# Parenteral Nutrition

Edited by F. W. Ahnefeld C. Burri W. Dick M. Halmágyi

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# Foreword

Nearly all medical specialities treat patients whose illnesses necessitate a means of nutrition which bypasses the gastrointestinal tract. Parenteral nutrition consequently means the administration of nutrient and building materials in qualitatively utilizable form and in quantitatively adequate amount by the intravenous route. This guarantees the requirements for energy and building materials under a variety of conditions, and compensates for any losses that might occur.

The basis for any parenteral nutrition is the knowledge of the biochemical processes of intermediary metabolism under physiological and pathophysiological conditions (e. g., starvation, post-stress metabolism, hypoxia, microcirculatory disturbances, etc.). Only taken in these contexts can nutrient and bodybuilding substances be combined, measured out, and administered in such a way as to be definitively useful to the body. Research into the biochemistry and the pathobiochemistry of intermediary metabolism has demonstrated possibilities, by means of which we may be able to "outwit" (to some extent) disturbances in utilization of certain nutrients under defined pathologic conditions. If the body receives and transforms substrate-precursors (e. g., sorbitol), it can maintain an adequate level of nutrient and life-support substances; this slow rate of transformation to the substrate makes allowance for the limited utilization capacity, and covers the needs of the body by roundabout means.

Some of the problems can now be considered solved, but a great many are still in the very early stages of elucidation, or await basic research.

It was the goal of this workshop (see also *Principles of Infusion Therapy* and *Fundamentals of Post-Operative Nutrition* – volumes 3 and 6, respectively, of this series of publications) to establish for the field of parenteral nutrition an inventory which states sure knowledge and which crystallizes the problems remaining. Even in this workshop, understandably, not all the controversial questions could be agreed upon; the very existence of controversial topics is the basis for present and future discussions, and gives hope for substantial advances.

We hope that this volume can impart recommendations for day-to-day clinical practice, not only to the practicing physician but also to nurses and paramedical personnel who are involved with the problems specific to parenteral nutrition; furthermore, we hope to have given some stimulus for further scientific research.

All the lectures have participated in the discussion. In order to keep the size of this volume within predetermined limits, only a summary of the most important points of discussion could be included; special attention has been given to controversial points of view.

We must again thank the Springer Publishing Company for its valuable suggestions, its always optimal cooperation, and its support of our efforts to publish the results of this workshop in the shortest possible time.

We thank Pfrimmer & Co. in Erlangen (West Germany) for making possible the realization of the workshop.

We extend our gratitude to Dr. Arthur A. BABAD, Assistant Clinical Professor, Department of Anesthesia, University of Claifornia, San Francisco, Visiting Professor of the Department of Anesthesiology at the University of Ulm, who cared about the translation of the present text.

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# Table of Contents

# Metabolism of the Nutrient Substances Used for Parenteral Nutrition

By K. H. Bässler

If one must present the bases of energy-metabolism - the quintessence of perhaps 200 textbook pages - in 40 minutes, one must naturally oversimplify things and present only the most essential facts. The following discussion will consider only those matters which are indispensable for problems of parenteral nutrition; this choice is necessarily subjective, does not pretend to be complete, and may not always describe complicated circumstances exactly because of the extreme simplification.

To begin with, let us briefly consider what we understand about metabolism. The living organism appears constant in form, but in reality everything exists in a dynamic state. The body consists of complicated organic molecules, which, according to the laws of thermodynamics, tend to break apart into simpler, energy-poorer fragments. This tendency is transformed into reality through the presence of the appropriate catalyst, the enzyme. A type of order is imposed by these enzymes, such that this fragmentation cannot occur in every possible way, but only in such ways as the existing enzymes direct. Thus the various organs of the body have different metabolic patterns, each according to its enzymatic make-up. In order to guarantee the constancy of the body, these catabolic processes must be compensated by synthetic processes. Nutrition furnishes the material and the necessary energy for such synthesis. This total chemical transformation is what we arbitrarily call metabolism.

