has to adjust dosages at an extreme health condition of a neonate. An important advantage is the elimination of calculation errors.

One major disadvantage of VIE–PNN is that the user cannot interrupt the nutrition calculation and carry on at the break point. This would be beneficial to the daily practical clinical use, where the physician may suddenly have to stop calculation for checking a patient.

During the evaluation we mentioned possible improvement. One example is the use of detailed information about the parenteral nutrition components of the different oral feeding products, which we do not account for explicitly at the moment. From the user interface point of view, the possibility to display trend data in graphical or numerical form during the composition phase would be helpful. An on–line connection to acquire laboratory measurements for the input is planned.

Acknowledgement

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time, and if the user interface and the dialogs are evident and self–explanatory. This step combines both the empirical and the subjective evaluation.

+ third step: on–site evaluation of VIE–PNN at the NICU in the calculation of the daily enteral and parenteral nutrition solution.

Currently we have accomplished the first two steps of evaluation and we are starting to have VIE–PNN in daily clinical use.

Step one was completed successfully after several enhancements of the knowledge base. These enhancements were motivated by the different views of the two experts about practical solutions to specific problems in the nutrition composition.

In step two we have tested 80 cases, six patients with different nutrition requirements and preconditions during a period of 10–15 days. We valued by (1) correct, (2) one component needed to be refined by the physician, (3) more than one component needed to be refined: 63 cases were correct, in 13 cases one nutrition element was adjusted and in 4 cases more than one component was adjusted.

The need for adjustments results from the design of VIE–PNN's knowledge base. It could not incorporate all possible complications for all patients. Consequently we designed an *interactive* support system. The physician has to adjust the dosage to reflect the complication of the many possible diseases (Schaffer 1965) which we could not account for by explicit rules. This has occurred in the 13 cases shown above. In such cases the physician does not have an exact solution to the nutrition problem, but often prescribes extreme doses. VIE–PNN, in contrast, operates more conservatively. In general, VIE–PNN's behavior seems acceptable from the user's point of view. Furthermore, VIE–PNN has proved not to prescribe dangerous dosages even for complicated circumstances.

Up to now, we have not really evaluated the aspect of time consumption systematically. At first view the time need to compose a nutrition solution with VIE–PNN is not much better compared to the manual calculation. Seidel et al. (1991) discovered a decrease in total time spent per parenteral nutrition solution after introduction of a computer program for a while. When looking at their results it is necessary to mention that in contrast we developed an interactive support system, which needs time for data input and validation of data. Furthermore the implementation in "I/C" has several performance problems which motivates the redesign in C++.

In summary VIE–PNN accomplished the desired goals of supporting a physician in parenteral nutrition planning. The advantage of VIE–PNN is that it is strictly maintenance value oriented and that all preconditions of the nutritional needs are represented in the knowledge base. Consequently it could not happen that e.g. a less experienced physician would prescribe vitamins before the second week of a neonate's life, or would forget trace elements. Finally, no more calculating mistakes occur.

6. Conclusions / Further Development

One major advantage of an expert system is its ability to combine the knowledge of multiple experts. The level of expertise may exceed that of a single human expert. VIE–PNN's main part of the knowledge base embodies the knowledge of an experienced physician, but during the first evaluation step the knowledge of a second expert with different experience has been added.

Additionally, VIE–PNN acts as an intelligent supervisor by considering all possible variants of parenteral nutrition composition and dependences. This supports a less experienced physician by avoiding the neglect of important nutritional requirements and needs. VIE–PNN is strictly maintenance value oriented, i.e. it ensures that the necessary life–preserving values of all nutrition components are delivered. Since the interactive support system is not able to account for all possible complications and diseases of a neonate, the physician

```
% RULE 14
reduce-intralipid-?  'ReduceG', 'ProposedQuantity'
   if      'ReduceG' = 0;
% RULE 15
 reduce-intralipid-?  'ReduceG', 'ProposedQuantity'
   if      'ProposedQuantity' := 'ProposedQuantity' - 'ReduceG';
```

