# THE FORMATION OF COMPOSITE HYPOTHESES IN DIAGNOSTIC PROBLEM SOLVING AN EXERCISE IN SYNTHETIC REASONING

Harry E. Pople, Jr.
Graduate School of Business
and
Decision Systems Laboratory
University of Pittsburgh
Pittsburgh, Pennsylvania 15261

### <u>Abstract</u>

The INTERNIST system, which is a computerbased diagnostic problem solver having Internal Medicine as its domain of discourse, employs a novel attention focusing heuristic in order to deal sequentially with the component parts of a complex clinical problem. The strategy of sequential problem formation and solution has proved to be effective in sorting out the complexities and rendering a correct diagnosis in the great majority of clinical cases tested. Experience with the system suggests, however, that many aspects of the search process could be significantly enhanced if it were possible to attend to the various component problems and their interrelationships simultaneously. Recent work on a successor system has been directed towards the development of strategies for the synthesis and analysis of composite hypotheses, which may be expected to yield more rapid convergence to the correct conclusion in many cases, and in at least some cases to prevent missed diagnoses.

#### 1, Introduction

We have for the past several years been engaged in a study of clinical decision making, for the purpose of providing computer-based diagnostic consultation for problems in Internal Medicine. In this domain, the more traditional approaches to computer-based medical diagnosis, such as pattern recognition, linear discriminant analysis, and statistical decision theory [1,2,3] cannot be directly applied. These methods assume an a priori specification of the full range of diagnostic categories into which individual patients are to be classified, an assumption that cannot be sustained in Internal Medicine. While the number of distinct disease entities known to a practicing clinician is not that large estimates range from two to ten thousand - the number of diagnostic categories required to classify arbitrary patients is substantially larger. The reason for this is that in many cases, especially those requiring diagnostic consultation, patients can present with a number of concurrent clinical problems. While certain patterns of co-occurrence of disease are more likely than others, one cannot exclude the possibility of encountering a dozen or more hitherto unrelated disease entities in any given If we assume for the sake of argument an upper bound of ten on the number of concurrent disease processes (in our investigation we have encountered this number and more), the number of diagnostic categories that would be required to

classify arbitrary patients is of the order of ten to the 40th, a respectable number of alternatives even by Al standards.

This then is the problem space in which the specialist in Internal Medicine operates. Given what to the untrained observer might appear to be an indiscriminant collection of findings (signs, symptoms, laboratory results) with respect to a particular patient, the clinician's job first of all is to decide what problems there are to be dealt with, then to employ whatever problem solving methods may be appropriate to select the correct alternative from each problem set.

In order to achieve a computer-based capability in this problem domain comparable to that of the skilled clinician, we have found it necessary to concentrate on the development of a model of synthetic reasoning, which emulates those aspects of the expert's behavior involved in the formation of composite problem hypotheses.

Methods for the formation, reduction, and synthesis of hypotheses have evolved over a number of generations of system design. Our purpose in this paper will be to chronicle the ontogeny of these concepts, and to provide descriptive accounts of the structure and behavior of the diagnostic problem solving systems in which they are incorporated.

About three years ago, we developed a system now called INTERNIST-I, which employs a simple attention focusing heuristic in order to deal sequentially with the component parts of a complex clinical problem. This strategy of sequential problem formation and solution has proved to be effective in sorting out the complexities and rendering a correct diagnosis in the great majority of clinical cases tested. It became clear on the basis of extensive testing, however, that many aspects of the system's performance could be significantly enhanced if it were possible to deal with the various component problems and their interrelationships simultan-This has led to the development of INTERNIST-II, a system embodying strategies of concurrent problem-formation which we expect will yield more rapid convergence to the correct diagnosis in many cases, and in at least some cases provide more accurate results.

In the following section, the information structures and heuristic processes underlying performance of the INTERNIST-I system will be reviewed briefly (a more complete description

can be found in Pople, et. al. [4]); this will be followed by a somewhat more detailed discussion of the methods of synthetic reasoning employed in the formation and synthesis of composite hypotheses in INTERNIST-II.