The most valuable components of the body, crucial for its functional capability, are the proteins. All proteins have defined functions, be it as structural components, as transport-proteins, as antibodies, etc. However, the predominant portion of the body's protein content exists as active enzyme-protein, essential for the regulation of the complex chemical interplay of metabolism. To reduce the problem to its kernel, one might - somewhat exaggeratedly - say: The task of nutrition is to guarantee the continuing existence and functional capability of the proteins - and if normal nutrition is not possible, that is the task of parenteral nutrition. Everything else must be subordinated to this viewpoint. To permit protein synthesis, we need amino-acids and energy sources; so that the enzymes can function, they need a specific ionic milieu, which must be made possible through the provision of electrolytes; they need co-enzymes, which come from vitamins, which must be supplied; and so forth.

Living requires a continuous supply of energy. The three main users of energy are (1) bio-synthetic processes, (2) mechanical work, and (3) osmotic work. This energy is supplied through the breakdown of nutrient substances or of stored substances (Fig. 1).

Only that portion of the energy which is preserved from the breakdown of energy-containing substances as ATP can be re-utilized for energy-consuming processes. Basically, life is a unique ATPase reaction, and the dynamic conditions in the living organism are maintained in an equilibrium by the ATP/ADP-system, as Fig. 1 shows. Energy-requiring processes are limited by the availability of ATP, and energy-producing processes are limited by the availability of ADP. As long as this coupling works, unnecessary breakdown of body substance will be avoided.

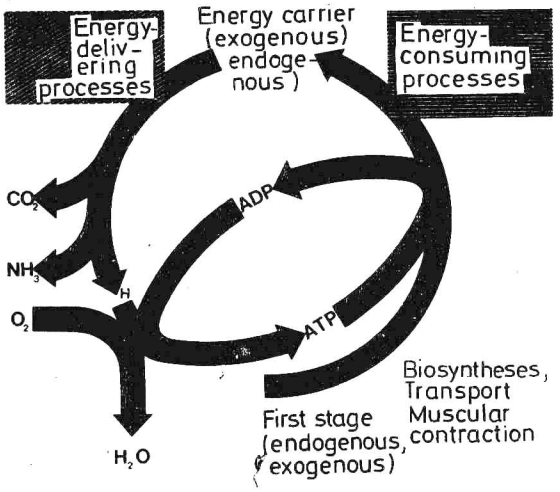


Fig. 1. Dynamic equilibrium of the body components

The energy-requiring processes cannot be completely turned off. This is manifested as the basal metabolic rate. Fig. 2 shows the contributions of some of the important organs to this basal metabolic rate.

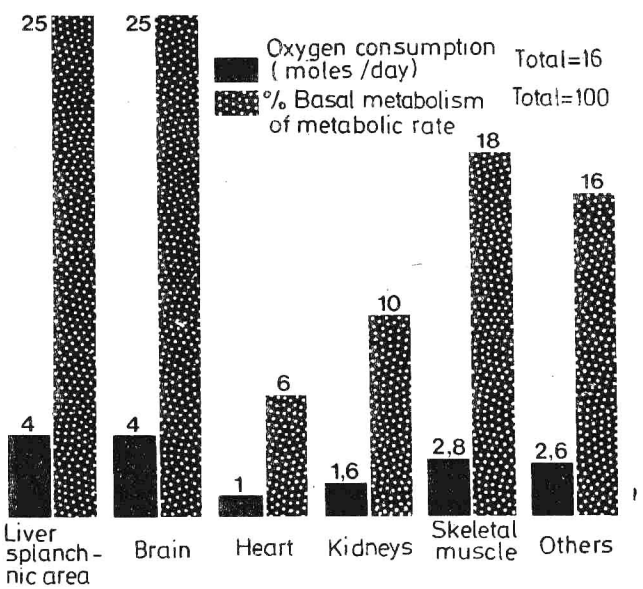


Fig. 2. Contributions of organs to the basal metabolic rate, in man

This energy-requirement is relatively constant for most organs. What we know as "increased performance" depends almost exclusively on the energy-bank-account of the musculature. Which substances can serve as

energy-sources for the various organs? A summary of this is given in Fig. 3.

| Organ | Energy-producing fuel | Metabolic capability for supplying other tissues |
|---|---|---|
| Liver | amino-acids | ketogenesis |
| | fatty acids | from amino-acids, lactate, glycerine |
| | glucose | gluconeogenesis |
| Kidney | fatty acids | |
| | glucose | gluconeogenesis |
| Fatty tissues | glucose | |
| | fatty acids | lipogenesis, lipolysis |
| Heart | glucose | |
| | fatty acids | |
| | ketone bodies | |
| Muscle | glucose | |
| | fatty acids | |
| | ketone bodies | |
| Brain | glucose | |
| | ketone bodies | |