The increasing or decreasing of the fat value depending on "triglycerides" is handled in detail by rules RULE 08–15. Normally the "intralipid" amount is increased by 0.5 units per day (RULE 08). Additionally, RULE 09–15 correct the "intralipid" value with respect to the measurement "triglycerides" (e.g. if the triglycerides are higher than 300 (mg/dl), the fat's supply is decreased by 1.5 units).

```
% RULE 16
first-nutrition-day-of-older-3-neonate   'ProposedQuantity'
   if      'Days' := (Days of AInfant)
      and 'ProposedQuantity' := ('Days' - 3) * 0.3
      and 'ProposedQuantity' <= 2.5 ;
% RULE 17
first-nutrition-day-of-older-3-neonate    'ProposedQuantity'
   if      'ProposedQuantity' := 2.5;
```

RULE 16–17 show the use of defaults in case the neonate is a new patient at the ICU and is older than three days.

```
% RULE 18
convert-g-to-ml  'GQuantity', 'Concentration', 'MlQuantity'
   if      get-neonates-body-weight  'G'
      and 'Kg' := 'G' / 1000
      and 'MlQuantity' := ( 'GQuantity' * 'Kg' * 100 ) / 'Concentration' ;
```

Finally, RULE 18 shows the influence of the body weight when converting the unit.

4. Implementation

VIE–PNN is an application system implemented on an IBM compatible PC using the Expert System Shell "Intelligence/Compiler (I/C)", Version 3.0, (IntelligenceWare, Inc., Los Angeles). VIE–PNN was developed by the Austrian Research Institute for Artificial Intelligence (ÖFAI), the Department of Medical Cybernetics and Artificial Intelligence, and the Department of Pediatrics, Neonatal Intensive Care Unit (NICU), University of Vienna. Currently we are starting to use VIE–PNN in the clinical routine at the NICU for calculating the daily nutritional composition.

Due to the problems with memory limitations and bugs in "I/C" a redesign of the system in C++ is currently in progress.

5. Evaluation

The objective of the knowledge–base evaluation is to determine the correctness, completeness, and consistency of the system. We evaluated VIE–PNN in three steps (compare e.g. Adelman 1992):

+ first step: technical evaluation of VIE–PNN on real problems by the knowledge engineer and two experts to determine whether the system comes up with the experts' viewpoints of parenteral nutrition planning;
+ second step: system testing by an experienced physician, who is directly involved in the daily parenteral nutrition calculation. We evaluated VIE–PNN for its correctness with respect to user's needs and requirements, e.g. if the theoretical concepts are corresponding to the practical routine work, if all necessary information about the neonate's health condition, laboratory values, etc. is available at the proper

RULE 02 shows the influence of age. It ensures that neonates who are younger than 3 days do not get any amount of fat. RULE 03–04 show how a specific disease, namely “acute sepsis”, is handled and how the value of the previous day is used. RULE 03 checks that the neonate does not have “acute sepsis”, gets the value of the previous day, and fires the rules which deal with the existing or missing previous values (RULE 05–07). RULE 04 sets the value of “intralipid” to 0.5 in the presence of “acute sepsis”.

```
% RULE 05
 react-to-last-value 'GYesterday',  'GQuantity'
   if       last-value-exists
      and decrease-of-last-value 'GYesterday';
% RULE 06
 react-to-last-value 'GYesterday',  'GQuantity'
   if       last-value-exists
      and how-are-the-triglycerides  'GYesterday',  'ProposedQuantity' ;
% RULE 07
 react-to-last-value 'GYesterday',  'GQuantity'
   if       not last-value-exists
      and  first-nutrition-day-of-older-3-neonate  'ProposedQuantity'
      and read-non-empty  'ProposedQuantity', 3,
            "First nutrition calculation day, but neonate is older than 3 days:  g/kg/d Intralipid ok?";
```

