absorption were avoided,

TABLE 4. ESTIMATED HEAT INCREMENTS OF TWO MEALS FED AT MAINTENANCE AND ABOVE[a]

Process	Carbohydrate meal	Mixed meal	Above[a] maintenance
	%		
Bond breakage	.5	.3	.3 to .4
Absorption (active transport)	2.6	1.3	1 to 2.5
Digestive secretions	2.0	2.0	1 to 2
Assimilation and(or) storage	....	....	1 to 2
Glucose as glycogen (.3 × 5%)	1.5	1.5	....
Glucose as fat (.5 × 15%)	7.5	....	....
Fat as fat (.5 × 3.0%)	....	1.5	....
Theoretical HI_m	14	6.6	3.3 to 7.0
Observed HI_m	10 to 15	6 to 8	25 to 45

[a]Adapted and updated from Baldwin and Smith (1974). A normal, balanced diet was considered for the above maintenance example.

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the necessity for assimilation or storage was alleviated and the heat increment was reduced to zero.

Efficiency of Gain. On the basis of our knowledge of metabolic pathways, it is possible to compute theoretical estimates of maximal efficiencies with which animals can perform productive functions. Baldwin (1968) Baldwin *et al.* (1970) Baldwin and Smith (1971a, b) Krebs (1964) and Milligan (1971) have made such calculations. Theoretical estimates of efficiencies of growth and lactation in rats and ruminants obtained in this fashion are presented in table 5. The theoretical efficiencies for growth in the rat range from 75 to 85%. Differences are due to assumptions regarding alternate metabolic pathways chosen for the synthesis of fat, in the case of growth, and of lactose and fat in the case of lactation. This emphasizes that there is no unique estimate of theoretical efficiency. Rather, one obtains a range of estimates. Estimates from the literature of observed efficiencies of growth and lactation in rats and ruminants are also presented in table 5. Maximum observed efficiencies are sometimes quite comparable to theoretical efficiencies. On the other hand, observed efficiencies considerably below theoretical are also observed. This variation in observed efficiencies raises two important questions: (1) Could we learn to identify animals that are capable of attaining maximum efficiencies and based on genetic selection improve the average efficiency of animal production? (2) If we knew exactly what types of unfortunate metabolic decisions the less efficient animals were making, could we manipulate the metabolism of those animals such that their efficiencies would approach those of the best animals? It would seem there is an opportunity here which is well worth exploring.

Another major source of variation in the HI_p or apparent efficiency of production is the balance of nutrients supplied to the animal. Relative efficiencies for conversion of acetate to fatty acids, glucose to fatty acids and diet fat to body fat are presented in table 6. One can see that the theoretical efficiency of fat synthesis can vary from 68 to 96%. Experimental estimates of efficiencies of fattening based on these substrates bear out the suggestion that considerable differences in efficiency of fattening can occur depending upon what substrate or nutrient serves as precursor. Similarly, glucose can be converted to lactose much more efficiently than propionate can be converted to lactose. This is one of the costs ruminants pay for the contribution of microbes to digestive function. These summary estimates of relationships among nutrients provided and net efficiency raises two more questions: (1) Can we provide animals an optimum balance of nutrients so as to attain maximal efficiencies? (2) Can we economically supply such a diet to our animals? We must know more before we can answer these questions or take appropriate actions.

In an earlier section, turnover and repair as elements of maintenance were discussed. Turnover costs also appear to contribute to the HI_p. The data presented in table 7 emphasize that turnover rates of protein vary considerably, depending upon age and body size, and also that turnover can be a very significant contributor to energy expenditures. For example, in the young rat, as much as 41% of liver protein must be replaced each day. In the young lamb, 8.4% of liver protein is replaced each day. High turnover rates certainly

TABLE 5. COMPARISON OF THEORETICAL AND REAL NET EFFICIENCIES OF PRODUCTION[a]

Function	Animal	Theoretical	Observed
		%	
Growth	Rat	75 to 85	30 to 70
	Ruminant	70 to 80	30 to 60
Lactation	Rat	84 to 88	70 to 85
	Ruminant	72 to 76	50 to 72

[a]Adapted from Baldwin and Smith (1974).