Fig. 3. Metabolic performance of individual organs with respect to production of energy and support of other organs

We can see from this Fig, that most of the organs can utilize various fuels for nutrition or for function. In addition, there are tissues, such as the blood cells, which live mainly on one fuel - glucose. We can also see that various tissues, because of special metabolic capability, contribute to the support of other tissues: for example, liver and kidney through gluconeogenesis; liver through ketogenesis; and fat through lipolysis. Thus we see a metabolic coordination of the organ-system which is very important for the normal functioning and the adaptability of the body. An example of such cooperation is the adaptation to starvation shown in Figs. 4 and 5.

During normal nutrition, these organs take their fuels from the blood independently of one another; however, during starvation, they are dependent on each other. We can see the role of the liver in the support of the brain through gluconeogenesis, and the roles of the fatty tissues (lipolysis) and the liver (ketogenesis) in supplying the musculature with fatty acids and ketone bodies. The musculature supplies amino-acids as precursors for gluconeogenesis. The CNS also utilizes ketone bodies, in proportion to the rise in blood ketone-body level, as can be seen in the diagram. A further example of the cooperation of organsystems is the Cori cycle (Fig. 6).

Blood cells break down glucose only as far as lactate. Also in musculature, during hypoxia, part of the glucose is broken down only to lactate. This lactate is delivered to the blood and is rebuilt in the liver to glucose, which is again made available to the blood cells and the muscles. This mechanism serves to economize on glucose, for the blood cells transform glucose in this fashion, but use up no glucose in the balance. Since the energy for the glucose-resynthesis in the

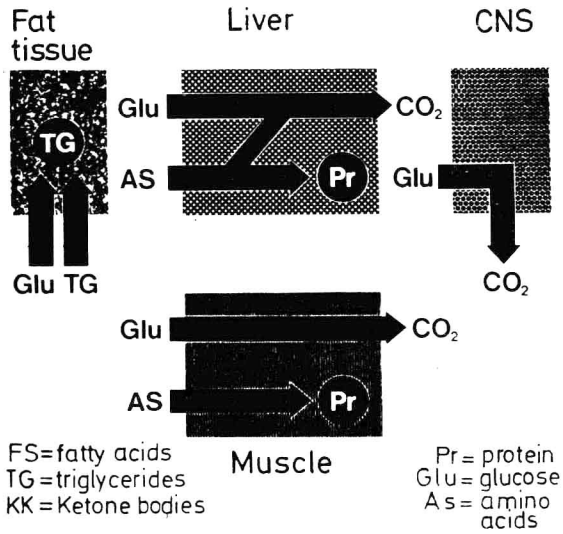


Fig. 4. Metabolism of organs after food intake

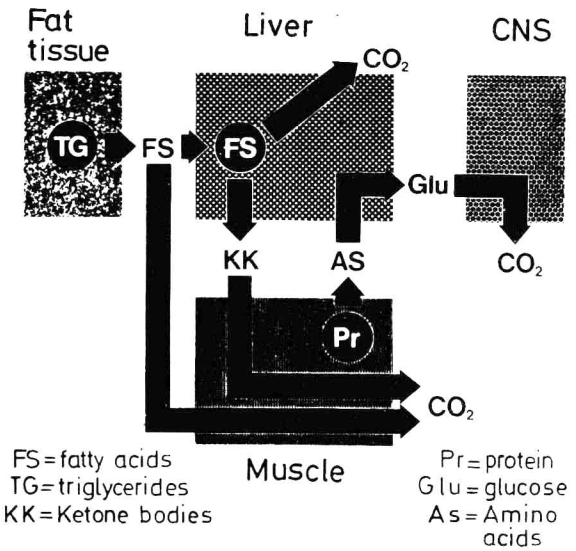


Fig. 5. Coordination of the metabolism of organs during starvation

liver comes from oxidation of fatty acids, the blood cells live off the energy stored in fat. A similar economy-circle with respect to glucose usage is also possible in the brain. Not because of hypoxia, but because of a metabolically regulated inactivation of pyruvate-dehydrogenase - glucose can be oxidized, not completely, but only to lactate. This constitutes a Cori cycle between brain and liver, the importance of which Dr. DIETZE will discuss later. During glucose metabolism in muscle, pyruvate can partially be transformed through transamination into alanine (rather than into lactate), and as alanine can be offered again to the liver as a glucose precursor. This gives us the alanine cycle (Fig. 7), which serves - as a modified Cori cycle - also to economize on glucose.

