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Adaptation Problems focusing on Endocrine Therapy Support

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Abstract. So far, Case-Based Reasoning has not become as successful in medicine as in some other application domains. One, probably the main reason is the adaptation problem. In Case-Based Reasoning the adaptation task still is domain dependent und usually requires specific adaptation rules. Furthermore, in medicine adaptation is often more difficult than in other domains, because usually more and complex features have to be considered. We have developed some programs for endocrine therapy support, especially for hypothyroidism. In this paper, we do not present them in detail, but focus on adaptation. We do not only summarise experiences with adaptation in medicine, but we want to elaborate typical medical adaptation problems and hope to indicate possibilities how to solve them.

1 Introduction

Case-Based Reasoning (CBR) has become a successful technique for knowledge-based systems in many domains, while in medicine some more problems arise to use this method. A CBR system has to solve two main tasks [1]: The first one is the retrieval, which is the search for or the calculation of similar cases. For this task much research has been undertaken. The basic retrieval algorithms for indexing [2], Nearest Neighbor match [3], pre-classification [4] etc. have already been developed some years ago and have been improved in the recent years. So, actually it has become correspondingly easy to find sophisticated CBR retrieval algorithms adequate for nearly every sort of application problem.

The second task, the adaptation means modifying a solution of a former similar case to fit for a current problem. If there are no important differences between a current and a similar case, a solution transfer is sufficient. Sometimes just few substitutions are required, but usually adaptation is a complicated process. While in the early 90th the focus of the CBR community lay on retrieval, in the late 90th CBR researchers investigated various aspects of adaptation. Though theories and models for adaptation [e.g. 5, 6] have been developed, adaptation is still domain dependent. Usually, for each application specific adaptation rules have to be generated.

Since adaptation is even more difficult in medicine, we want to elaborate typical medical adaptation problems and we hope to show possibilities how to solve them.

2 Medical Case-Based Reasoning Systems

Though CBR was not as successful in medicine as in some other domains so far, several medical systems have already been developed which at least apply parts of the Case-Based Reasoning method. Here we do not want to give a review of all these systems (for that see [7, 8, 9]), but we intend to show the main developments concerning adaptation in this area.

2.1 Avoiding the Adaptation Problem

Some systems avoid the adaptation problem, because they do not apply the complete CBR method, but only a part of it, namely the retrieval. These systems can be divided into two groups, retrieval-only systems and multi modal reasoning systems.

Retrieval-only systems are mainly used for image interpretation, which is mainly a classification task [10]. However, retrieval-only systems are not only used for image interpretation, but for other visualisation tasks too, e.g. for the development of kidney function courses [11] and for hepatitic surgery [12].

Multi modal reasoning systems apply parts of different reasoning methods. From CBR they usually incorporate the retrieval step, often to calculate or support evidences [13], e.g. in CARE-PARTNER [14] CBR retrieval is used to search for similar cases to support evidences for a rule-based program.

2.2 Solving the Adaptation Problem

So far, only a few medical systems have been developed that apply the complete CBR method. In these systems three main techniques are used for adaptation: adaptation operators or rules, constraints, and compositional adaptation. Furthermore, abstracting from specific single cases to more general prototypical cases sometimes supports the adaptation.

Adaptation rules and operators. One of the earliest medical expert systems that use CBR techniques is CASEY [16]. It deals with heart failure diagnosis. The most interesting aspect of CASEY is the ambitious attempt to solve the adaptation task. Since the creation of a complete rule base for adaptation was too time consuming, a few general operators are used to solve the adaptation task. Since many features have to be considered in the heart failure domain and since consequently many differences between cases can occur, not all differences between former similar cases and a query case can be handled by the developed general adaptation operators. So, if no similar case can be found or if adaptation fails, CASEY uses a rule-based domain theory.

However, the development of complete adaptation rule bases never became a successful technique to solve the adaptation problem in medical CBR systems, because the bottleneck for rule-based medical expert systems, the knowledge acquisition, occurs again.