TABLE 6. COMPARISON OF THEORETICAL AND REAL PARTIAL EFFICIENCIES[a]

Precursor → product	Theoretical	Real
	%	
Acetate → fatty acids	68 to 72	30 to 60
Glucose → fatty acids	82 to 85	60 to 80
Diet fat → body fat	94 to 96	90+
Amino acids → protein	75 to 85	33 to 80
Glucose → lactose	95	....
Propionate → lactose	75 to 80	....

[a]Adapted from Baldwin and Smith (1974) and Milligan (1971).

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TABLE 7. PROTEIN TURNOVER RATES FOR SEVERAL RAT AND LAMB TISSUES[a]

Tissue	Rat		Lamb	
	Age, days	Turnover, %/day	Age, days	Turnover, %/day
Liver	10	41	10	8.4
	100	18	200	5.3
Heart	10	4.7	10	1.2
	100	3.0	200	.9
Gut	10	16	10	3.1
	100	9.0	200	2.6
Muscle	10	2.3	10	.5
	100	1.2	200	.3

[a]From Baldwin and Black (1979).

lower the net efficiency with which protein accretion occurs. Thus, potential benefits through the reduction of protein turnover rates apply not only in the maintenance state as discussed above, but also to the net efficiency of protein accretion.

To illustrate the benefit that might be obtained from the manipulation of rates of protein turnover, the following example is presented. If protein accretion simply required the digestion, absorption, transport and uptake of amino acids and, finally, the synthesis of a peptide bond, net efficiency of protein accretion would fall in the range of 75 to 84% (6 to 10 ~P/peptide bond synthesized). Turnover costs can reduce this efficiency by 15 to 40%. As a result, net efficiency of protein synthesis varies between 35 and 70%. Factors in addition to turnover which might reduce net efficiency of protein accretion include the use of amino acids as energy sources and rearrangements among nonessential amino acids that might be required to match the balance of nonessential amino acids of the diet to that of the protein synthesized. Losses associated with the use of amino acids as energy sources can be minimized in diet formulation. Our calculations of reductions in net efficiency produced by rearrangements among nonessential amino acids suggests that these losses are relatively small.

The major factor beyond cost of synthesis that affects net efficiency of protein accretion appears to be turnover under normal conditions. Hence, the only real opportunity for increasing efficiency of protein accretion in growing animals may be to decrease protein turnover. Several limitations must be imposed when one considers manipulation of protein turnover rates. The first is that adaptations of organisms to new physiological states, new dietary challenges, etc, require that protein turnover occur. For example, when diet shifts require a change in enzyme patterns in the liver, the synthesis of some enzymes must increase while others decrease. In addition, rates of degradation must remain the same or increase to achieve a rapid adjustment in enzyme patterns. We would not want to interfere with protein turnover to the extent that it would limit or depress the ability of an animal to adapt to new dietary and physiological conditions. A second limitation that one must consider is osmoregulation. Continuing turnover of albumin, for example, assures that the animal can respond to differing states and maintain osmotic balance. A third limitation is that turnover helps the animal maintain homeostasis in amino acid patterns in blood. Turnover modifies effects that imbalanced diet proteins have upon blood amino acid patterns, preventing severe fluctuations in patterns and concentrations of amino acids in blood. Before we undertake studies directed at regulation of protein turnover, a study of how much of a reduction in protein turnover can be safely accomplished should be undertaken.