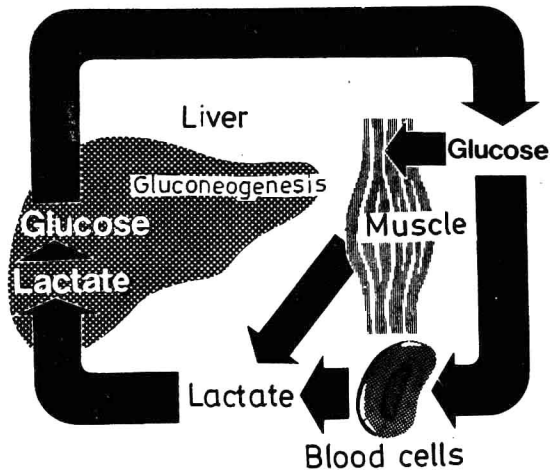


Fig. 6. The Cori cycle as an example of the coordination of organs

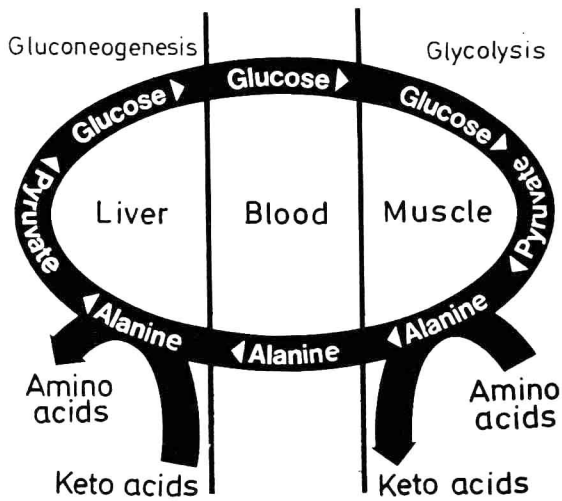


Fig. 7. Alanine cycle as a modified Cori cycle

You can see that these economy mechanisms work only in the body as a whole; one cannot demonstrate them in the individual organ. This makes the investigation of these questions quite difficult.

We must now direct our attention to describing more closely the essential pathways of energy-metabolism. This can only be done step-wise, and with extreme simplification. So that we don't lose our orientation by studying these individual pictures out of context, let us first look at a summary of energy-metabolism; then we can subsequently realign the individual segments into the total picture (Fig. 8).

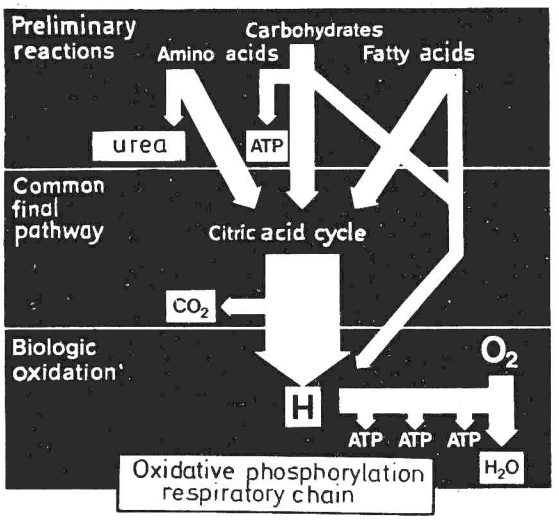


Fig. 8. The three steps of energy-producing metabolism

Shown here is the energy-producing metabolism, divided into three steps: Step 1: preparatory reactions. In this category come (1) the breakdown of carbohydrates through glycolysis, the pentose-phosphate-shunt and other pathways leading to glycolysis, (2) the various metabolic pathways for amino-acids, and (3) the ß-oxydation of fatty acids. It would take half a textbook on intermediary metabolism to cover this category. All these metabolic pathways then meet with the same intermediary products in a final common pathway, the citric-acid cycle. This is Step 2, the main area of metabolic change; on this turntable, many substances can be converted, one into the other. The dehydrogenase reactions in the citric-acid cycle constitute the body's main source of hydrogen, which is bound to coenzymes. Step 3, most of the energy production finally takes place, as the oxydation of hydrogen in the respiratory chain is coupled with the phosphorylation of ADP to ATP. Here in the mitochondria, oxygen enters into the metabolic activity. The largest part of the body's oxygen requirement is used in this pathway. Adequacy of energy-production is thus dependent upon an adequate oxygen supply, as Fig. 9 points out.