The above three rules (RULE 05–07) show the reaction to existing or missing yesterday’s values. The clause **last-value-exists** becomes true if there is a yesterday’s value, otherwise it fails. RULE 05 checks, in the case of existence of the last value, whether it has been decreased in the past (**decrease-of-last-value** 'GYesterday', the description of this rule is not mentioned here.). RULE 06 accounts for fat value, in which case the measurements of triglycerides have to be taken into consideration. This is handled in detail by rules RULE 08–15. RULE 07 is fired if no yesterday’s value exists and the amount of fat is estimated (RULE 16–17) depending on the neonate’s age.

```
% RULE 08
how-are-the-triglycerides  'GYesterday',  'ProposedQuantity'
   if       'TG' := (TG of AJonogramm)
      and are-triglycerides-too-high  'TG',  'ReduceG'
      and reduce-intralipid-?  'ReduceG', 'ProposedQuantity'
      and 'ProposedQuantity' := 'ProposedQuantity' + 0.5;

% RULE 09
are-triglycerides-too-high  'TG', 'G'
   if       'TG' >  300
      and 'G' :=  1.5
      and store-Intralipid-has-been-reduced-TG;
% RULE 10
 are-triglycerides-too-high   'TG', 'G'
   if       'TG' > 250  and  'TG' <= 300
      and 'G' :=  1
      and store-Intralipid-has-been-reduced-TG;
% RULE 11
 are-triglycerides-too-high  'TG', 'G'
   if       'TG' > 200 and  'TG' <= 250
      and 'G' :=  0.5
      and store-Intralipid-has-been-reduced-TG ;
% RULE 12
 are-triglycerides-too-high    'TG', 'G'
   if        'TG' > 100 and  'TG' <= 200
      and 'G' := -0.5;
% RULE 13
are-triglycerides-too-high  'TG', 'G'
   if       'TG' <= 100
      and 'G' := -0.5;
```

3.3 Representing Theoretical and Practical Knowledge about Parenteral Nutrition in Rules

During the design of VIE−PNN we tried to represent the theoretical knowledge about nutrition solution composition and the practical knowledge of experienced physicians by one single mechanism, namely backward chaining rules.

The notation of rules is briefly summarized in the following. The backward rules are interpreted in a Prolog−like manner, where variables are denoted by quotes (e.g. 'Days'), and constants are any string of up to 80 characters (e.g. Monday, female, 12). The scope of each variable extends to only one rule. A backward rule begins with the conclusion (goal) followed by the reserved word "if" and then the premise.

In General:

```
---------
 conclusion
      if     premise ;
```

An Example:

```
----------
intralipid -calculation
      if        older-than-three-days  'Days', 'GQuantity'
          and   energy-rate 'GQuantity';
```

A clause (or goal) consists of a predicate and a number of arguments (e.g. **older-than-three-days** 'Days', 'GQantity'). Predicates are written in bold. Arguments to clauses may be constants or variables. Clauses may be joined together by the logical connectives "and" and "or" to form compound clauses. Clauses are negated by using "not".

In the example below we show how the domain problems described in chapter 2 are solved by this representation. The example presents the calculation of the nutritional component fat, namely "intralipid". The calculation of fat includes the interesting preconditions of neonate's age, neonate's body weight, the disease "acute sepsis", the values of the previous days, whether these values have changed or not, the course of laboratory measurement "triglyceride", past "intralipid" dosages, and the decreasing or increasing of "intralipid" dosage with respect to laboratory measurement "triglycerides". (The rules in the example are translated from German)

```
% RULE 01
intralipid -calculation
    if        'Days' := (Days of AInfant)
       and days-of-life  'Days', 'GQuantity'
       and convert-g-to-ml  'GQuantity', 20 , 'MlQuantity'
       and store-intralipid-quantity   'MlQuantity'
       and energy-rate 'GQuantity' ;
```

RULE 01 controls the calculation of the fat "intralipid". The first calculation requirement is the neonate's days of life. In the variable 'GQuantity' the amount of "intralipid" is returned. "Intralipid" is dosed in different units as it is displayed and stored. Therefore the amount has to be converted from 'g' to 'ml'. The last fired clause calculates the statistical value of the energy rate.

```
% RULE 02
days-of-life 'Days', 'GQuantity'
    if       'Days' <= 2
       and 'GQuantity' := 0;
% RULE 03
days-of-life  'Days', 'GQuantity'
    if       acute-sepsis  'YesNo'
       and 'YesNo' = No
       and last-intralipid-value  'GYesterday',
       and react-to-last-value 'GYesterday',  'GQuantity'
       and check-allowed-intralipid-limits  'GYesterday' , 'GQuantity';
% RULE 04
days-of-life 'Days', 'GQuantity'
    if       'GQuantity' := 0.5;
```

The knowledge base is divided into the static and the dynamic knowledge. The static knowledge is represented by backward chaining rules. It consists of the essential rules for the composition of the parenteral nutrition.