Constraints. A more successful technique is the application of constraints. In ICONS, an antibiotics therapy adviser [17], adaptation is rather easy, it is just a reduction of a list of solutions (recommended therapies for a similar, retrieved case) by constraints (contraindications of the query patient).

Another example for applying constraints is a diagnostic program concerning dysmorphic syndromes [18]. The retrieval provides a list of prototypes sorted according to their similarity in respect to the current patient. Each prototype defines a diagnosis (dysmorphic syndrome) and represents the typical features for this diagnosis. The provided list of prototypes is checked by a set of explicit constraints. These constraints state that some features of the patient either contradict or support specific prototypes (diagnoses).

A typical task for applying constraints is menu planing [19], where different requirements have to be served: special diets and individual factors, not only personal preferences, but also contraindications and demands based on various complications.

Compositional adaptation. A further successful adaptation technique is compositional adaptation [20]. In TA3-IVF [21], a system to modify in vitro fertilisation treatment plans, relevant similar cases are retrieved and compositional adaptation is used to compute weighted averages for the solution attributes.

In TeCoMed [22], an early warning system concerning threatening influenza waves, compositional adaptation is applied on the most similar former courses to decide whether a warning against an influenza wave is appropriate.

Abstraction. As one reason for the adaptation problem is the extreme specificity of single cases, the generalisation from single cases into abstracted prototypes [18] or classes [23] may support the adaptation. The idea of generating more abstract cases is typical for the medical domain, because (proto-) typical cases directly correspond to (proto-) typical diagnoses or therapies. While in GS.52 all prototypes are organised on the same level, in MNAOMIA [23], a hierarchy of classes, cases, and concepts with few layers is used. MEDIC [24], a diagnostic reasoner on the domain of pulmonology, consists of a multi-layered hierarchy of schemata, of scenes, and of memory organisation packets of individual cases.

