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Possibilities and necessities of parenteral nutrition with amino acid mixtures

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With 15 figures

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I. Physiological fundamentals

Physically, the human organism is an "open system", compared to the classical systems of thermodynamics. All that is excreted as degradation products must be replaced by food intake, so that a constant substrate flow is maintained within the body. Homeostasis, i.e. the maintenance of many concentrations, is only possible if intake balances output. Contrary to the "stationary state" in closed systems we encounter a "steady state" which is a dynamic equilibrium (7).

As soon as the balanced substrate intake adapted to the requirements is disrupted – whether voluntarily or not – numerous reactions will take place in the body to maintain the vital functions as long as possible by special regulatory mechanisms.

The least endangered is the supply of energy, as considerable quantities of energy stores are distributed throughout the body in the form of fat depots which will be mobilized by increased lipolysis during fasting. Carbohydrate stores, however, are rather limited at 300 to 400 g glycogen and scarcely cover the basal metabolism for one day. Because fats cannot be used in gluconeogenesis, protein is used to cover the brain's daily requirements of 100 to 150 g of glucose. This requires approximately 250 g of protein. There is not much protein, however, available for mobilization. Those that are readily available, the ones with a short half-life, are indispensable structural proteins for the organism. The so-called labile protein pool consists mainly of the most important enzyme proteins of the liver, the pancreas, and the intestinal mucosa. Even a short-term interruption of protein intake leads to a drastic change of the enzyme pattern and a drastic decrease in the ribonucleinic acid (RNA) level of the liver, thus damaging the catalytic system. *Munro* reported, in fact, an impairment to the liver function at low protein intakes (54, 55).

The common practice of expressing nitrogen losses in terms of loss of muscular tissue ($N \times 6.25 \times 5$) does not apply to the acute state, as fig. 1

Fig. 1. Contribution of different tissues to the total nitrogen deficit in protein-depleted rats (from data of *Waterlow* and *Stephen,* 1966) (55).

Tissue	Protein loss (%) 3 days depletion	5–8 weeks depletion
Nitrogen deficit	760 mg	1920 mg
Liver	8 %	4 %
Other viscera	16 %	10 %
Muscle	0	26 %
Skin and hair	35 %	35 %

shows. Thus a vicious circle develops which can only be broken by parenteral supply of amino acids (fig. 2).

The presumption that it is nonsense to supply substrates in the so-called catabolic phase – formerly considered almost a dogma by surgeons – and that fasting is even beneficial for the organism, is today known to be false. It is also known today that anabolism and catabolism, i.e. the building and degradation of tissue, enzymes, etc., always go together, and that what is clinically described as an anabolic or catabolic state is merely the relative predominance of a particular tendency (fig. 3).

In catabolism, substrates given are also utilized (35, 36, 37). Protein deficiency has a drastic influence on wound healing and the albumin pool. In the classical studies of the research groups of *Cannon, Ravdin, Rhoads,* and many others, protein deficiency was shown to cause a delay in wound healing. Recent studies by *Dudrick* and colleagues once more proved clearly the correlation between wound healing, the albumin pool, and protein intake (13), and demonstrated the influence of infusion therapy on circulating serum albumin and anastomotic resistance. According to *Munro,*

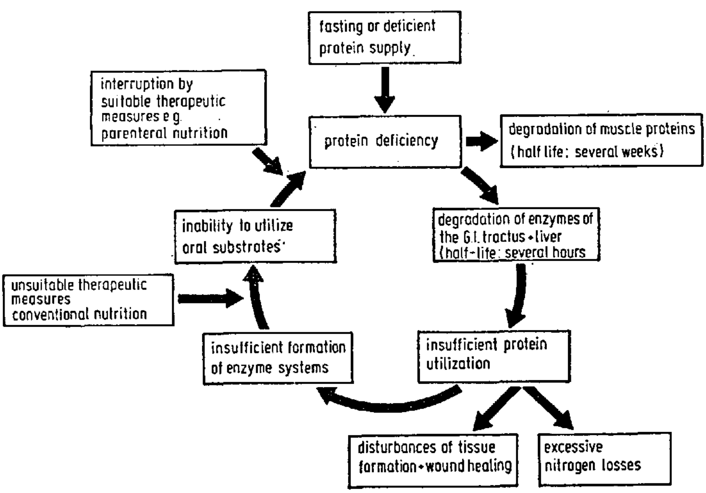

Fig. 2. Development interruption of a vicious circle caused by lack of protein supply.

decreased protein intake already delays the regeneration of connective tissue. The size of the albumin pool is not only an important index of the supply of protein, but also very important for the resistance of the organism to various noxae and especially for metabolic stability. Hypoalbuminaemia is a real risk factor. It develops after stress from various causes, burns, infections (especially peritonitis and sepsis), in liver diseases, and numerous disturbances in protein metabolism. As *Jarnum* and colleagues demonstrated in a *WHO* study in India, hypoalbuminaemia and a low rate of albumin synthesis in patients with tropical sprue can be effectively treated with infusions of requirement-adapted amino-acid mixtures (43) (fig. 4).