The dynamic knowledge contains all the data of the parenteral nutrition solution (PNS) of each neonate, which combines the neonate's personal description, the nutrition solution, the nutritional calculation requirements, and the statistical measurements, as shown in Figure 2. These data are represented in a frame structure. The values of the PNS are written to the slots of the frames by the backward chaining rules. All these data are printed on the PNS schedule form.

The knowledge acquisition facility provides means for the expert to enhance the static knowledge base by entering new bypasses and oral feeding products.

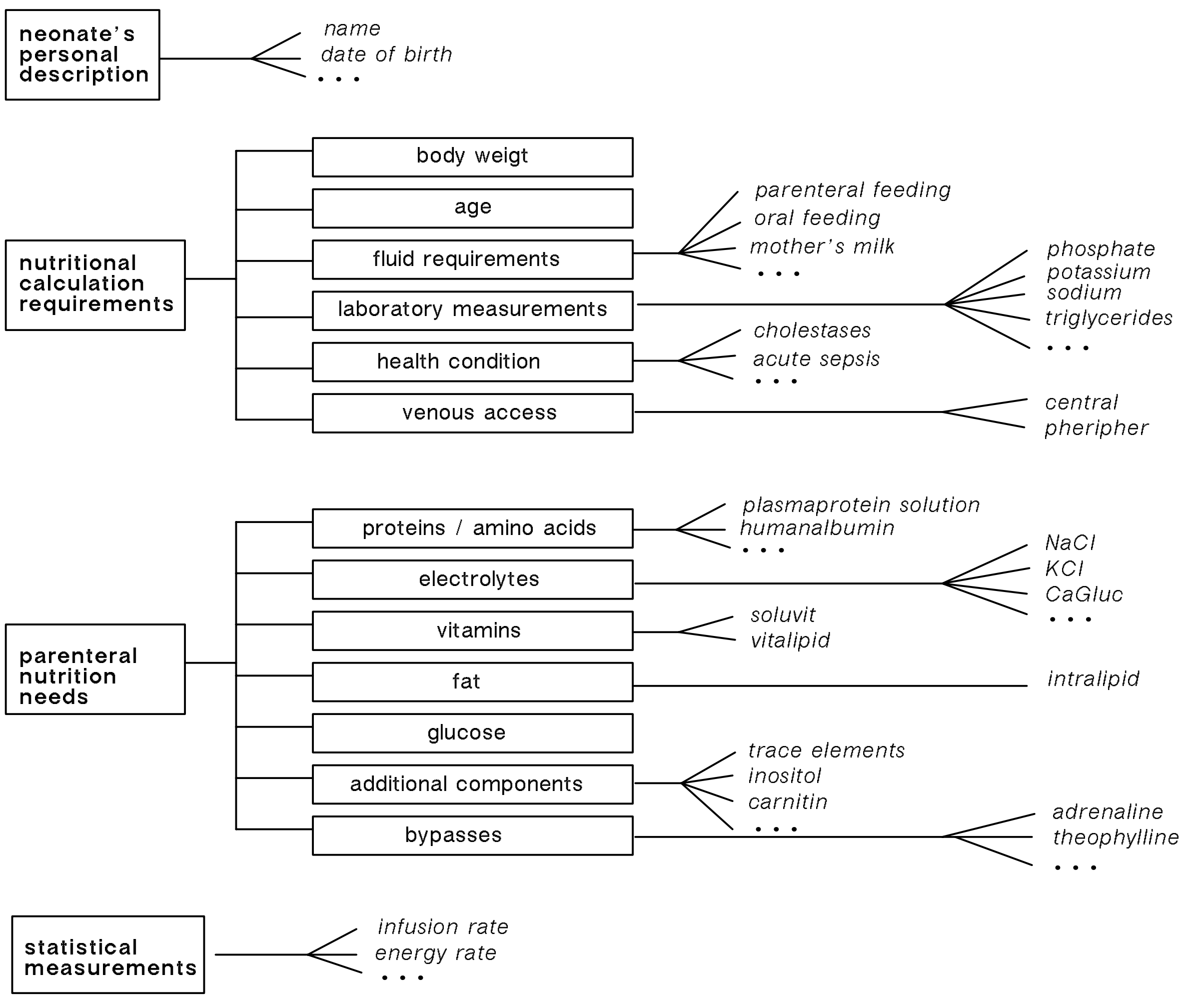

Figure 2: Nutrition components of the parenteral nutrition solution (PNS)