Adipose Tissue. Adipose tissue metabolism in both meat - and milk - producing animals is of interest. In growing animals, adipose tissue determines composition of gain. In lactating animals, adipose tissue can determine the availability of energy for milk synthesis. In figure 2, a diagram of adipose metabolism in a lactating cow is presented. This diagram accommodates three observations not presented in a previous analysis (Baldwin *et al.*, 1976). The first observation is that turnover of triacylglycerol is elevated in cow adipose tissue during lactation. Triacylglycerol turnover contributes to total animal energy expenditures (see below). The second point emphasized in the diagram is that considerable lactate release from adipose tissue occurs (Yang and Baldwin, 1973). From the standpoint of preservation of glucose precursors within the animal, this is a desirable function. On the other hand, lactate released by adipose tissue must be converted to glucose in liver and this is an energy requiring function. The third point illustrated in the figure is that the cost of triacylglycerol synthesis can vary significantly (60 to 65% when

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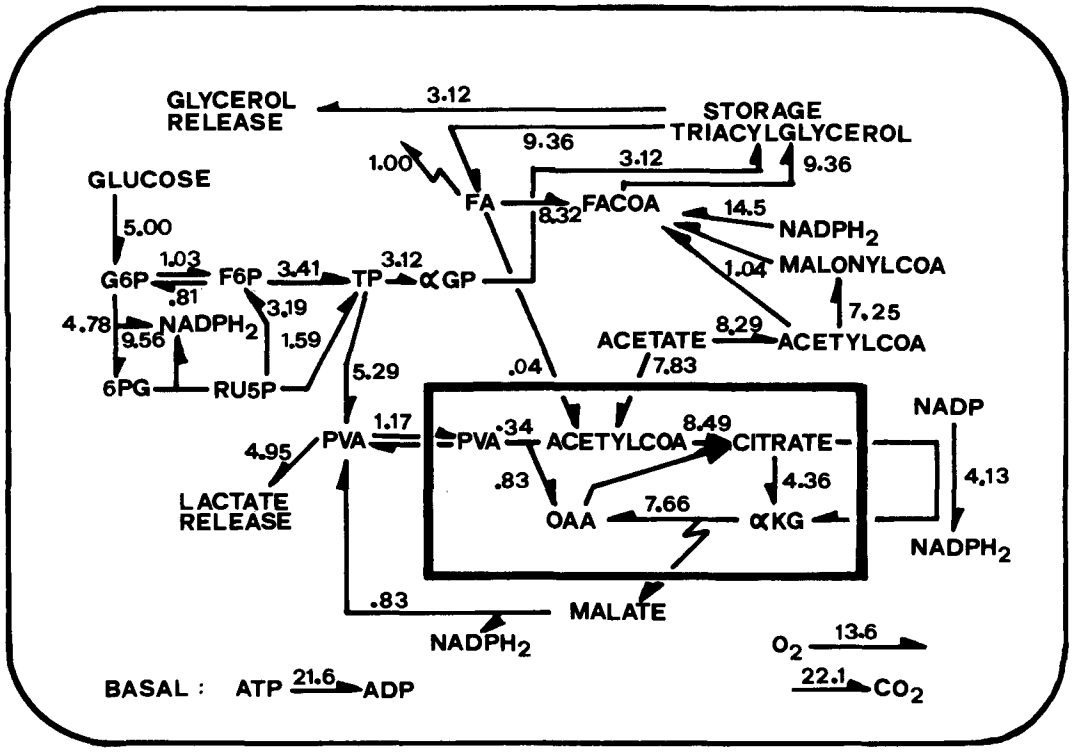

Figure 2. Diagrammatic representation of the essential aspects of adipose tissue metabolism in a lactating cow. Fluxes expressed as moles per 24 hr on the basis of the work of Baldwin *et al.* (1976).

acetate is the precursor, 95% when diet fat is the precursor; table 6).