# 2. Sequential Problem Formation in INTERNIST-I

#### 2.1. Background

A principle that is often invoked in clinical decision making is that of Occam's razor. This is the maxim requiring that the simpler of competing hypotheses be preferred to the more complex. As interpreted in the practice of medical diagnosis, this rule adjures the clinician to seek a unitary cause if possible to account for all observed findings in a patient. This does not necessarily call for the identification of a single disease entity, as we have used this term previously. A unitary hypothesis can include a number of distinct entities, which are interrelated via some pathophysiological (i.e. causal) mechanism.

Because of the significance attached to this principle in clinical decision making, our first approach to computer-based diagnosis (which predates INTERNIST-I) was strongly oriented towards the identification of unitary hypotheses. procedure described formally in Pople [5] was developed to search causal networks, structured on the basis of pathophysiological concepts, in order to formulate unitary hypotheses - possibly comprising a number of interrelated components to explain the findings in a clinical problem. The program employed heuristic hypothesis formation methods very similar to the problem reduction techniques employed in other Al domains, and a novel technique referred to as 'synthesis' was used to merge conjunctive hypotheses into more parsimonious units.

The main problem with this precursor system was its inability to deal with real world clinical problems. As long as test cases were limited to artificial problems contrived to exercise the various known synthesis pathways of the network. results appeared most encouraging. However, the analysis of actual patient data frequently led to the wrong conclusion, even in relatively uncomplicated clinical problems. What became obvious in comparing the behavior of this system with that of an expert clinician was the latter's uncanny ability to disregard major portions of the clinical findings of a case, while focusing on the problem and/or problems implicit in a subset of the data. While not ignoring the imperative of Occam's razor, the clinician clearly exercises judgment in the application of this rule and is not misled, as the program often was, by a compulsion to search out unitary hypotheses that can explain all the data. There are, after all, clinical cases that involve unrelated problems for which one must posit two or more independent hypotheses.

In an effort to emulate the skilled clinician's capability to partition a clinical

problem into 'obvious' sub-problems that could be considered separately or together at will, we developed a problem-formation and attention focusing heuristic and incorporated this in the system now called INTERNIST-I.

An extensive medical data base was compiled in order to enable thorough testing of the heuristic diagnostic procedure in a representative assortment of clinical problems in Internal Medicine.

In the following section, the structure of medical knowledge in the INTERNIST data base will be briefly outlined. This will be followed by a description of the heuristic problemformation and attention-focusing heuristic mechanisms of the diagnostic program. Finally, we consider the strengths and weaknesses of this approach that have influenced the design of a successor system.

# 2.2 The INTERNIST Knowledge Base

The knowledge base underlying both INTERNIST systems is composed of two basic types of elements: disease entities and manifestations (history items, symptoms, physical signs, laboratory data). In addition, there are a number of relations defined on these classes of elements. At present, there are approximately four hundred disease entities encoded in the knowledge base and over two thousand manifestations.

Each disease entity has an associated list of manifestations known to occur in that disease, recorded along with an estimate on a scale of 1 - 5 of the frequency of occurrence. The inverse of this relation is also recorded explicitly in the knowledge base; thus, each manifestation is associated with the list of diseases in which the manifestation is known to occur, again with a weighting factor (in this case on a 0 - 5 scale) intended to reflect the strength of association. We refer to this weight as the 'evoking strength' by which a manifestation is related to each disease on its 'evokes-list'.

There is also recorded a hierarchy of disease categories, organized primarily around the concept of organ systems, having at the top level such categories as 'liver disease', 'lung disease', 'kidney disease', etc. Each of these areas is divided into more specific categories, which may in turn be further subdivided any number of times until the terminal level representing individual disease entities is reached. The reason for including such a hierarchy of categories in the knowledge base is to enable the hypothesis and conclusion of higher level descriptions of disease process in cases where the data do not permit more precise judgment.