Particularly interesting studies by *Kudlicka* and *Dobersky* (14, 50, 51) of the Institute for Metabolic Studies and Nutrition and the Research Institute for Clinical and Experimental Medicine, Prague, have shown rather unexpected results. It became evident that the administration of balanced amino acid mixtures was the most effective method to normalize the protein reserves (albumin pool). This proved even more effective than the

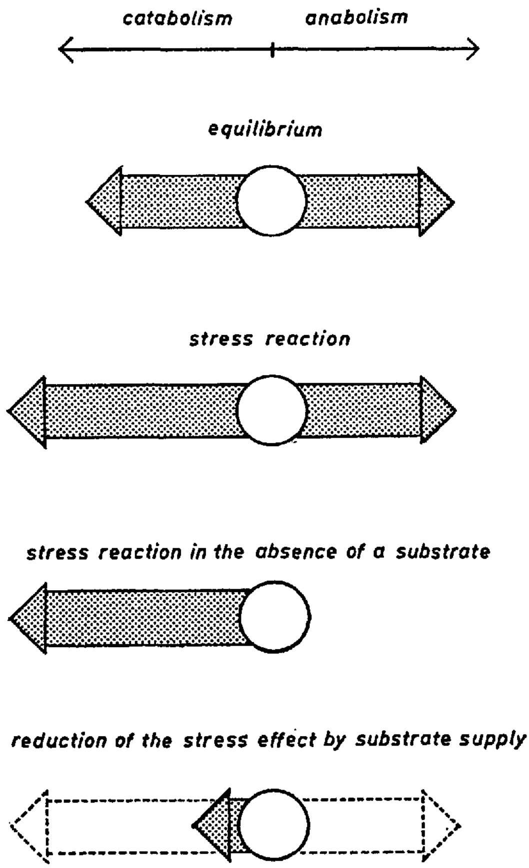

Fig. 3. Catabolism, anabolism.

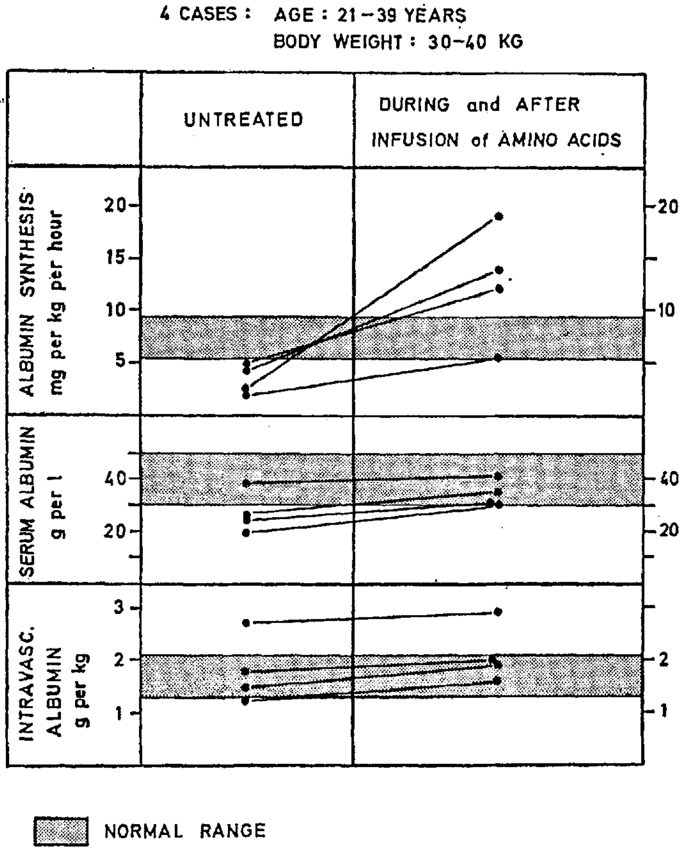

Fig. 4. Albumin synthesis in 4 cases of tropical sprue before and during infusion of balanced L-amino acids (43).

Fig. 5. Comparison of the effect of parenteral nutrition with amino acids and plasma proteins (51).
(Mean percentual change of the observed parameters in a day of therapy.)

		Plasma Proteins	Balanced AA mixture	
		(n = 7)	(n = 7)	(n = 7)
	Anabolics	+	–	+
Body weight	(kg)	0.215	0.24	0.55
Broca index	(%)	0.215	0.24	0.51
Body surface	(m^2)	0.090	0.10	0.204
Plasma volume	(ml)	0.473	0.58	1.36
Serum albumin	(g%)	0.064	0.50	0.30
Albumin total	(g)	0.609	0.67	2.23
Albumin intravasc.	(g)	0.549	1.15	1.20
Albumin extravasc.	(g)	0.845	0.65	2.42

Fig. 6. Indications for artificial food supply (the patient can, will or must not eat (9).

Examples	
Patient cannot eat	unconsciousness prolonged anaesthesia stenoses
Should not eat	therapeutic measure recent anastomoses perforation atony
Does not want to eat	anorexia mental disease or psychosis physical exhaustion fever

exogenous supply of albumin and almost twice as effective as the infusion of isonitrogenous lyophilized plasma (fig. 5).

Moreover, the infusion of amino acids markedly improved erythropoiesis. The findings listed above show distinctly that, not only in long-term mandatory fasting, but also at short-term interruption of the oral substrate intake, parenteral alimentation, especially the infusion of suitable amino acid solutions, is most important to warrant an adequate provision of the organism with substrates to prevent the undesirable degradation of body substrates (endogenous cannibalism according to *Peaston*). The most important indications for parenteral nutrition may be seen from fig. 6.

II. Criteria for the evaluation of amino acid solutions

Dietary protein supplies the amino acids necessary for the biosynthesis of endogenous proteins and for numerous metabolic reactions (e.g. detoxication). It is not, in fact, the protein that is required, but amino acids, which is why in parenteral nutrition suitable amino acid mixtures can easily meet the corresponding requirements (25, 52, 53).

Which criteria must be met by amino acid solutions for the most efficient treatment of patients under severe stress (e. g. following severe trauma, burns, surgery, severe malnutrition, etc.)?

A German group of experts of the "International Society of Parenteral Nutrition" (ISPN) worked out a number of recommendations some years ago which need some supplementation, but are nevertheless basically valid today (21).