The data in table 8 were gathered to attempt an assessment of the potential benefit in efficiency that could be gained through manipulation of adipose tissue functions. A change in diet composition could result in a 2 to 3% decrease in total energy expenditures due to decreased fatty acid synthesis in adipose tissue. Depression in triacylglycerol turnover rates could yield a reduction of 1 or 2%. A reduction in rates of lactate resynthesis in liver would reduce whole animal energy expenditures by less than 1%. In the case of reducing lipolysis, we must emphasize that this is a homeostatic mechanism and has regulatory significance. The maximum overall benefit in energy expenditures that could be gained through manipulation of adipose tissue metabolism in the example used here is only 3 to 5%. Thus, in terms of whole animal energy expenditures, manipulation of adipose tissue metabolism is not an attractive target. The most important reason for studying adipose tissue is the potential the tissue has for regulating composition of gain and affecting the partition of nutrients between milk production and fattening.

Patterns of Nutrient Use. Earlier in this presentation, it was suggested that costs of maintenance and production can vary depending upon the nutrients provided to the animal and(or) the patterns of nutrient use within an animal. An example of the impact that alternate patterns of nutrient use could have upon

TABLE 8. ENERGY EXPENDITURES IN ADIPOSE

Function	% total[a]
Lipogenesis	3.7
Triacylglycerol turnover	2.6
Maintenance	2.0
Lactate resynthesis	.8
	9.1

[a]For cow producing 23 Mcal heat/day (Baldwin and Smith, 1971b).

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estimated efficiencies of production is presented in table 9. If volatile fatty acids were used for maintenance, amino acids for protein gain and dietary fat for fattening, the HI_p would be 15.4%. If, as an alternative, dietary fat were used for maintenance, amino acids were used for protein and fat were synthesized from volatile fatty acids, the resulting HI_p would be 27.6%. This represents almost a twofold difference in the energy cost of gain.

It was shown that 20% differences in the ME requirement for maintenance can occur depending upon the nutrients provided or used to support maintenance functions. In table 9, it is shown that the HI_p can vary twofold, depending upon the pattern of nutrient utilization.

TABLE 9. EXAMPLE EFFECT OF METABOLIC DECISIONS UPON NET EFFICIENCY

Case	HI_p, %
Case 1	
VFA → maintenance	
Amino acids → protein	15.4
Fatty acids → fat	
Case 2	
Fatty acids → maintenance	
Amino acids → protein	27.6
VFA → fat	

Because of the magnitude of differences in apparent efficiency, it seems appropriate to examine factors that determine patterns of nutrient use within the animal. In figure 3 we have attempted to depict some of the driving forces that influence patterns of nutrient utilization within an animal. Tissue work, which might be work associated with maintenance or biosynthetic functions, results in the conversion of ATP to ADP. It is well established that ADP concentration within a mitochondrion is a primary driving force resulting in the oxidation of available nutrients (Atkinson, 1977). One might suppose, on the basis of available metabolic data, that there is a maximum rate at which an organism can oxidize a given substrate. Also, rate of oxidation at any given point in time might be a function of the affinity of enzymes which utilize that substrate within each tissue. Thus, capacity of tissues to utilize and oxidize substrates, ADP concentrations and tissue or enzyme affinities to nutrients might be important determinants of rates and patterns of nutrient utilization.

Several factors may operate to determine the concentration of an intracellular metabolite or nutrient. One might suggest that rate of uptake of a nutrient is a function of its concentration in blood; in the capacity of carriers, or enzymes involved in transport and(or) affinities of carriers and enzymes for that nutrient. These