3 Adaptation Problems in Endocrinology Diseases Therapy Support

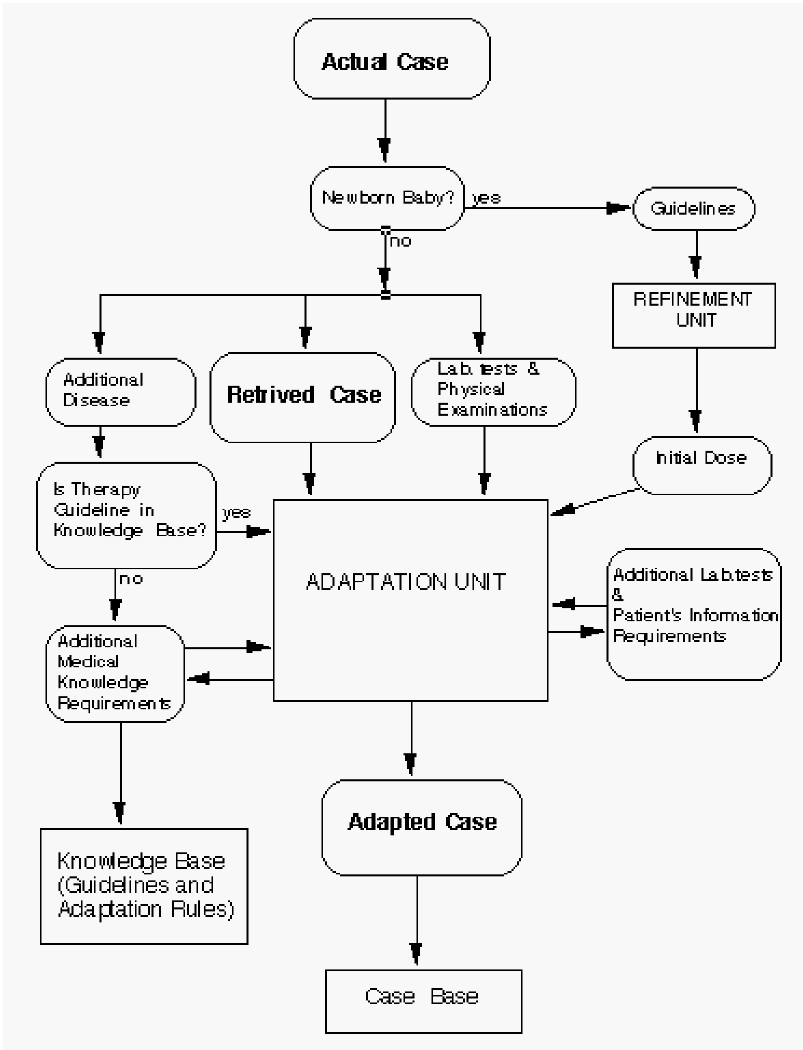

Fig. 1. Architecture of our endocrine therapy support system

We have developed an endocrine therapy support system for a children's hospital. The architecture is shown in figure 1, for technical details see [25]. Here, we focus on adaptation problems within it to illustrate general adaptation problems in medicine.

All body functions are regulated by the endocrine system. The endocrine gland produces hormones and secrets them in blood. Hypothyroidism means that a patient's thyroid gland does not produce enough thyroid hormone naturally. If hypothyroidism is undertreated, it may lead to obesity, brachicardia and other heart diseases, memory loss and many other diseases [26]. Furthermore in children it causes mental and physical retardation. If hypothyroidism is of autoimune nature, it sometimes occurs in combination with further autoimune diseases such as diabetes. The diagnosis hypothyroidism can be established by blood tests. The therapy is inevitable: thyroid hormone replacement by levothyroxine. The problem is to determine the therapeutic dose, because the thyroxin demand of a patient follows only very roughly general schema and so the therapy must be individualised [27]. If the dose is too low, hypothyroidism is undertreated. If the dose it too high, the thyroid hormone concentration is also too high, which leads to hyperactive thyroid effects [26, 27].

There are two different tasks of determining an appropriate dose. The first one aims to determine the initial dose, while later on the dose has to be updated continuously during a patient's lifetime. Precise determination of the initial dose is most important for newborn babies with congenital hypothyroidism, because for them every week of proper therapy counts.