The decisive factor is, of course, the correct pattern of the essential amino acids. The available types of preparations may be classified as follows:

a) protein hydrolysates,
b) amino acid mixtures adapted to plasma,
c) amino acid mixtures according to the so-called potato-egg (p. e.) pattern,
d) requirement-adapted amino acid mixtures.

a) Protein hydrolysates are practically out of date. Their pattern was limited in effectiveness because of the proteins used as the basic mate-

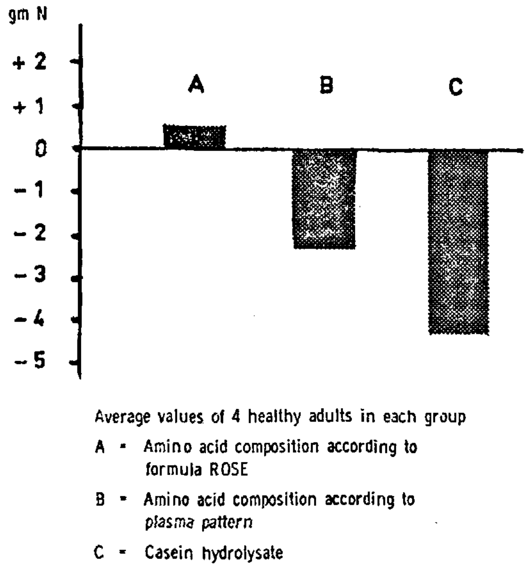

Fig. 7. Nitrogen balance with different amino acid solutions.

Pre-period:	3 days, 10 g N orally
Test period:	1 day, 10 g N parenterally

Total caloric supply daily: 2400 calories

rial (mostly casein). Their high content of non-utilizable peptides led to heavy urinary losses and subsequently to incompatibility reactions.

b) The concept of limiting the pattern of the plasma free amino acids soon proved to be wrong (see fig. 7).

Although these preparations were further improved, the amino acid pattern is certainly not optimal yet, considering certain amino acids. For example, these preparations have not enough sulphur-containing amino acids which are especially important for wound healing. This may be seen from the resulting decrease in plasma methionine below normal (see fig. 8).

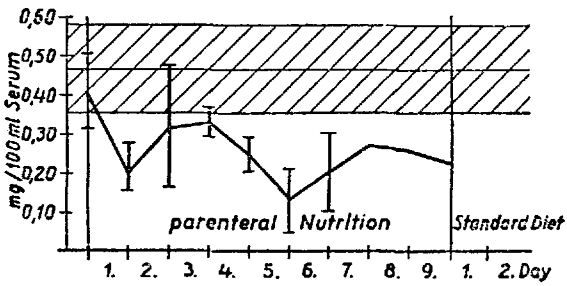

Fig. 8. Serum methionine after infusion of an amino acid solution adapted to plasma (normal range shaded) (according to *Dolif, D.* and *P. Juergens*, 17).

Fig. 9. Estimated requirements to produce positive nitrogen balance.

Amino Acid	Requirement for Zero Balance, mg/day	Requirement for Positive Balance of 0.5 g/day, mg/day	% Increase
Tryptophan	168	270	160
Phenylalanine	258	550	213
Threonine	375	1,750	465
Isoleucine	550	1,700	310
Lysine	544	1,750	321
Methionine	700	3,450	493
Valine	622	1,000	161
Leucine	727	2,600	367

According to *D. M. Hegsted* (16).

c) The very concept of the p. e. (potato-egg) solutions show that these solutions are not optimal for most indications of intensive care. The potato and egg protein mixture developed by *Kofranyi* (49) which *Kluthe* (48) used in renal therapy at a ratio of 2 : 1 is valid only if a minimal supply of nitrogen is necessary as e. g. in a uraemic diet. When higher nitrogen supplies become necessary following trauma, surgery, and especially burns, those solutions designed for and tested at the minimum would only show a suboptimal amino acid pattern.

Hegsted (38) showed that in passing from zero balance to a positive nitrogen balance, i.e. with higher nitrogen intakes, the requirement

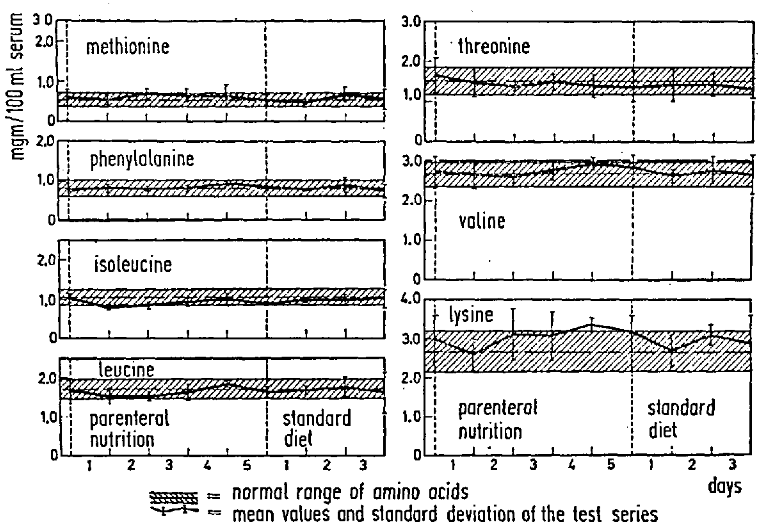

Fig. 10. Levels of the essential amino acids (except tryptophan) in fasting serum under standard diet and under parenteral nutrition with a requirement-adapted amino acid mixture (test group F) (according to *Dolif, D.* and *P. Jürgens,* 46).

of each amino acid rises disproportionally. Methionine which is the limiting amino acid in solutions of the types b) and c) shows the greatest increase.