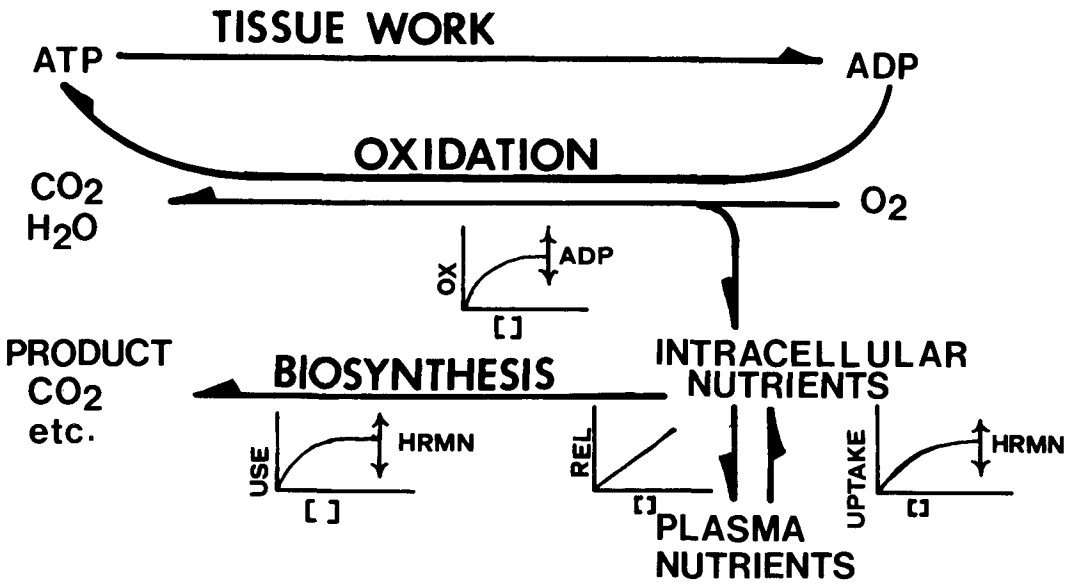

Figure 3. Driving forces that influence patterns of nutrient utilization in animal systems. HRMN for hormone effects.

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might vary as a function of hormonal state. If a nutrient were to attain high intracellular concentrations, rate of release into plasma might become a significant factor and it would be expected to be a linear function of intracellular concentration. The other major factor affecting intracellular concentrations of nutrients would be rates of utilization of this nutrient for oxidative and biosynthetic functions in that tissue. Again, one would expect that enzymes involved in the utilization of a nutrient, for oxidative and biosynthetic functions, would have specific affinities and that there would be a maximum capacity for utilization of that substrate. If the suggestions presented above and depicted in figure 3 are valid, we can conclude that nutrient uptake by a tissue depends upon affinity, energy state of the tissue as reflected in ADP concentration and biosynthetic or oxidative capacity.

We are suggesting (figure 3) that use of Michaelis-Menten type kinetics to describe a tissue's ability to oxidize or otherwise utilize nutrients might be a useful approach to analysis of factors that influence patterns of nutrient utilization within the animal. Figures 4 and 5 present data which indicate that total rates of utilization and oxidation of at least some metabolites follow Michaelis-Menten type kinetics in the whole animal. In figure 4, concentration of plasma acetoacetate is plotted *versus* total rates of ketone body utilization, a Michaelis-Menten type relationship. The data

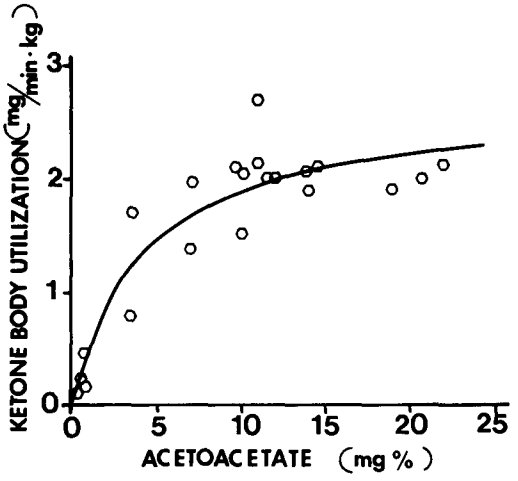

Figure 4. Relationship between plasma acetoacetate concentration and rates of ketone body utilization. Data from Barry *et al.* (1963) and Kronfeld *et al.* (1968).