Other relations are defined on the set of disease entities to record the causal, temporal, and other patterns of association by which the various disease entities are interrelated. There

are also several auxiliary relations defined on the class of manifestations to record properties of interest (such as the type and importance of a manifestation) and relations among manifestations (such as the derivability of one from another).

## 2.3 Problem Formation Methods

In discussing the strategy of problem formation in INTERNIST-I, it is important that we have a clearly defined interpretation of what is meant by the terms used. The term 'problem' is taken to mean a collection of disease entities, one and only one of which is considered possible in the case being analyzed. As mentioned previously, in many computer-based diagnostic systems, the problem (so-defined) is pre-determined and the program's job is simply to select one of a fixed list of disease entities that best fits the facts of a case. In cases where more than one disease may be present, however, it is necessary to partition the set of disease entities evoked by a given set of observed manifestations into disjoint subsets, each of which meets the 'problem' specification given above.

The approach taken in INTERNIST-I has been to focus on one problem at a time, with each successive problem dynamically determined by the facts of the case developed up to that point. The process is as follows. First, disease entities that can explain any or all of the observed findings are weighed individually and assigned scores reflecting their goodness of fit with the data. In this scoring process, the 'evoking strength' and 'importance' of manifestations explained by a disease are counted in its favor; 'frequency' weights count against those disease hypotheses in which the corresponding manifestations are expected but not found present in the case.

Given a ranked list of disease hypotheses, a problem is then formulated on the basis of the most highly rated of these items, using the following heuristic criterion: two disease entities are considered to be alternatives to one another (hence part of the same problem definition) if, taken together, they explain no more of the observed findings than are explained by one or the other separately.

The set of alternatives so determined, with scores within a fixed range of the top ranked disease hypothesis on the list, are then composed into a problem which becomes the focus of problem solving attention.

The program then selects questions that will help to discriminate among entities in the problem set, re-evaluates all diseases evoked (whether in or out of the problem focus) on the basis of new information obtained, and then reformulates the problem focus. Depending on which disease entity emerges as most highly rated on successive iterations of the process, the focus of attention may shift from one problem to another - but at any one time, there is a

single problem under active consideration.

Whenever a problem becomes solved, it is entered into a list of concluded diagnoses; all manifestations explained by that disease are marked 'accounted for'; and the process recycles until all problems present in the case have been uncovered.

As was pointed out earlier, because of causal, temporal, or other interrelationships, certain combinations of disease entities are more likely to occur than others. This fact is recognized in INTERNIST-I by the scoring algorithm, which on each iteration of the process, gives additional weight to any disease entity that is in any way linked to some already concluded disease.

# 2.4 Discussion

Though exceedingly robust and proven effective in solving a wide range of difficult clinical problems, the sequential approach to problem formation and solution incorporated in INTERNIST-I is not without its shortcomings.

In monitoring the reactions of clinicians who have interacted with the system over the past two years, several major performance deficiencies have been detected. Of primary concern is the tendency of the program, in complex cases, to begin its analysis by considering wholly inappropriate problems, on which it may spend an inordinate amount of time. This rarely leads to a false conclusion but does prolong the sessions of terminal interaction unnecessarily. There are several reasons to account for this phenomenon, all of which are related to the system's inability to perceive the multiplicity of problems in a case all at once.

If, for example, it were possible to structure several problems at the same time, heuristics might be employed to focus problem solving attention on the most 'solvable' of these, rather than the one that happens to receive the highest goodness of fit rating as described above. Moreover, the scoring process itself could be made more effective if the findings of a case could be distributed among the several concurrent problem areas in accordance with some notion of relevancy. At present, lacking the perspective of a multiple problem focus, INTERNIST-I assigns credit in the scoring of a disease hypothesis to all manifestations explained by that disease, however rare that association. Hence in a case, say, involving obvious liver and gastrointestinal involvement, the singular focus of INTERNIST-I will invariably favor those liver problems that also generate gastrointestinal findings and those gastrointestinal disorders that give rise to what are predominantly liver manifestations. clinician, able to recognize that both problem areas are involved, can attribute findings to the most relevant problem areas, thereby coming in many cases to a far better ranking of the alternatives 1n each sub-problem. The clinician can also take prior cognizance of the

interrelationships among disease entities in order to come more quickly to specific hypotheses than would otherwise be the case.