Besides, it should be noted that the amino acid composition of the so-called p. e. solutions does not at all correspond to that of a real 2 : 1 potato egg protein mixture, regarding the essential amino acids, and even more so regarding the non-essential amino acids.

d) Those amino acid solutions most commonly used in Europe today, are the so-called requirement-adapted amino acid mixtures. The aim is really just to meet certain requirements in view of a clinically relevant nitrogen intake.

In the beginning, the most widely used preparation of this kind was based on the requirement figures according to *Rose* (57). It was, however, continually improved during the 14 years of its clinical application by special sensitive methods. Although today nitrogen balance remains the decisive criterion for such preparations, differentiated methods become necessary to fully understand the amino acid metabolism. One of these is the assessment of the plasma free amino acids in the "steady state". At first, the object was to optimize the proportions of the essential amino acids. As fig. 10 shows, these remain in the normal range when a balanced mixture is given, whereas an imbalanced mixture causes the corresponding changes (fig. 8).

The role of the non-essential, i.e. non-specific amino acids should not be underestimated. The *FAO/WHO* Report on "Protein Requirements" (22) states regarding the non-essential amino acids: "... which, in spite of their being so designated, are necessary parts of the protein molecule and hence needed for protein synthesis ... Even in the case of the human infant the limiting factor at low levels of milk intake has proved to be unessential nitrogen rather than any of the essential amino acids."

Therefore, some of the authors are wrong in trying to evoke the impression that the higher the content of essential amino acids in an amino acid mixture (expressed in the so-called E/T ratio), the higher the biological value.

The *FAO/WHO* Report cited which introduced the E/T ratio

$$\text{E/T ratio} = \frac{\text{g essential amino acids}}{\text{g total protein nitrogen}}$$

stresses that in many problems the E/T ratio is higher than optimal. For example, egg protein with an E/T ratio of 3.2 may be diluted by ammonium salts as the source of non-essential nitrogen to an E/T ratio of only 0.6 without losing its biological value.

Several research groups found that glycine is unsuitable as the only source of non-essential nitrogen. In fact, the addition of glycine to an optimal mixture of essential and semi-essential amino acids caused marked changes in plasma amino acids (fig. 11) which could be avoided by using a balanced mixture of glycine, alanine, and proline. The latter two substances seem to be essential in parenteral nutrition. This was evident in the behaviour of the plasma amino acids (fig. 11).

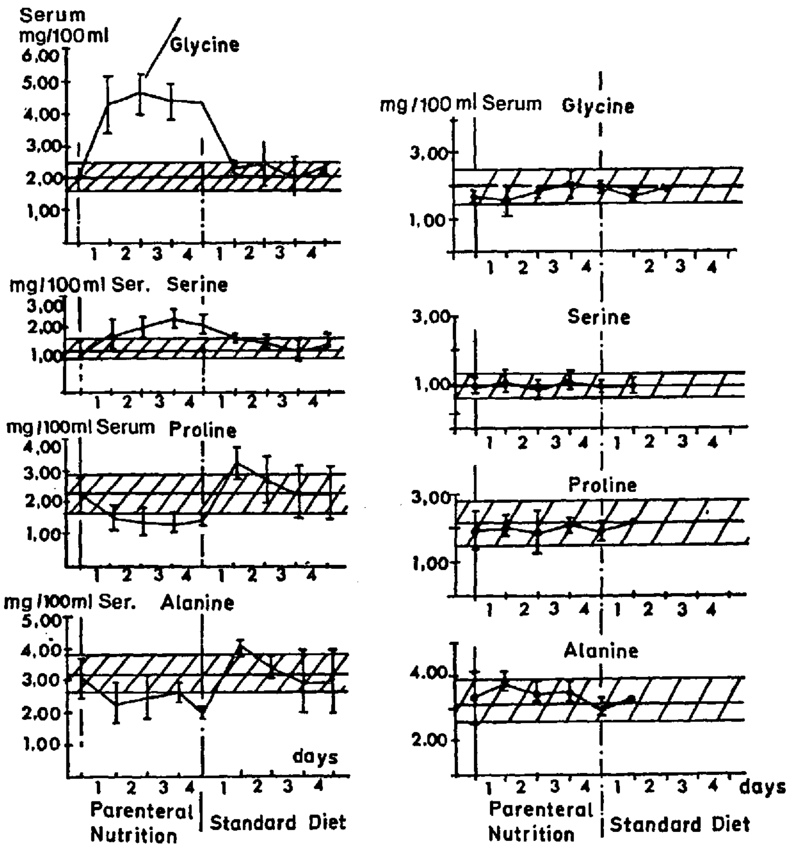

Fig. 11. Behaviour of the plasma level of some non-essential acids after infusion of an amino acid mixture containing glycine as the only non-essential N source (left column) and after infusion of a balanced amino acid mixture (right column) (16, 17).

The nitrogen balances in the two test groups showed marked differences. Nitrogen excretion of patients of the left group was, in fact, higher than their intake. This effect is particularly drastic with an absolutely imbalanced commercial preparation still produced and sold because the essential amino acid tryptophan is completely omitted (fig. 12, left column). Instead of supporting the organism's regeneration, the administration of such preparations additionally induces disadvantageous nitrogen losses.