(5) to check data input limitations, but to tolerate extreme values on users' request;

(6) to produce a printed schedule including parenteral and enteral fluid needs (the PNS), that can be used directly in the case history of neonates. It allows the nurses to compose the daily mixture of the parenteral nutrition infusion;

(7) to enable the expert to extend the list of bypasses and oral feeding products;

(8) to collect and to keep the input and calculated data for further statistical analysis.

3.2 System Description

The system consists of four major components, as given in Figure 1:

1) the user interface
2) the inference engine
3) the knowledge base
4) the knowledge acquisition module.

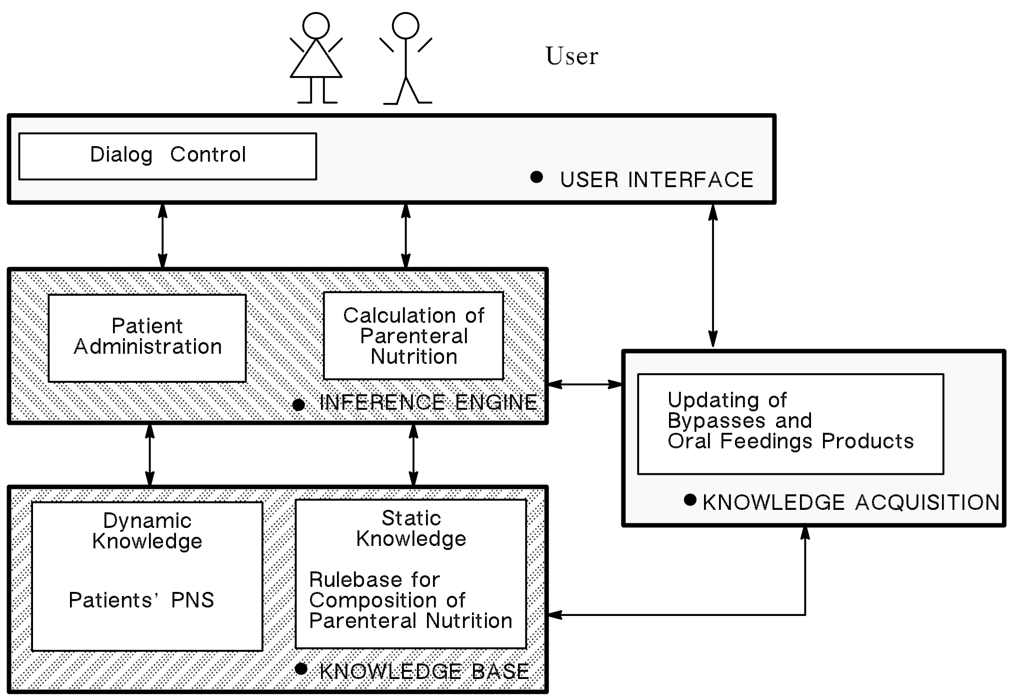

Figure 1: System Structure of VIE-PNN

The user interface uses the menu system of the Expert System Shell "Intelligence/Compiler (I/C)". One of the main design problems is caused by the impossibility to fit the whole PNS onto a single screen, which would be optimal. We had to divide the values of the PNS into connected parts, which are displayed on one screen. A similar problem occurs with the input of the relevant nutrition calculation requirements. We split it into parts having the same context.

The inference engine consists of two modules:

- a module for patient administration, which allows to add new patients, and to file and to retrieve old ones;
- a module for nutrition calculation, which applies backward chaining to the rules given below;

with the practical clinical knowledge of experienced physicians. Consequently we developed standardized schemata, which define the maintenance dosage of nutritional components of neonates. These schemata are enhanced by rules reacting to abnormal laboratory measurements. These rules furthermore include the dependences of age, body weight, neonate's health condition, and nutritional components of the previous days. The rules are derived from the clinical experience in combination with well–known standards of nutrition needs (Niemer et al. 1992). As a result the reaction schemata enforce at least the prescription of the maintenance dosage of the parenteral nutrition components. These dosages are sometimes overlooked at manual calculation. The solutions are merely proposals and the physician may accept or adjust them. The accepted or changed values are used as a basis for the nutritional composition of the next days.