3.1 Computing an Initial Dose

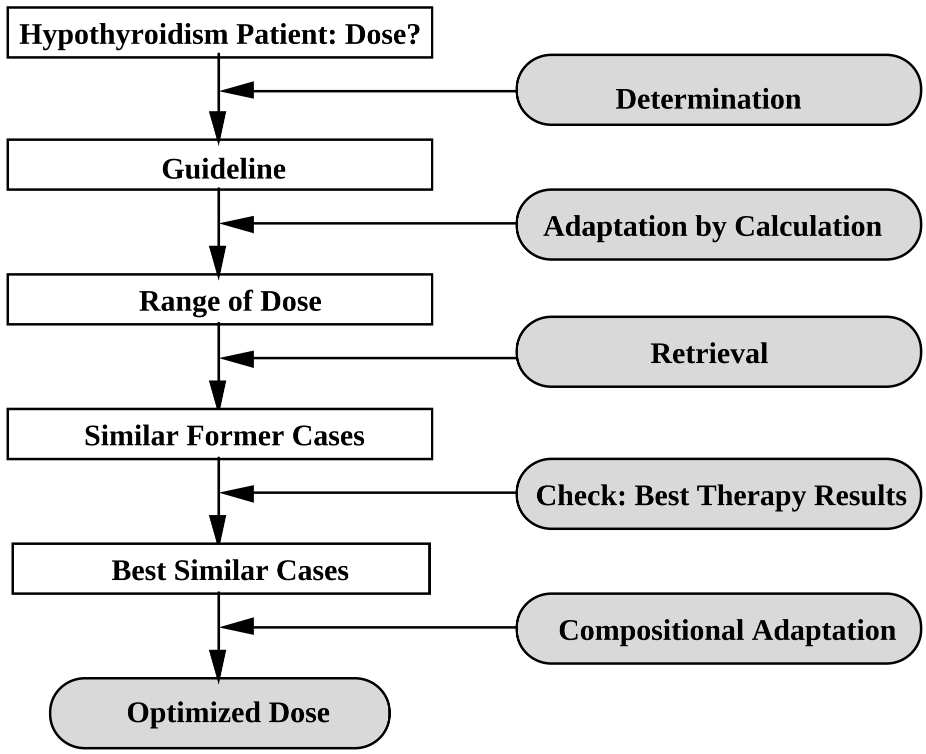

Fig. 2. Determination of an initial dose

For the determination of an initial dose (fig. 2), a couple of prototypes, called guidelines, exist, which have been defined by commissions of experts. The assignment of a patient to a fitting guideline is obvious because of the way the guidelines have been defined. With the help of these guidelines a range for good doses can be calculated.

To compute an optimal dose, we retrieve similar cases with initial doses within the calculated ranges. Since there are only few attributes and since our case base is rather small, we use Tversky's sequential measure of dissimilarity [28]. On the basis of those of the retrieved cases that had best therapy results an average initial therapy is calculated. Best therapy results can be determined by values of another blood test after two weeks of treatment with the initial dose. The opposite idea to consider cases with bad therapy results does not work here, because bad results may be caused by various reasons.

So, to compute an optimal dose recommendation, we apply two forms of adaptation. First, a calculation of ranges according to guidelines and patients attribute values. Secondly, we use Compositional Adaptation. That means, we take only similar cases with best therapy results into account and calculate the average dose for these cases, which has to be adapted to the query patient by another calculation.

Example for computing an initial dose. The query patient is a newborn baby that is 20 days old, has a weight of 4 kg and is diagnosed for hypothyroidism. The guideline for babies about 3 weeks age and normal weight recommend a levothyroxine therapy with a daily dose between 12 and 15 μg/kg. So, because the baby weighs 4 kg, a range of 48-60 μg is calculated. The retrieval provides similar cases that must have doses within the calculated range. These cases are restricted to those where after two weeks treatment less than 10 μU/ml thyroid stimulating hormone could be observed. Since these remaining similar cases are all treated alike, an average dose per kg is computed which subsequently is multiplied with the query patient's weight to deliver the optimal daily dose.

3.2 Updating the Dose in a Patient's Lifetime

For monitoring the patient, three laboratory blood tests have to be made. Usually the results of these tests correspond to each other. Otherwise, it indicates a more complicated thyroid condition and additional tests are necessary. If the tests show that the patient's thyroid hormone level is normal, it means that the current levothyroxine dose is OK. If the tests indicate that the thyroid hormone level is too low or too high, the current dose has to be increased resp. decreased by 25 or 50 μg [26, 27]. So, for monitoring adaptation is just a simple calculation according to well-known standards.

Example. Figure 3 shows an example of a case study. We compared the decisions of an experienced doctor with the recommendations of our system. The decisions are based on the basic laboratory tests and on lists of observed symptoms. Intervals between two visits are approximately six months.