III. Administration of amino acid solutions

Numerous cases of long-term parenteral nutrition show that all factors relevant to an adequate parenteral nutrition are known today. *Jarnum* (44) recently reported the almost complete intravenous alimentation of a patient based on a requirement-adapted amino acid solution for over

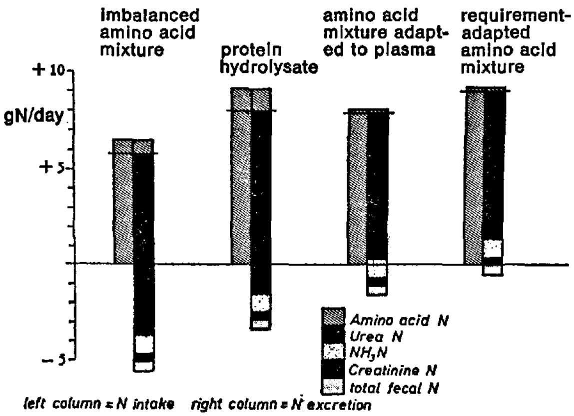

Fig. 12. Nitrogen balance after various amino acid solutions (17).

three years. Such cases are, of course, relatively rare, but they demonstrate the achievements in this field particularly well.

Amino acid therapy is of considerable importance in the compensation of larger nitrogen losses, as they occur following trauma of any kind, particularly after fractures and, to the greatest extent, after burns. These losses were beautifully shown in the well known studies of *Kinney* (47, fig. 13).

Certainly, there is no need to further discuss the effects of those nitrogen losses on wound healing, liver detoxication, the albumin pool, etc. An adequate supply of high quality proteins is especially important for

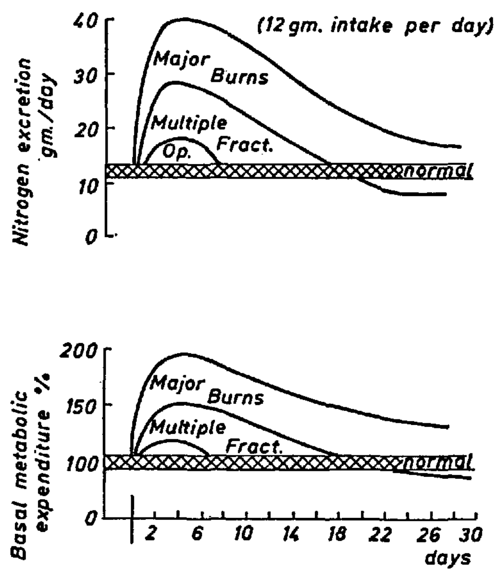

Fig. 13. Influence of trauma on nitrogen excretion and metabolic expenditure (47).

Fig. 14. Amino acid requirements during parenteral nutrition (g/kg body weight/day) (21).

Adults	0.8–1.6
Infants, pregnant women, patients during the postoperative period	1.6–2.0
Premature infants, hypotrophic new-borns and new-borns	2–3
Renal insufficiency (here for meeting the endogenous nitrogen minimum)	0.4

strengthening to body's resistance against infection (particularly the bilding of antibodies) which is also stressed in the *WHO* Report no. 57 (1968). Further indications for the provision of amino acids are nutritional problems of pregnant women, premature infants, severe maldigestion and malabsorption states, uraemia, and, of course, the care of the unconscious patient. Basically, most indications may be seen from fig. 6. A simple dosage scheme is given in fig. 14, corresponding to the recommendations of the ISPN (21).

The standard value for the infusion rate of amino acids (expressed as g nitrogen) is: 0.02–0.03 g/kg/h.

The question of caloric intake together with amino acid infusions still is to be discussed. If suitable carbohydrates are not infused simultaneously, amino acids are burned, as indicated in chapter I, or used for gluconeogenesis and are thus kept from performing their tasks in protein synthesis and several other essential metabolic functions. The liver, as the "laboratory of the body", must be of primary interest. As parenteral amino acids are mostly administered in stress situations, the special metabolism of stress must be considered when choosing the carbohydrates.

In this context, the often considerable disturbance of glucose metabolism is rather important. In stress, glucose is no longer a substrate for the liver, but a product; this means that, if glucose homeostasis is to be maintained, the liver must be given substrates utilizable under these conditions (such as fructose, sorbitol, xylitol). Otherwise the liver would be forced to use the amino acids for gluconeogenesis (*Förster,* 28, 29, 30). There is a deficiency of glucose utilization despite increased levels of blood insulin under stress (*Schultis;* 60, 61, 62). Apart from the danger of sensibilization, this is another reason why additional insulin doses are not the ultimate solution to the problem.

Therefore, it may be dangerous in the stress phase to cover carbohydrate requirements with large amounts of glucose. In the U.S., there have been reports of dangerous, even lethal, syndromes caused by infusion of hypertonic glucose in complete parenteral nutrition which were described as „hyperosmolar, non-ketotic, hyperglycemic comas" (64). *Dudrick* (18) gave the critical indications shown in fig. 15.

Patients at the Institute for Anaesthesiology of the University of Mainz also showed increases in blood glucose following glucose infusions in the postoperative phase in accordance with the American results (33).

Today, especially in Germany, sugar substitutes are preferred in parenteral nutrition, as they are easily utilizable precursors of glucose. It became apparent that a maximum infusion rate of 0.25 g/kg/h for each car-

Fig. 15. Conditions associated with the hyperosmolar hyperglycemic non-ketotic coma of parenteral alimentation (18).

Excessive total quantity of dextrose infusion
Excessive rate of dextrose infusion
Overt or latent diabetes mellitus
Intraoperative response to anesthesia and surgery
Immediate postoperative response to anesthesia and surgery
Focal infection or generalized sepsis
Shock
Severe blunt trauma
Major or multiple fractures
Major full-thickness burns
Intracranial disorders, trauma, operation
Acute or chronic renal failure
Hepatic disorders or insufficiency
Pancreatic disorders or insufficiency
  Acute or chronic pancreatitis
  Primary or metastatic malignancy
  Pancreatic fibrosis
Geriatric patients
Premature infants or full-term neonates

bohydrate is desirable to avoid side effects. The polyols sorbitol and xylitol have the advantage that they can be sterilized with amino acids without producing the so-called *Maillard* reaction, leading to a devaluation of the amino acid mixture e. g. by destruction of lysine or development of biologically different – perhaps toxic – substances.