In summary, the design of INTERNIST-I was motivated by the need to formulate and focus attention on individual components of complex clinical problems. Experience with this system suggests, however, that a multi-problem focus and prior attention to the interrelationships among hypothesized disease entities might yield patterns of behavior that would appear more reasonable hence more acceptable to the clinician users of the system. These observations set the stage for the design of the successor system described in the following section.

#### Concurrent Problem Formation in INTERNIST-I

# 3.1. The 'Constrictor' Concept

Clinicians have a term 'pathognomonic' that refers to any manifestation distinctively characteristic of a particular disease; the occurrence of such a finding is sufficient to warrant the conclusion of the associated disease. Unfortunately, such pathognomonic associations between manifestations and disease entities are rare, and are by and large derived from special laboratory or invasive procedures that are expensive and/or dangerous for the patient. Hence, one cannot indiscriminantly seek pathognomonic findings in order to enhance the problem formation capability of a diagnostic problem.

We can, however, extend the concept of pathognomonic association to achieve a very useful tool for generation of multiple hypotheses. If the focus of attention is directed at higher levels of the disease hierarchy rather than at the terminal level nodes, quite specific associations between very commonplace manifestations and these higher level disease descriptors can often be established. For example jaundice, which is a readily observed physical sign, is a reasonably strong cue that some problem within the general category of liver disease is present, although it provides virtually no help in further discrimination within this sub-area. Similarly, bloody sputum, while not pathognomonic with respect to any particular lung problem, provides ample justification for serious consideration of the lung area as a problem focus.

The existence of these specific patterns of association between certain commonly observed manifestations and higher-level disease descriptors has led to the conjecture that the clinician's facility in delineating the multiproblem structure of a clinical case derives, at least in part, from his attention to what we have come to call the 'constrictors' of a case those findings that strongly cue the hypothesizing of some unspecified problem within each of several categories of the disease hierarchy.

We have analyzed the pattern of constrictor relationships among manifestations and disease categories in the INTERNIST data base and have incorporated the resulting set of associations as an additional information structure accessible to the diagnostic programs. In reviewing the data, we found that while many manifestations are uniquely associated with particular high level categories of the hierarchy, other associations are merely 'predominant' - i.e., though rare, the possibility exists of certain findings being explained in areas other than the one to which they have been assigned in the constrictor relation. As might be expected, the occurrence of 'strict' constrictor associations becomes less frequent as one considers more specific disease categories, and by the time terminal nodes are reached, the constrictor relation is essentially limited to the pathognomonic manifestations.

Because constrictors come with varying degrees of certitude, it is important to recognize the heuristic nature of any multi-problem formation strategy based on this concept. Hence, it is still necessary to view the problem-formation process as conjectural, and have provision for retreating from any multiple problem hypothesis that might be adduced, in order to consider other alternatives.

#### 3.2. The Multi-Problem Generator

INTERNIST-II employs a hypothesis generator that uses the concept of constrictor to delineate the top-level structure of a complex problem, and a modified scoring algorithm that considers within each sub-problem only those findings judged to be relevant in that context.

The process, briefly, is as follows. First, each evoked disease category is weighed on the basis of the importance of those observed manifestations explained by some disease in that category, with negative findings causing reductions in the score where appropriate. a multiple problem generator is invoked to formulate what we refer to as the root-structure of the overall problem. This generator constructs a conjunctive set of category hypotheses by selecting first on the basis of constrictor certitude, then on the basis of the score assigned to each area. A running record of unexplained findings is progressively reduced as successive hypotheses are entered into the root structure, and the generator eventually terminates when all findings have been covered by at least one hypothesis. Because this construction is a heuristic process, these generators are maintained in readiness so that alternative root-structures may be generated if called for at some later time.