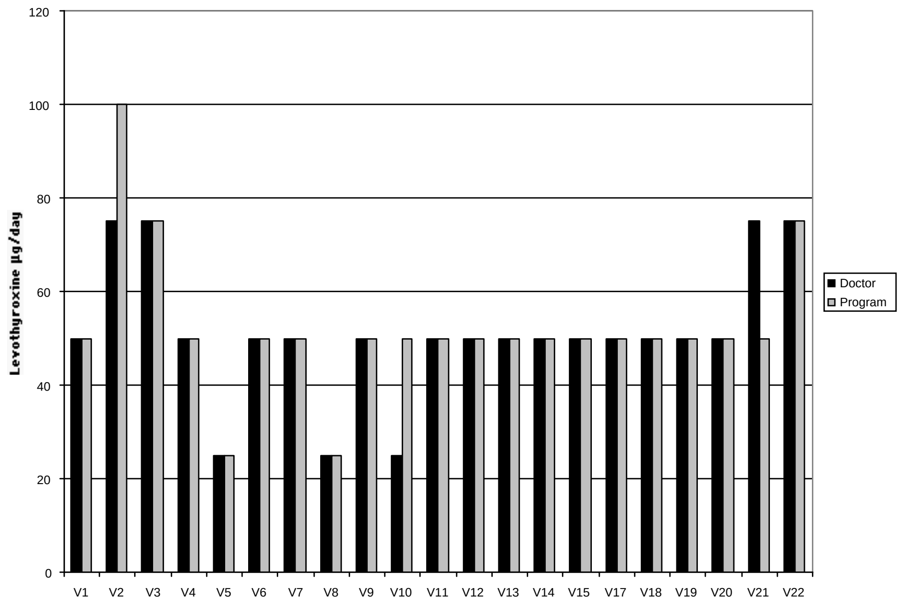

Fig. 3. Dose updates recommended by our program compared with doctor's decision. V1 means the first visit, V2 the second visit etc.

In this example there are three deviations, usually there are less. At the second visit (v2), according to laboratory results the levothyroxine should be increased. Our program recommended a too high increase. The applied adaptation rule was not precise enough. So, we modified it. At visit 10 (v10) the doctor decided to try to decrease the dose. The doctor's reasons were not included in our knowledge base and since his attempt was not successful, we did not alter any adaptation rule. At visit 21 (v21) the doctor increased the dose because of some minor symptoms of hypothyroidism, which were not included in our program's list of hypothyroidism symptoms. Since the doctors decision was probably right (visit 22), we added these symptoms to the list of hypothyroidism symptoms of our program.

3.3 Additional Diseases or Complications

It often occurs that patients do not only have hypothyroidism, but they additionally suffer from further chronic diseases or complications. So, the levothyroxine therapy has to be checked for contraindications, adverse effects and interactions with additionally existing therapies. Since no alternative is available to replace levothyroxine, if necessary additionally existing therapies have to be modified, substituted, or compensated (fig. 4) [26, 27].

In our support program we perform three tests. The first one checks if another existing therapy is contraindicated to hypothyroidism. This holds only for very few therapies, namely for specific diets like soybean infant formula, but they are typical for newborn babies. Such diets have to be modified. Since no exact knowledge is available how to do it, our program just issues a warning saying that a modification is necessary.

The second test considers adverse effects. There are two ways to deal with them. A further existing therapy has either to be substituted or it has to be compensated by another drug. Since such knowledge is available, we have implemented corresponding rules for substitutional resp. compensational adaptation.

The third test checks for interactions between both therapies. Here we have implemented some adaptation rules, which mainly attempt to avoid the interactions. For example, if a patient has heartburn problems that are treated with an antacid, a rule for this situation exists that states that levothyroxine should be administered at least 4 hours after or before an antacid. However, if no adaptation rule can solve such an interaction problem, the same substitution rules as for adverse effects are applied.