The mixture of 50 % sorbitol + 50 % xylitol proved to be especially favourable as these two substrates follow different metabolic pathways after the first – at normal infusion rates not limiting – metabolic step (oxidation).

In order to ensure particularly high caloric carbohydrate supply to supplement amino acid infusions without overstraining glucose tolerance, efforts have been made to find optimized carbohydrate mixtures to suit the various conditions. At three different institutes, i.e. the Department of Metabolism and Nutrition at the University Hospital of Erlangen, and the Institutes for Anaesthesiology of the Universities of Mainz and Ulm, optimal results have been achieved using a mixture of 50 % fructose, 25 % xylitol, and 25 % glucose (5, 33, 34). Doses of a total of 0.5 g of carbohydrates/kg/h neither had a negative effect on the aid-base balance nor on the parameters of sugar metabolism nor liver function (5).

Fat emulsions are unsuitable as source of energy in stress, certainly in adults. As with glucose, there seems to be malutilization accompanied by increased mobilization. *Schultis* observed (60, 61, 62) that partial substitution of carbohydrate calories by fat calories in postoperative parenteral alimentation leads to negative nitrogen balance. This finding could be confirmed by *Halmagyi* at the Institute for Anaesthesiology of the University of Mainz, as well as by *Heller* whose recent tests on female patients receiving X-ray therapy had similar results (41). *Eckart* (20) further confirmed these findings by his tests with isotope labelled fat emulsions. It became evident that only a maximum of 30 % of the posttraumatically infused fat is utilized within 24 hours. The remaining 70 to 80 % is partly stored in the RES and partly in the fat depots. *Kupffer* cells and the liver parenchyma have been identified among others as storage cells. More recently, there have again been reports of deaths from "fat overloading syndrome" after comparatively short-term parenteral alimentation with fat emulsions (*Födisch*, 27) which must be seriously considered. From the anaesthetist's point of view, there is also a danger in a reduced gas transport between the alveolar space and the erythrocytes after fat infusions, as demonstrated by *Greence* (32) and colleagues.

As far as the techniques of infusing amino acid solutions are concerned, it should be noted that short-term parenteral alimentation may be infused through peripheral veins, whereas in long-term infusions, especially when administering highly hypertonic sugar solutions, the superior vena cava catheter should be used. Because of the infectious and thrombotic effect, however, use of the veins of the lower extremities is to be avoided (for details see *Burri*). The basilic, jugular, and subclavian veins are to be preferred. Previously injured tissue (e. g. by burns, trauma, haematoma) must also be avoided when introducing the catheter because of the increased risk of infection.

The following conclusions from the above deserve attention:

1. Optimal regulation of the body's homeostasis seems to be possible only by maintaining the substrate intake, above all the substrates of protein metabolism.
2. The so-called requirement-adapted amino acid mixtures make it possible to ensure an optimal intravenous supply even at increased protein requirements, and – at the same time – to normalize such important biological parameters as the albumin pool and the liver function.
3. Even if positive or equilibrated nitrogen balance can not always be achieved, it seems important to keep nitrogen losses as low as possible from the beginning to avoid protein depletion which is often accompanied by lowered resistance to infections, disturbances in wound healing etc.
4. Large amounts of glucose to cover energy requirements are dangerous in stress situations. Mixtures with sugar substitutes (e. g. fructose, xylitol, glucose with a ratio of 2 : 1 : 1) are to be preferred, and in amino acid mixtures above all xylitol or sorbitol or xylitol + sorbitol, as they do not produce side products during sterilization.
5. Fat is unsuitable as a calorie source in the posttraumatic phase.
6. In short-term infusions a supply of amino acids may be given peripherally, whereas long-term parenteral nutrition and highly hypertonic sugar solutions should be administered through a central vein. With modern techniques, parenteral nutrition may be carried out for practically unlimited periods.

Summary

In recent years, there have been conclusive findings in the field of maintaining homeostasis following trauma, bleeding, nutritional and metabolic disturbances and infections. These findings can help save the lives of an in-

creasing number of injured and sick by enlarging the therapeutic possibilities which have previously been unimaginable.

This development has been made possible by the good cooperation of both basic research and clinical staff whose common aim was to achieve advances in this field of intensive care.

The aim of the present study is to make a relevant theoretical and practical contribution to the widening possibilities and necessities in this field.

Zusammenfassung

Die letzten Jahre haben auf dem Gebiet der Aufrechterhaltung der Homöostase im Schock, nach Traumen, nach Streß, nach Blutungen, nach Ernährungs- und Stoffwechselstörungen und nach Infekten entscheidende Erkenntnisse gebracht. Diese gewinnen bei einer steigenden Zahl von Verletzten und Kranken lebensrettende Bedeutung durch Erweiterung der Therapiemöglichkeiten, wie sie bisher nicht denkbar waren.

Entscheidend beigetragen hat zu dieser Entwicklung die kollegiale Zusammenarbeit von Grundlagenforschern (vor allem physiologischen Chemikern) einerseits und Klinikern andererseits (vor allem Anästhesiologen, Chirurgen, Internisten, Reanimatologen usw.), vereinigt in gemeinsamen Bemühungen um Fortschritte auf dem Gebiet der Intensivtherapie.