The root-level hypotheses may or may not constitute 'problems' in the technical sense that this term was used in the previous section. That is, there is no assurance that the conjecture of a problem within some high level

disease category makes reference to a single disease entity there. For example, cirrhosis of the liver and cirrhotic portal hypertension - both disease entities in the liver area - often co-occur in the same patient.

Thus the need exists for some method of refining the root-level hypothesis structures by the introduction of sub-problem conjectures where appropriate. Provided that there are suitable constrictor cues in the data to justify such subdivision, the multi-problem generator just described can be employed in this hypothesis reduction task.

There are obvious analogies that can be drawn between this hypothesis formation and reduction procedure and the more familiar problem-reduction methods employed in other Al domains [6]. What we are dealing with is a search space that can be viewed as an AND/OR graph, with a single reduction operator represented by the multi-problem generator, and a terminating condition with respect to each branch of the graph that is satisfied when there is no reason to suspect the co-occurrence of two or more disease entities in that region of the search space.

# 3.3 Scoring of Disease Hypotheses

Manifestations are considered relevant for a disease category if there occurs within that region of the hierarchy some specific association of manifestation and disease characterized by either high evoking strength or high frequency of occurrence. Other findings having weaker associations with a category are assigned there for accounting purposes in those cases where no other element of the root structure accounts for that same finding. If a finding is weakly associated with two or more elements of the root structure, it is considered to be part of the 'float' - which means it will not be considered in the scoring of any of the related hypotheses.

Individual disease entities within each category of the problem root structure are scored on the basis of those findings either assigned or judged to be relevant to that category. This context sensitive scoring procedure provides a greatly improved ranking of the alternatives within each area than would otherwise be possible. However, certain interdependences across conjunctive elements of the root structure are introduced by this process of attribution. In particular, it can happen that the property of a manifestation being relevant to a particular category of disease will fail to be inherited by the sub-categories used to 'reduce' that node of the ANDOR graph. Such 'decommittment' of accountability often requires a re-assigment of responsibility for coverage of manifestations to other elements of the root structure, and in some cases may entail the generation of additional conjunctive hypotheses elsewhere in the root structure.

In order to facilitate the bookkeeping required to support this type of interdependency, we have adopted a state-space formulation of the search space in which each state represents a partially expanded ANDOR graph, having appropriate attributions of findings to each problem hypothesis. State transformation operators then perform the reduction operation with respect to hypothesis nodes of the embedded graph structure and make whatever modification in attribution of responsibility these changes in the structure of the problem may entail.

# 3.4. Goal of the Search Process

The 'goal' of the state-space search is achievement of a state in which each terminal of the associated AND/OR graph corresponds to what we refer to as a 'simplex' problem, one having the presumption of a single disease occurrence (each problem focus developed by the INTERNIST-I heuristic would be reckoned a simplex, by this definition). Clearly, a great many states can be created that would satisfy this 'goal' criterion of the problem-formation process, so additional criteria and procedures must be devised to focus attention on the most useful formulation from among those satisfying the goal criterion.

The reason for introducing the new terminology above is to distinguish the simplex type of problem specification from that of a 'complex', where the latter term refers to a problem conjecture comprising two or more interrelated diseases, all of which are thought to occur. In order to develop a complex hypothesis, causal, temporal and other relationships that reflect common associations among disease entities are used to combine two or more simplex problems into a single unit.

The procedure by which separate simplex problem specifications become combined into a single complex can be thought of as an additional type of state - transformation operator. Like the hypothesis-reduction operator described earlier, the synthesis operator typically yields an instantiation of category hypotheses on which it operates, i.e. the elements of the problem sets comprising a complex constitute proper subsets of the simplexes from which the complex is derived. Hence the focus is typically much more sharply defined after invoking the synthesis operation than would otherwise be the case.