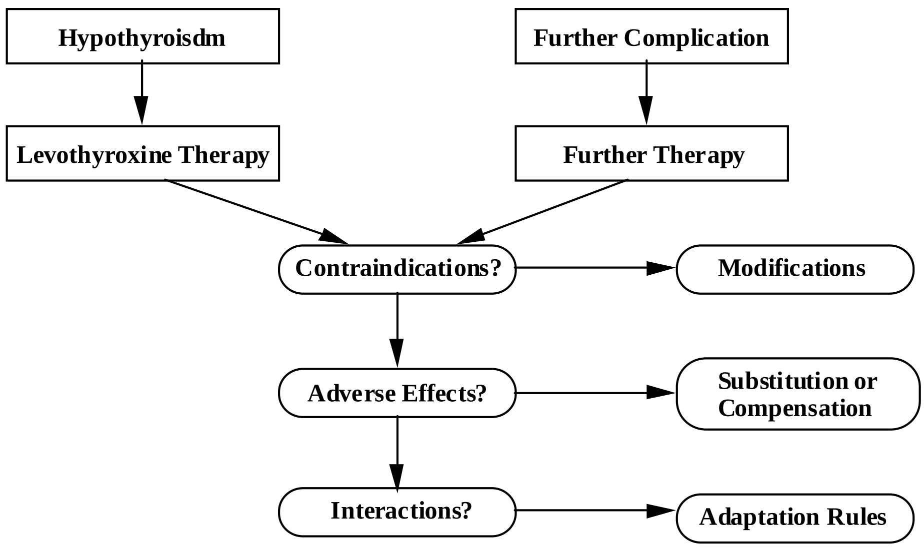

Fig. 4. Levothyroxine therapy and additionally existing therapies

4. Conclusion: Adaptation Techniques for Medical Therapy Problems

Our intention is to undertake first steps in the direction of developing a methodology for the adaptation problem for medical CBR systems. However, we have to admit that we are just at the beginning. Furthermore, our experience concerning the adaptation problem is mainly based on therapeutic tasks. Indeed, in contrast to ideas of many computer scientists, doctors are much more interested in therapeutic than in diagnostic support programs.

So, in this paper, we firstly reviewed how adaptation is handled in medical CBR systems and secondly enriched the experiences by additional examples from the endocrinology domain, where we have recently developed support programs.

For medical therapy systems, that intend to apply the whole CBR cycle, at present we can summarise useful adaptation techniques (fig. 5). However, most of them are promising only for specific tasks.

Abstraction from single cases to more general prototypes seems to be a promising implicit support. However, if the prototypes correspond to guidelines they may even explicitly solve some adaptation steps (see section 3.1).

Compositional Adaptation at first glance does not seem to appropriate in medicine, because it was originally developed for configuration [20]. However, it has been successfully applied for calculation therapy doses (e.g. in TA3-IVF [21] and see section 3.1.).

Constraints are a promising adaptation technique too, but only for a specific situation (see section 2.2), namely for a set of solutions that can be reduced by checking e.g. contraindications (in ICONS) or contradictions (in GS.52).

Adaptation rules. The only technique that seems to be general enough to solve many medical adaptation problems is the application of adaptation rules or operators. The technique is general, but unfortunately the content of such rules has to be domain specific. Especially for complex medical tasks the generation of adaptation rules often is too time consuming and sometimes even impossible.

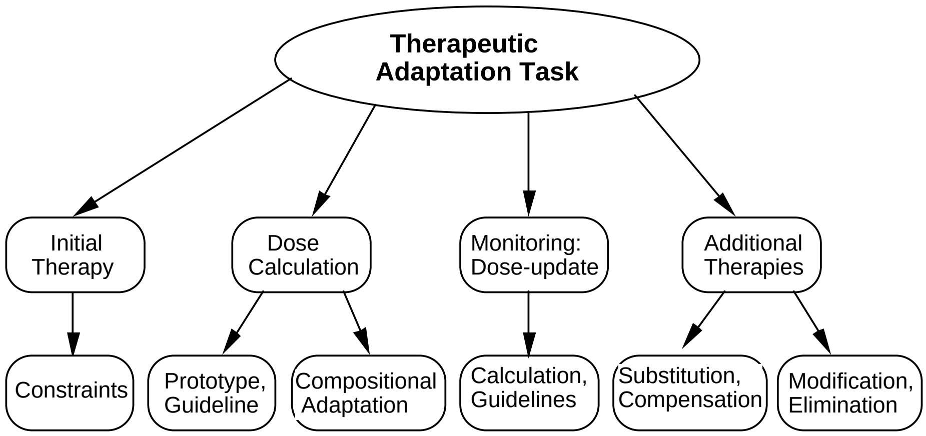

Fig. 5. A task oriented adaptation model

However, for therapeutic tasks some typical forms of adaptation rules can be made out, namely for substitutional and compensational adaptation (e.g. section 3.3.), and for calculating doses (e.g. section 3.2.). So, a next step might be an attempt to generate general adaptation operators for these typical forms of adaptation rules.

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