Die vorliegende Arbeit möchte einen speziellen nicht nur theoretisch, sondern auch praktisch wichtigen Beitrag leisten zu dieser Entwicklung: Die Zurückdrängung der Bluttransfusion (gefährlich wegen der schlechten Haltbarkeit, häufigen Unverträglichkeit und der Gefahr der Übertragung von Infektionskrankheiten wie Hepatitis, Syphilis usw.) durch die heute vorhandenen verbesserten Aminosäurengemische. Diese sind gut verträglich, lange lagerfähig und bei vielen neuen Indikationen wirkungsvoller als das bisher hierfür verwendete Blut und seine Derivate. Die neuen Aminosäurengemische sind deshalb berufen, besonders in der Katastrophenmedizin und in der postoperativen Behandlung eine bedeutende Rolle zu spielen und eine bisher oft bedrückende Lücke in der Versorgung der uns anvertrauten Kranken zu schließen. Einen Überblick über diese neuen Möglichkeiten zu geben, ist das Ziel dieser Arbeit.

References

1. *Bässler, K. H.*, Z. Ernährungswiss. Suppl. **10**, p. 57–72 (Darmstadt 1971). – 2. *Bässler, K. H., W. Fekl, K. Lang*, Grundbegriffe der Ernährungslehre (Berlin–Heidelberg–New York 1973). – 3. *Bauer, B. L.* und *K. Schultis*, Actuelle Chirurgie **1**, 281–286 (1966). – 4. *Beisbarth, H.* and *W. Fekl*, Z. Ernährungswiss. Suppl. **10**, p. 73–88 (Darmstadt 1971). – 5. *Berg, G., H. Bickel, F. Matzkies*, Dtsch. med. Wschr. **98**, 602–610 (1973). – 6. *Bergmann, H., St. Necek, D. A. Coats* and *K. Lang*, Wiener Klin. Wschr. **84**, 708–712 (1972). – 7. *Bertalanffy, L. v.*, Kolloid Z. **139**, 86–91 (1954). – 8. *Bickel, H., H. Bünte, D. A. Coats, P. Misch, L. v. Rauffer, P. Scranowitz*, Dtsch. Med. Wschr. **96**, 809–813 (1973). – 9. *Bünte, H.*, Möglichkeiten und Grenzen der künstlichen Ernährung. Materia Medica Nordmark XVI, 479–491 (1964). – 9 a. *Burri, C.*, Der zentrale Venendruck. Wiss. Schriftenreihe 4, 3rd ed. 1971. – 10. *Cannon, R. R.*, Some Pathologic Consequences of Protein and Amino Acid Deficiencies (Springfield, Ill., 1948). – 11. *Coats, D. A.*, Z. Ernährungswiss. **9**, 401–402 (1969). – 12. *Coats, D. A.*, Langenbecks Archiv Chir. Suppl. Chirurg. Forum p. 175–178 (1972). – 13. *Daly, J. M., A. B. Harry, M. Vars* and *S. J. Dudrick*, Surg. Forum Vol. XXI (1970). – 14. *Dobersky, P., V. Kudlicke, M. Vulterinova, V. Parikova, V. Kudlicková*, Fortschritte der parenteralen Ernährung. Ed.: *Berg, G.*, p. 146–152 (Stuttgart 1970). – 15. *Dölp, R., F. W. Ahnefeld* and *L. Fodor*, Die Infusions-