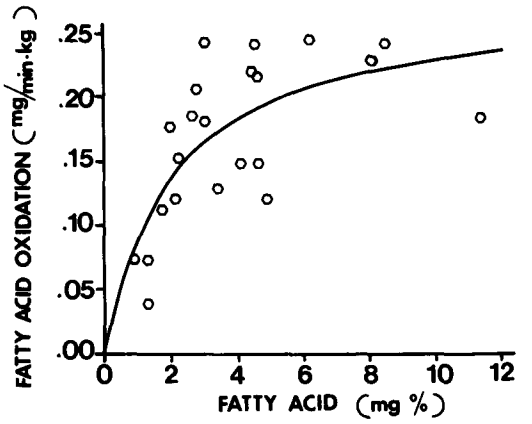

Figure 5. Relationship between plasma free fatty acid concentration and rates of fatty acid oxidation. Data from Barry *et al.* (1963), Hartmann and Lascelles (1964, 1965), Kronfeld *et al.* (1968) and Yang *et al.* (1978).

depicted in this figure come from a number of sources and are based on radioisotope tracer estimates of total ketone body utilization rates. In figure 5, similar data depicting the relationship between fatty acid concentrations in plasma and fatty acid oxidation are plotted. Again, a Michaelis-Menten type equation describes the data fairly well. Note that there is significant variation in this case. This may be so because most of the data used are for single fatty acids. Data obtained with palmitate, oleate and stearate are depicted; perhaps, curves for each of these differ. Also, the data presented in this figure were collected from animals in differing physiological and metabolic states in which blood patterns of alternate nutrients were not constant. Overall, however, it is clear that at least on a whole animal basis, the utilization of some metabolites can be depicted as Michaelis-Menten type of relationships.

The data depicted in figures 6 to 10 summarize a number of mammary data from the literature. In figure 6, it can be seen that there is no evidence whatsoever that Michaelis-Menten kinetics apply within the physiological range of concentrations of acetate in plasma. Rather, a simple linear relationship is indicated. In figures 7 to 10, Michaelis-Menten kinetics best fit data relating uptakes of glucose, ketone bodies, triacylglycerol and amino acids by mammary tissue to plasma concentrations. Statistics defining relative fits of a linear equation ($y = ax$) *versus* a Michaelis-Menten equation for these substrates are presented in

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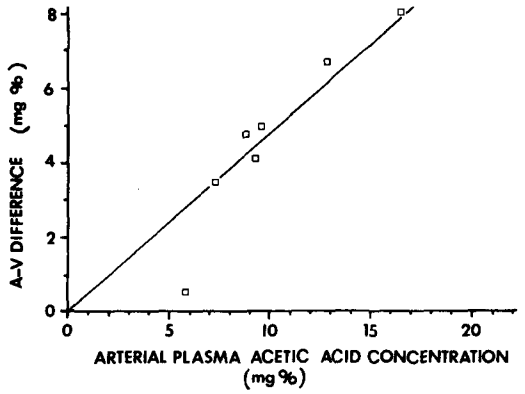

Figure 6. Relationship between plasma acetic acid concentration and arteriovenous difference in acetic acid across the mammary gland. Data from Annison (1954) and Kronfeld *et al.* (1968).