By use of the synthesis procedure whenever a sufficiently strong simplex is adduced, the resolution of other related sub-problems can be conjectured even in the absence of discriminating primary evidence. Thus for example if there is reasonably strong evidence that a patient has congestive heart failure and also some form of ascites, the strong link between heart failure and the transudative form of ascites can be invoked to resolve the ambiguity with respect to the latter problem.

The mechanism of synthesis also provides an additional criterion that can be used to weigh alternative hypothesis states: namely the cardinality of the problem description contained in that state, with each simplex and each complex contributing equally to the score. This criterion is clearly heuristic; as discussed previously, the unitary hypothesis is not necessarily better than several independent ones, particularly when it is incorrect. However, within the structure of the INTERNIST-II state space, it is possible to attend to the imperative of parsimony, while reserving the option of retreating to alternative formulations when the evidence so requires.

# 3.5 Status of INTERNIST-II

As of this writing, the heuristic multiproblem formation and reduction procedures described above have been implemented and tested on a large number of cases (three-hundred or so), with resulting initial problem formulation that surpasses INTERNIST-I performance in all complex cases.

The synthesis procedure has been incorporated in the system only recently, however, and is not currently being exploited to the full extent anticipated. The intention is to invoke the synthesis heuristic during the course of state-space expansion in order to bias sub-problem selection towards potentially unified constructs. At present, the procedure is invoked only in an ex-post-facto fashion after all conjunctive problems have been reduced to simplex form.

The system is incomplete in other respects as well; for example, it has not yet been fitted with the type of inquiry capability used in INTERNIST-I to test and evaluate hypotheses. However, we expect that the improved problem focus already demonstrated by INTERNIST-II can be counted on to provide much more discriminating information gathering capability than was possible in the predecessor system.

The effect of the problem formation and synthesis heuristics of INTERNIST-II is best illustrated by example. The case analysis presented below uses data from the clinical pathological conference published in the New England Journal of Medicine, Vol. 290, page 1071. Several other published CPC's have also been tested with comparable results.

## 3.6 Case Analysis

The important diagnoses for this case included primary cardiomyopathy, congestive heart failure with pleural effusion, transudative ascites, cardiac cirrhosis resulting from chronic hepatic congestion, and acute tubular necrosis of kidneys caused by cardiogenic shock. There is also evidence of systemic embolism.

After initial findings are read in, INTERNIST-II develops two multi-problem formulations, the first without use of the synthesis

procedure, and the second using synthesis in the fashion described above. Both formulations are correct. However, it can readily be seen that several of the simplex problems, viewed as independent entities, contain little in the way of discriminating data. Invoking parsimony, the clinician would have little trouble in tentatively narrowing these simplexes on the basis of apparent relationships between specific diseases of the several problem areas.

As can be seen in the second set of problem foci displayed below, the problem formation, reduction, and synthesis methods of INTERNIST-II, working together, show promise of exhibiting comparable synthetic reasoning behavior.