therapie, spec. issue 2, p. 79–84 (1973). – 16. *Dolif, D.* und *P. Jürgens*, Med. Ern. **11**, 67–71 (1970). – 17. *Dolif, D.* and *P. Jürgens*, Z. Ernährungswiss. Suppl. **10**, Parenterale Ernährung. Hrsg.: *Lang, K.* u. *W. Fekl*, S. 24–56 (Darmstadt 1971). – 18. *Dudrick, S. J., B. V. MacFayden, C. T. van Buren, R. L. Ruberg, A. T. Maynard*, Ann. Surg. **176**, 259–264 (1972). – 19. *Dudrick, S. J.* (Ed.), Current Concepts in Parenteral Feeding. Symp. Philadelphia (USA) Okt. 1971. Z. Ernährungswiss. Suppl. in press (Darmstadt). – 20. *Eckart, J., G. Tempel, Schurnbrand, H. Schaaf, A. Kaul* and *G. Witzke*, Investigations on Metabolism of Radioactive Labeled Fat Emulsions in the Postoperative and Posttraumatic Period. Summaria IX Int. Congr. of Nutr. (Mexico 1972). – 21. Empfehlungen zur parenteralen Ernährung. Med. Ern. **8**, 193–195 (1967); **9**, 217–218 (1968); **10**, 65–66 (1969); **11**, 201–205 (1970). – 22. FAO Protein Requirements. Report of Joint FAO/WHO Expert Group. WHO Technical Report, Series No. 301. Food and Agriculture Organization of UN (Rome 1965), 2. Ed. (1969). – 23. *Fekl, W.*, Diskussionsbeitrag. Verh. Dtsch. Ges. Inn. Med. 72. (München, 1966). – 24. *Fekl, W.*, Med. Ern. **11**, 2–6 (1970). – 25. *Fekl, W.*, Z. Ernährungswiss. Suppl. **13**, Rehabilitation durch Ernährung. *Doberský, P.* (Darmstadt 1972). – 26. *Fekl, W.*, Diskussionsbeitrag, in: Parenterale Ernährung. *Beisbarth, H., K. Horatz,* P. *Rittmeyer* (Stuttgart, in press). – 27. *Födisch, H. J., A. Probst* and *G. Mikuz*, Verh. Dtsch. Ges. Pathol. **56.** Tg. *G. Seifert*, p. 431–435 (Stuttgart 1972). – 28. *Förster, H.*, Med. Ern. **13**, 7–15 (1972). – 29. *Förster, H.*, Dtsch. Med. Wschr. **98**, 839–844 (1973). – 30. *Förster, H.*, Stoffwechsel von Monosacchariden und Polyolen unter verschiedenen Bedingungen. – 31. *Fürst, P., B. Josephson* und *E. Vinnars*, Scand. J. Clin. Lab. Invest. **26**, 319–326 (1970). – 32. *Greence, H., D. Hazlett, R. Dermarre, J. Dramesi*, Effect of Intralipid on Pulmonary Function in Normal Humans and on Election Microscopy of Rabbit Lung and Liver. Summaria IX Intern. Congr. of nutrition, Mexico, S. 197 (1972). – 33. *Halmagyi, M.*, Komplette parenterale Ernährung Traumatisierter. Grundlagen u. Praxis d. parenteralen Ernährung (Stuttgart 1974 i. Dr.). – 34. *Halmagyi, M.*, Bilanzierte Substitutionstherapie durch Infusionen (Elektrolyte, Aminosäuren und Energieträger) bei schwerkranken traumatisierten Patienten. Die Infusionstherapie, spec. issue 2 (1973) (Erlangen 1973 i. Dr.). – 35. *Hartig, W.*, Z. Exper. Chirurgie **2**, 102–113 (1969). – 36. *Hartig, W., K. Wetzel, O. Gebhardt, H.-D. Czarnetzki* and *G. Hübner*, Z. Exper. Chirurgie **3**, 56–72 (1970). – 37. *Hartig, W., G. Hübner, H.-D. Czarnetzki, O. Gebhardt* and *K. Wetzel*, Z. Exper. Chirurgie **3**, 170–176 (1970). – 38. *Hegsted, D. M.*, Variation in Requirements of Nutrients-Amino-Acids. Fed. Proc. **22**, 1424–1430 (1963). Nutrition Symposion, Food and Nutritional Problems in Prolonged Space Travel. – 39. *Heller, L.*, Geburtsh. u. Frauenheilkunde **28**, 848–862 (1968). – 40. *Heller, L.*, Scand. J. Gastroenterol. **4**, Suppl. 3, 7–16 (1969). – 41. *Heller, L.*, Die Bedeutung intravenös applizierter Fettemulsionen für die parenterale Ernährung. Grundlagen u. Praxis d. parenteralen Ernährung (Stuttgart 1974). – 42. *Holt, L. E., P. György, E. L. Pratt, S. E. Synderman, W. M. Wallace*, Protein and Amino Acid Requirements in Early Life (New York 1960). – 43. *Jarnum, S.*, Parenteral Nutrition, S. 93–98. Ed.: *A. W. Wilkinson, Churchill* (Edinburgh 1972). – 44. *Jarnum, S., K. N. Jeejeebhoy, A. V. Borkar* and *H. Westergaard*, Scand. J. Gastroenterology **4**, Suppl. 3, 35–39 (1969). – 45. *Jürgens, P.* and *D. Dolif*, Klin. Wschr. **46**, 131–143 (1968). – 46. *Jürgens, P.* and *D. Dolif*, Med. Ern. **11**, 6–11 (1970). – 47. *Kinney, J. A.*, Energy Deficits in Acute Illness and Injury. Proceedings of a Conference on Energy Metabolism and Body Fuel Utilization, pp. 167–177 (1966). – 48. *Kluthe, R.*, Bilanzierte Ernährung in der Therapie, S. 244–251. *Lang, K., W. Fekl, G. Berg* (Stuttgart 1971). – 49. *Kofranyi, E.*, Die Nahrung **11**, 863–873 (1967). – 50. *Kudlicka, V., P. Doberský, M. Vulterinová* und *V. Kudlickova*, Z. Ernährungswiss. Suppl. **13**, p. 53–64 (1972). – 51. *Kudlicka, V., P. Doberský, V. Kudlickova*, A New Approach of Evaluate the Final Effect of Parenteral Nutrition, i. Dr. – 52. *Lang, K.* und

W. Fekl, Med. Ern. **10,** 205–212 (1969). – 53. *Lang, K.* and *W. Fekl,* Z. Ernährungswiss. Suppl. **10,** Parenterale Ernährung, S. 1–23 (Darmstadt 1971). – 54. *Munro, H. N.,* Bilanzierte Ernährung in der Therapie, p. 1–21. *Lang, K., W. Fekl, G. Berg* (Stuttgart 1971). – 55. *Munro, H. N.,* Anaesthesiologie u. Wiederbelebung Vol. 58, p. 20–31. Hrsg.: *Lang, K., R. Frey* und *M. Halmagÿi,* Stoffwechsel, Pathophysiologische Grundlagen der Intensivtherapie (1972). – 56. *Peaston, M. J. T.,* Postgrad. Med. J. **43,** 317–338 (1967). – 57. *Rose, W. C.,* Physiological Review **18,** 109–136 (1938). – 58. *Sall, S., B. Brofmann* and *M. L. Stone,* Amer. J. Obstet. Gynec. **114,** 500–506 (1972). – 59. *Schultis, K.* und *B. L. Bauer,* Z. Prakt. Anaesthesie u. Wiederbeleb. **2,** 228–239 (1967). – 60. *Schultis, K.,* Excerpta Media, International Congress Series No. 242, p. 196–200 (1970). – 61. *Schultis, K.,* Komplette parenterale Ernährung in der Chirurgie. Grundlagen u. Praxis d. parenteralen Ernährung (Stuttgart 1974). – 62. *Schultis, K., H. Bickel, H. Beisbarth* und *O. Brand,* Infusionstherapie, spec. issue 2, p. 65–69 (1973). – 63. *Vinnars, E.* and *P. Fürst,* Acta Anaesth. Scand. **14,** 259–271 (1970). – 64. *Wyrick, W. J., W. Rea* and *R. McClelland,* Arch. Surg. **101,** 436 (1970); Amer. J. Obstet. Gynec. **114,** 500–506.

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