The clinical course of neonates is of special importance for the nutrition calculation, especially the trends of laboratory measurements and the prescribed values of the nutritional components. As an example the calculation of fat "intralipid" depends on the supply of the preceding days, on whether these values have changed or not, and on the actual measurement of triglycerides. Additionally, the preconditions of age, body weight, and health condition (fat restriction during acute sepsis) are involved.

Another often missed feature is the need to add a clearance volume to an infusion. There is always an amount of fluid left in the bottle, pump or line. In theory, there are different strategies to allow for the clearance volume, which we discussed. As a practical solution we decided to increase the amount of one nutrition component, namely glucose. The calculation of this compensatory factor is further complicated by the type of infusion bottle used and the actual glucose concentration. The use of the compensation factor results in a change of the glucose amount and the glucose concentration. This is taken into consideration by the program's rules. It is easy to see that these calculations are difficult to do by hand.

A great problem is the adjustment of the necessary glucose supply in case of restricted total fluid allowances. Neonates need an adequate glucose supply, but depending on the venous access (central or peripheral) only specific glucose concentrations are allowed. Considering the restricted total fluid allowance and/or peripheral venous access there often occurs a fluid–glucose–concentration–needs problem and the physician has to change other parenteral nutritional components. This is a very time–consuming task, which is usually not done systematically by hand, because it results in a recalculation of the amounts of previously defined nutritional elements. We offer five possible changing alternatives: reduction of proteins and/or amino acids, reduction of oral feeding, increasing of total fluid, changing of the total glucose amount, and changing of the glucose concentration of bypasses. The user could choose single or mixed strategies.

3. System Structure of VIE–PNN

3.1 VIE–PNN's Aims

The aims of this project were:

(1) to support a physician in planning the daily nutrition composition of neonates;

(2) to develop an interactive system, which is able

- + to reduce the risk of calculation errors and of the absence of necessary nutritional components;
- + to consider the nutrition plans and laboratory measurements of preceding days;
- + to propose calculated values according to special requirements, but to give the physician the choice to correct or to accept them;
- + to take into consideration very specific nutrition problems, like reduction of parenteral nutrition due to oral feeding, clearance volume of infusion's bottle, strategies for fluid restricted cases. These tasks are to be handled on users' request only;

(3) to reduce the time needed for the calculation;

(4) to reduce the data input to the problem specific situation needs and to develop a user–friendly and easy–to–use interface;

1. Introduction

Parenteral nutrition can be a major adjunct in homeostatic control of fluid, electrolyte, caloric, and nitrogen needs. There exist some schemata of parenteral nutrition composition which can be used for elder children and adults (Gardner et al. 1989, Levin et al. 1990). But sick newborn infants need a special treatment according to their health conditions, their body weights, their ages, their metabolic and underlying nutrition status and the effects in response to the previously prescribed parenteral therapies. The influence on their health condition depends on small–scale changes of their infusion composition, individual tolerance, and past parenteral and enteral nutrition solutions (Niemer et al. 1992). It is important to evaluate the child's metabolic and underlying nutrition status before initiating the parenteral nutrition. To meet each neonate's nutritional needs, nutrition composition is a time consuming job, which needs expert knowledge and involves the risk of introducing possibly fatal calculation errors.

During the past few years a number of computer–assisted parenteral feeding support programs have been developed. All these systems try to reduce the time needed to compose the parenteral nutrition solutions, and to eliminate errors. Nevertheless none of these systems takes into account all important factors relevant at a neonatal intensive care unit. We want to mention the criticism shortly. The nutrition planning system by Vandenplas et al. (1989) deals only with total parenteral nutrition and does not take into consideration the oral feeding component. Yamamoto et al. (1989) deal with emergency management guidelines for pediatric and adult patients as against the daily routine of parenteral nutrition composition. PEDINFUS (Kuchenbecker 1991) calculates the nutritional amount for children up to 18 years. It does not provide for the important requirements and needs of neonates. The computer program by Picart et al. (1989) combines parenteral and enteral nutritional needs of neonates and children by using food composition tables. It lacks an in–depth analysis of the trend of laboratory measurements and the amount of nutritional components. Piert et al. (1989) developed a nutrition planning program in an intensive care burn unit. The burn unit's preconditions cannot be easily applied to the needs of a neonatal intensive care unit.