# 3.6.1 Manifestations Entered for Analysis

AGE 26 TO 55

SEX MALE DYSPNEA EXERTIONAL HEART OUTPUT DECREASED HEART CATHETERIZATION LEFT VENTRICLE BND DIASTOLIC PRESSURE INCREASED HEART FAILURE CONGESTIVE HX PRESSURE ARTERIAL SYSTOLIC LESS THAN 90 THROMBOPHLEBITIS LIVER ENLARGED MODERATE EKG PREMATURE ATRIAL CONTRACTION (S) EKG VENTRICULAR CONTRACTION (S) EKG HEART BLOOK FIRST DEGREE BKG LEFT BUNDLE BRANCH BLOOK EKG LOW VOLTAGE EKG ATRIAL FIBRILLATION COUGH **TACHYCARDIA** PRESSURE VENOUS CENTRAL GTR THAN 10 PRESSURE VENOUS INCREASED INSPECTION RHONCHI DIFFUSE HEART SOUND (S) SUMMATION GALLOP LEFT VENTRICULAR HEART PERCUSSION LEFT BORDER LATERAL DISPLACEMENT HEART IMPULSE APICAL FORCEFUL ABDOMEN TENDERNESS RIGHT UPPER QUADRANT HEART XRAY LEFT VENTRICLE ENLARGEMENT HEART XRAY RIGHT VENTRICLE ENLARGEMENT WBC 14000 to 30000 PLATELET (S) 50000 TO 200000 CHEST XRAY LUNG (S) CONGESTED CHEST XRAY PLEURAL EFFUSION (S) URINE OUTPUT LESS THAN 400 CC PER DAY UREA NITROGEN BLOOD 30 TO 60 BILIRUBIN CONJUGATED BLOOD INCREASED SGOT GTR THAN 400 LDH BLOOD INCREASED CPK BLOOD INCREASED ABDOMEN FLANK (S) BULGING BILATERAL ABDOMEN FLANK (S) HEAVY BILATERAL ABDOMEN DULLNESS SHIFTING PROTHROMBIN TIME INCREASED CALCIUM BLOOD DECREASED PHOSPHATE BLOOD INCREASED ELECTROPHORESIS SERUM ALBUMIN DECREASED ALKALINE PHOSPHATASE INCREASED UP TO 2 TIMES NORMAI URINE SEDIMENT RBC

# $\frac{3.6.2}{\text{Synthesis}}$ Problem Focus of INTERNIST-II Without

PROBLEM:

CHYLOUS ASCITES 26
EXUDATIVE ASCITES 26
TRANSUDATIVE ASCITES 26
ACUTE GENERALIZED PERITONITIS 12

PROBLEM:

CHRONIC CONGESTIVE LEFT HEART FAILURE 185

PROBLEM:

ALCOHOLIC HEPATITIS 116
LEPTOSPIROSIS WITH HEPATIC INVOLVEMENT 112
HEPATOCELLULAR CARCINOMA 111
SECONDARY NEOPLASM OF THE LIVER 106
ACUTE VIRAL HEPATITIS 106
HEPATIC VEIN OBSTRUCTION 106
HEPATIC MILIARY TUBERCULOSIS 106
CHRONIC ACTIVE HEPATITIS 106
HODGKIN'S DISEASE OF THE LIVER 101
DRUG HYPERSENSITIVITY HEPATOCELLULAR REACTION 100
INFECTIOUS MONONUCLEOSIS 100
HEPATIC CONGESTION 100
PRIMARY BILIARY CIRRHOSIS 100
ACUTE VIRAL HEPATITIS CHOLESTATIC TYPE 100

PROBLEM:

EMPYEMA 56
SECONDARY PULMONARY MALIGNANT NEOPLASM (LYMPHOGENOUS TYPE) 55
HEMOTHORAX 50
PLEURAL EFFUSION TRANSUDATE 46
PLEURAL EFFUSION CHYLOUS 46
PRIMARY BRONCHOGENIC CARCINOMA 42
BRONCHIOLAR-ALVEOLAR CELL CARCINOMA 42
PLEURAL EFFUSION EXUDATE 40

PROBLEM:

ACUTE CARDIOGENIC SHOCK 158

PROBLEM:

ACUTE MASSIVE PULMONARY EMBOLISM 92

PROBLEM:

CARDIOMYOPATHY PRIMARY 144
CARDIOMYOPATHY SECONDARY 130

PROBLEM:

LEPTOSPIROSIS WITH RENAL INVOLVEMENT 82 ACUTE TUBULAR NECROSIS 70

UNEXPLAINED:

CALCIUM BLOOD DECREASED 3

3.6.3 Problem Focus of INTERNIST-II Using Synthesis

SIMPLEX:

ACUTE MASSIVE PULMONARY EMBOLISM

COMPLEX:

ACUTE CARDIOGENIC SHOCK CAUSING ACUTE TUBULAR NECROSIS COMPLEX:

ONE OF THE FOLLOWING: CARDIOMYOPATHY PRIMARY

CARDIOMYOPATHY SECONDARY

CAUSING

CHRONIC CONGESTIVE LEFT HEART FAILURE CAUSING

PLEURAL EFFUSION TRANSUDATE

ALSO CAUSING

TRANSUDATIVE ASCITES

ALSO CAUSING

HEPATIC CONGESTION

#### 3.7 Discussion

The verdict is not yet in with respect to the heuristic methods used to accomplish the objectives set for INTERNIST-II. The primary goal has been to achieve a concurrent problem formation capability in order that improved scoring methods and attention to the principle of parsimony might be exploited in the development of what will be perceived by clinicians to be reasonable problem conjectures.