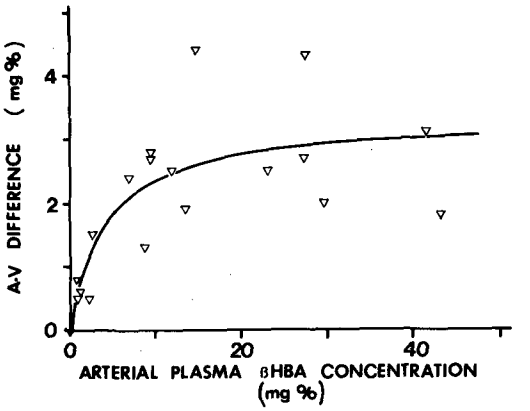

Figure 8. Relationship between plasma β-hydroxybutyric acid (HBA) concentration and arteriovenous difference in HBA across the mammary gland. Data from Barry *et al.* (1963), Hartmann and Lascelles (1965) and Kronfeld *et al.* (1968).

table 10. In the case of glucose, the Michaelis-Menten equation provides only a slight improvement over a linear relationship, with terrific scatter around both relationships. This suggests that factors in addition to plasma glucose concentration affect glucose uptake. In the case of β-hydroxybutyrate, the Michaelis-Menten equation fits the data much better than a linear equation does. The same is true for triacylglycerol and amino acids.

Yang and Baldwin (1973), using isolated ruminant adipocytes, assessed the value of employing Michaelis-Menten type relationships to describe the uptake and utilization of nutrients. In that case, a single Michaelis-Menten relationship did not apply for a single substrate under all conditions because of interactions among glucose, acetate and insulin. Interactions among nutrients and hormone effects must be accommodated. Perhaps with additional data these can be accommodated by similar equations which provide for nutrient interactions and hormone effects upon apparent affinities and capacities. Thus, linear and Michaelis-Menten equations can be applied usefully in some, but not all, analyses of patterns of nutrient use within animals. Additional data and equations are required for

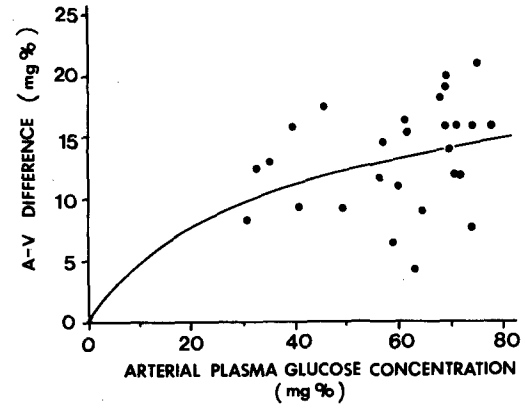

Figure 7. Relationship between plasma glucose concentration and arteriovenous difference in glucose across the mammary gland. Data from Hartmann and Lascelles (1965), Hartmann (1966), Kronfeld *et al.* (1968) and Yang *et al.* (1978).

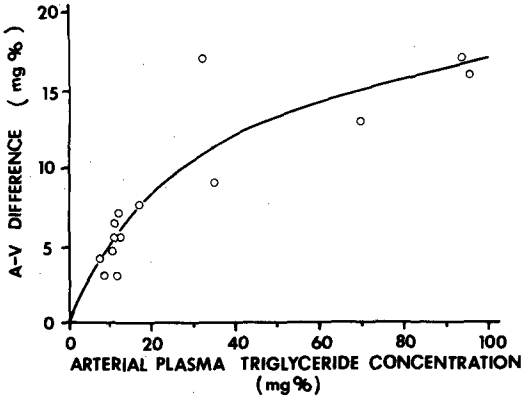

Figure 9. Relationship between plasma triglyceride concentration and arteriovenous difference in triglyceride across the mammary gland. Data from Hartmann and Lascelles (1964, 1965) and Yang *et al.* (1978).