Our goal was to consider the special parenteral therapy needs of neonates (e.g. to react to the specific diseases of neonates, to overhydration, and to immature organs) and to take care of the influence of small–scale changes. We developed the knowledge–based system VIE–PNN (Vienna Expert System for Parenteral Nutrition of Neonates) which contains the essential rules for the composition of the parenteral nutrition solution (PNS). VIE–PNN represents knowledge about textbook rules of nutrition composition, which is combined with the practical knowledge of experienced physicians.

2. Problem Domain

The parenteral nutrition solution is mainly composed of amounts of fat, carbohydrates, proteins, and amino acids. Then a basic supply of electrolytes and other micro nutrients (e.g. vitamins, trace elements, carnitin, inositol) are added. Furthermore, several drugs have to be administered continuously as bypasses. However the parenteral nutrition composition for ill neonates cannot be reduced to a simple calculation of metabolic, electrolyte, caloric and nitrogen needs as it is possible for elder children and adults. Besides the patient's body weight and its age the physicians have to bear in mind the labile homeostatic control of neonates, especially if they are seriously ill. Moreover, the daily determination of serum electrolytes, triglycerides and proteins, the venous access, the glucose tolerance, the total fluid allowances, the proportion of oral feeding, the clearance volume of an infusion and the daily increase of nutritional components according to the neonate's metabolic tolerance have to be considered. An appropriate dosage of the nutrition elements depending on the individual needs is necessary for the neonate's effective recovery, and a tiny incorrectness could cause fatal decline of the health condition of the newborn infant.

There are a lot of possible therapies depending on the individual tolerances of the neonates. Our aim was not to implement merely the classical theory of parenteral nutrition composition, but to combine textbook rules

VIE-PNN

An Expert System for Parenteral Nutrition of Neonates

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Abstract: The planning of an adequate nutritional support for meeting the metabolic requirements of sick neonates is a tedious time consuming calculation, needs practical expert knowledge and involves the risk of introducing possibly fatal errors. We therefore developed the interactive support system VIE–PNN for calculating the composition of parenteral nutrition solutions (PNS) for neonates at intensive care units. The aims were to avoid errors within certain limits, to save time, and to keep data for further statistical analysis.

We combined textbook rules of nutrition planning with the knowledge of experienced physicians. The dynamic and static knowledge is represented in frame structure and backward chaining rules.

The daily requirements are determined in units per kilogram body weight and have to be adjusted according to the patient's age, its body weight, and its clinical conditions (e.g. specific diseases, past and present–day blood analysis). The system uses default values and strategies of estimation in the absence of real values. The physician has the possibility to accept or to adjust proposed values on the screen. VIE–PNN offers the possibility to adjust compositions of the PNS to the total fluid intake, which is often difficult when total fluid allowance is restricted. This task is time consuming if done systematically by hand. Finally, the PNS may be reduced according to the proportion of oral feedings. The final output is a PNS schedule form, which can directly be used in the case history of neonates. A knowledge acquisition module supports the input of new bypasses and new oral feeding products.

A technical, empirical and subjective evaluation of the system was performed. It proved VIE–PNN's soundness, its ability to provide a standard for the composition of parenteral nutrition, and its clinical applicability.

AI topic: *Configuration and Planning, Decision Support*

Domain area: *Medicine, Neonates, Intensive Care, Parenteral Nutrition*

Language/Tool: *Expert System Shell "Intelligence/Compiler (I/C)", Version 3.0, (IntelligenceWare, Inc., Los Angeles), IBM compatible PC*

Status: *fully implemented and currently under clinical testing*

Effort: *2 persons years*

Impact: *VIE–PNN implements a standard for the composition of parenteral nutrition of neonates, eliminates possible errors and frees the physician from time–consuming calculations.*