At least in the development of initial problem formulations, early results suggest that we can expect performance surpassing that of predecessor systems. What remains to be seen is the adequacy of the state-space formalism as a framework within which appropriate re-formulation of the problem-set can be recognized and/or developed in those cases when the initial focus is, at least in part, incorrect.

One of the great strengths of INTERNIST-I is its ability to shift the focus of attention from one problem to another on the basis of newly derived data. This is achieved by the simple expedient of re-formulating the problem focus after each round of information gathering activity. To attain comparable facility in the multiple problem context of INTERNIST-II will require much more elaborate control strategies, because new evidence will be expected in most cases to call for alteration of only one component of the total problem structure. Quite radical re-structuring of the total problem focus may be called for in some cases, however; e.g. where doubt arises with respect to some problem conjecture, and that problem had been used, via synthesis, to reduce and render more specific other problem conjectures.

In the case analysis given above, another type of decision problem is illustrated for which special control strategies will have to be devised. In the major problem complex - the one dealing with heart failure - a choice remains to be made between the primary and secondary forms of cardiomyopathy. This is a common type of decision problem in medicine, requiring a strategy of search that calls for the conclusion of the primary (or idiopathic) form of a disease only after other etiologies have been excluded. Hence in this case, the clinician should seek evidence of sarcoidosis, amyloidosis, or other cause of a secondary cardiomyopathy before

coming to the judgment of the primary form of this disease. Similar search strategies, involving directed investigation of the INTERNIST-II state space, will need to be incorporated in the system in order to deal with this class of decision problem.

One further consideration that has emerged from the analysis leading to design of INTERNIST-II deserves mention. This is the clearly perceived need for extending in some manner the dimensionality of the hierarchy of disease categories so that additional constrictor relationships, not now capable of representation, may be made available to the diagnostic programs. There are presently no categories with labels such as 'infectious disease', 'chronic disease', 'cancer', 'hypertension' - yet each of these categories possesses a number of associated findings that could be viewed as constrictors. Until this representational problem has been solved, the full power of the constrictor-based multi-problem generator will not be achieved.

Much of the machinery needed to carry out critical experiments with respect to the issues discussed above is already in place, and additional results may be expected in the near future.

# 4. Observations and Conclusions

Computational support for INTERNIST systems research and development work has been provided over the past three years by the NIH sponsored SUMEX-AIM resource, which offers PDP-10 hardware and the TENEX operating system. The primary language used for implementation of the diagnostic programs has been INTERLISP, with interfaces to the data base, which is structured in external files, coded in assembly language.

Program execution times for INTERNIST-I typically range from three to seven minutes of CPU time for reasonably complex case analyses. For the initial problem formation phase of INTERNIST-II, execution times vary from twenty seconds to two minutes depending on the complexity of the case; the example of the preceeding section required approximately ninety seconds.

We have found INTERLISP to be an extremely friendly environment for this development work. In particular, the control primitives associated with the INTERLISP 'spaghetti stack' [7] have proved to be most useful in the context-management required for support of the INTERNIST-II state space search.

The main conclusion that can be drawn from our experience in building INTERNIST is that any conclusion is probably premature, and should be resisted. It seems to be in the nature of the enterprise that the attainment of each new level of system performance gives rise to greater expectations and more subtle challenges [8]. The study of diagnostic reasoning processes has proved to be an exceedingly rich domain, and we

expect it will continue to yield interesting results for some time to come.

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