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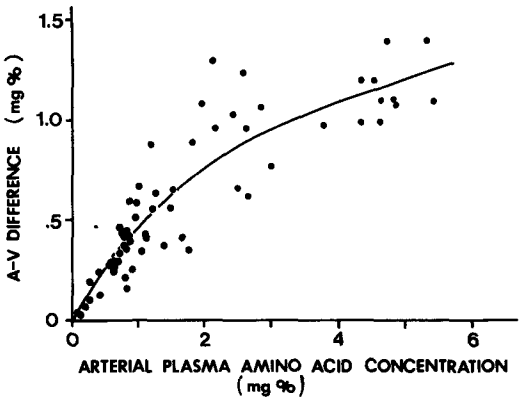

Figure 10. Relationship between plasma amino acid concentration and arteriovenous difference in amino acid across the mammary gland. Data from Sheldon-Peters and Barry (1956), Verbeke and Peeters (1965), Mepham and Linzell (1966), Clark *et al.* (1977) and Yang *et al.* (1978).

analyses of other aspects of metabolic patterns (Baldwin and Smith, 1971a). For example, effects of hormones or physiological state upon the capacities and affinities of tissues to nutrients must be accommodated.

It was suggested above that there might be potential for enhancing average animal efficiencies through improvement of the set of metabolic decisions made or by adjustment of patterns of nutrient utilization. Before we can undertake experiments directed at manipulation of patterns of nutrient utilization in the animal, however, we need much more information regarding capacities and affinities of tissues to nutrients and factors that might modify both of these.

Futile Cycles. There has been considerable interest among animal biochemists in recent years in evaluating contributions of futile cycles to energy expenditures. In table 11, we have summarized the contributions of several futile cycles to maintenance requirements of animals. The major futile cycle is sodium transport across membranes, which contributes 20 to 30% of the maintenance energy expenditures. The significance of this futile cycle was discussed above. Other futile cycles discussed above included protein turnover and triacylglycerol turnover within adipose tissue. These three futile cycles contribute significantly to maintenance energy expenditures and, in the case of protein, to apparent costs of protein accretion. Some benefit may be obtained through manipulation of these, but the role of protein turnover in osmoregulation and adaptation, the role of sodium transport in the maintenance of membrane potentials and the metabolic significance of triacylglycerol turnover in energy metabolism have to be considered as constraints upon manipulation.

Additional futile cycles have been considered. One is the conversion of glucose to glucose-6-phosphate in liver followed by hydrolysis of the glucose-6-phosphate by glucose-6-phosphatase. The contribution of this futile cycle to total energy expenditures of the animal is less than 2%. The contribution of the cycle involving the pyruvate kinase and pyruvate carboxylase and PEP carboxykinase reactions results in an energy expenditure of less than 1%. The phosphofructokinase, fructose-1, 6-diphosphatase cycle makes a contribution to energy expenditures of less than 2% (Katz and Rognstad, 1976). It is generally considered that these cycles perform an important regulatory function in providing for

TABLE 10. SUMMARY STATISTICS ON RELATIONSHIP BETWEEN BLOOD NUTRIENT CONCENTRATIONS AND MAMMARY UPTAKE

Substrate	Linear[a]		Michaelis-Menten[a]		
	A	WSSQ	V_{max}	K_m	WSSQ
	mg/ 100 mg		mg/ 100 ml		
Glucose	.21	631	21	36	575
β-hydroxybutyrate	.98	34	3.3	4	10
Acetate	.47	5.9	10^{13}	10^{13}	5.9
Triacylglycerol	.21	240	22	32	61

[a]A is the coefficient in the linear equation Y = AX; WSSQ = weighted sums of errors squared; V_{max} = maximum velocity; K_m = apparent affinity.

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TABLE 11. CONTRIBUTIONS OF FUTILE CYCLES TO MAINTENANCE ENERGY EXPENDITURES[a]

Futile cycle	% contribution
Na+/K+ transport	20 to 30%
Protein turnover	10 to 15%
Triacylglycerol turnover	2 to 3%
Glucose/G6P	<2%
Pyruvate/PEP	<1%
F6P/F16DP	<2%

[a]From Baldwin and Smith (1974) and Katz and Rognstad (1976).

rapid adaptations to changes in metabolic demands. In view of the fact that energy expenditures in these functions constitute less than 5% of the maintenance energy expenditures, it is probably not desirable to attempt to improve efficiency through manipulation of these cycles.

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