The oxydation of fatty acids and the oxydation of carbohydrates by way of pyruvate is possible only if the reduced coenzymes can be re-oxidized in the respiratory chain through the presence of oxygen. ATP is created by this process. Only one process can continue even in the absence of oxygen: glycolysis - the breakdown of glucose to lactate, because here reduced NAD is re-oxidized through the conversion of pyruvate to lactate. Thus, lactate becomes the end-product of carbohydrate metabolism during hypoxia. Even in this process, ATP can be produced, through the phosphorylation reactions of glycolysis. The quantitative importance of this process, in comparison with aerobic metabolism is shown in a comparison of ATP-production during aerobic and anaerobic glucose metabolism (Fig. 10).

We can see from the preceding summary the extraordinary importance of the oxygen supply; carbohydrates can be metabolized only to lactate; the energy-yield is minimal. Other energy-carriers such as fatty acids or alcohol cannot be utilized at all without oxygen. Since oxygen rarely enters directly into the reaction with the substrate, but acts mostly by re-oxydizing reduced coenzymes in the respiratory chain (in the

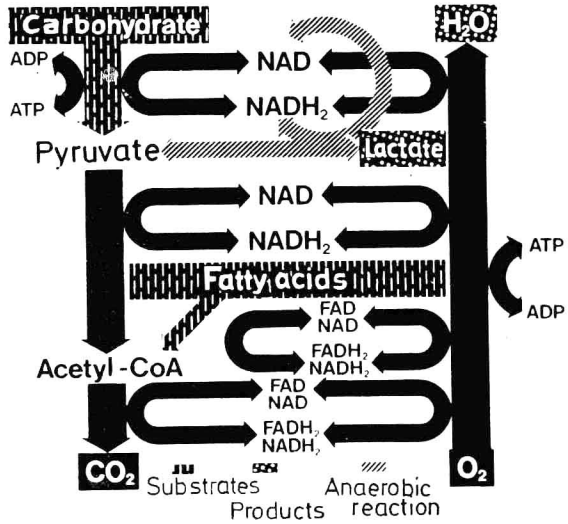


Fig. 9. The role of oxygen in energy-metabolism

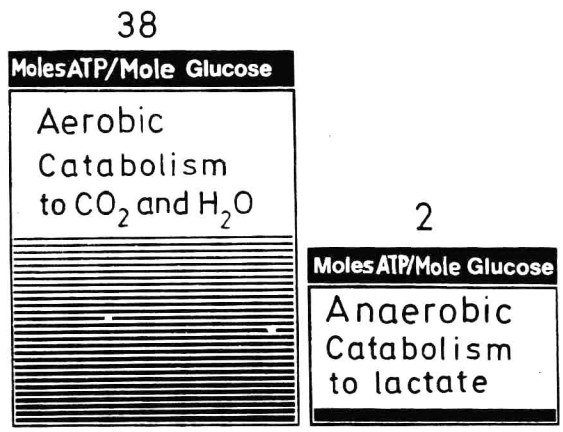


Fig. 10. Theoretical ATP-yield during aerobic and anaerobic glucose metabolism

mitochondria), the high proportion of reduced coenzymes during hypoxia sets up substrate-equilibria in the dehydrogenase reactions: we find high ratios of lactate/pyruvate, glycerophosphate/dihydroxyacetone-phosphate, malate/oxaloacetate, ß-hydroxybutyrate/acetoacetate, etc.

At this point, I must call your attention to a fact which is not apparent from these simplified diagrams. Most of the dehydrogenase reactions take place in the mitochondria, and there too the reduced coenzymes have direct access to the respiratory chain. A number of dehydrogenases are also located in the cytoplasm, for example, the dehygenases of ethanol or the poly-alcohols sorbitol and xylitol. In these cases, the hydrogen must be transported from the cytoplasm into the