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Object oriented partitioning for a medical vocabulary based on semantic network

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ABSTRACT

OBJECT ORIENTED PARTITIONING FOR A MEDICAL VOCABULARY BASED ON SEMANTIC NETWORK

by
Mansnimar Singh

Computers have become ubiquitous and indispensable part of everyday life both for personal use and in the workplace. Medicine is one of the few domains that has not fully adopted computerization. One impediment to this emanates from a communication gap between the computer science professional and the medical professional. Besides, medical terminology is full of synonyms and medical professionals use them according to their personal preferences. This lack of common terminology has prevented sharing of knowledge and automating data processing, resulting in the healthcare information explosion.

Semantic network models have been developed to represent medical concepts and to provide a common repository of medical terms. These networks are huge collections of terms and deal with the concepts individually. The semantic models, however, have not resolved management and comprehension difficulties associated with large number of terms and their complex semantics.

Object-Oriented modeling, as demonstrated in this thesis, provides a mature technology to model complex concepts for a computerized medical vocabulary. Object class abstraction, that represents objects in the same context, promises to solve the comprehension and management problems. Such a vocabulary would facilitate exchange of information, data processing and building decision support systems.

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by
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To my beloved family

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CHAPTER 1

INTRODUCTION

1.1 Objective

Large semantic networks like medical vocabularies are difficult to comprehend and maintain because of the huge number of concepts and the complex semantics associated with them. The objective of this thesis is to analyze the concepts in a semantic network based medical vocabulary and to partition them into logical units. These logical groups can then be represented by object class hierarchies. The class model reduces the number of concepts and semantic relationships in the network and facilitates comprehension and management of medical information. The source of the concepts for this model is the Columbia Presbyterian Medical Center's Medical Entities Dictionary (MED).

1.2 Background Information

The origin of modern medicine can be traced to ancient Greece where Hippocrates of Cos laid its foundation. Medical science has expanded and become more sophisticated as knowledge has accumulated over the millennia. This has led to the evolution of a highly complex terminology. In the recent decades medicine has advanced at a meteoric pace and so has the medical terminology.

In order to share knowledge, information has to be distributed and exchanged between different organizations and information systems. This can only be accomplished if a common terminology is available to facilitate the integration process. However, conventional data models do not fully capture the essence of medical concepts. The

problem has been compounded by the need for terminology concepts to be pooled from various sources and interpreted by computer systems.

There is therefore a pressing need to build a computerized medical vocabulary that would provide a common language for conversation between organizations or computer systems and accommodate the perspectives of all its users.

CHAPTER 2

COMPREHENSION DIFFICULTIES OF MEDICAL TERMINOLOGY

A terminology is a set of words or phrases that are used to describe the concepts in a domain. The basic domains of medicine that are required to be represented in any medical vocabulary are the diseases, their diagnostic procedures and treatment modalities. The main factors that lead to difficulties in understanding medical terminology are the number of terms and their semantics.

2.1 Size of the Medical Vocabulary

Medical terminology has continued to grow as knowledge has accumulated over the centuries. In other vocabularies some terms become obsolete as the domain evolves and new terms are coined. But in medicine the domains have expanded without making some terms obsolete. This is due to the fact that humans have continued to suffer from the same maladies and only one major disease, Smallpox, has been eradicated from the world. The major form of Diabetes (Diabetes Mellitus characterized by excessive urine which is sweet) had been discovered centuries ago and continues to be an important cause of morbidity and mortality.

A number of human factors have led to the rapid expansion of the medical vocabulary. The average human life span has increased dramatically in the last few decades and this has led to the recognition of diseases associated with old age like Alzheimer's Disease, Paget's Disease and numerous malignancies [2, 14]. The rapid growth of human population and tourism has led people to venture into previously

uninhabited terrain with its own microcosm. This has led to the discovery of new pathogens (disease causing agents) whose primary hosts are immune but now have a new unprotected human host at their disposal.

Advancements in technology have led to the identification of many diseases and also contributed to new conditions. Industrialization has added new classes of toxic and disease causing substances that are responsible for many occupational diseases like Coal Miners Lung or Asbestosis. Introduction of compact cars led to cases of Window Slash Fracture occurring when a person with his elbow protruding out of the car window was sideswiped by a passing car. Computers themselves have their share of blame and Repeated Traumatic Injury to the wrist has become a well recognized syndrome among computer professionals engaged in continuous typing on keyboards.

Even sports, due to extreme stress placed on body parts that were not conditioned for these forces, has led to new medical afflictions. Golfer's elbow and Tennis Elbow result from excessive strain on certain tendons and ligaments [1, 2]. In fact, sports medicine has become a highly specialized field in its own right.

Another culprit responsible for comprehension difficulties in medical terminology is the lack of standardized rules for coining new terms. In the absence of accepted taxonomy guidelines, there are many sources of inspiration for coining new terms. Some concepts bear the name of the person who discovered the condition (Crigler-Najjar Syndrome describes a deficiency of an enzyme in bilirubin metabolism) while others describe the place of discovery (Rocky Mountain Spotted Fever). Some concepts describe the organ and pathological manifestation of the disease (Gastritis describes the inflammation of the stomach) and some have roots in mythology and religion (Saint

Vitus' dance describes the sudden, aimless, irregular movements in Rheumatic Heart Disease) [2, 12, 14]. These diverse naming conventions make new terms difficult to interpret. To add to this confusion are the abundant synonyms that arise because different people encountered the diseases independently and named it according to their interpretation. Furthermore, many conditions were named after the same discoverer so these names need additional qualifications to avoid confusion. For example, Paget's disease can occur in bones or breast but the etiology and pathology of both are very different [12, 14].

The need to treat all the diseases has led to an explosive growth in pharmacological preparations. In the pharmacy domain once again there are few rules for naming compounds and pandemonium reigns. Many names are based on the chemical family of the constituents (aminoglycoside refers to amino sugars linked by glycoside linkage to hexose nucleus) while some refer to the source of the chemical in the human body (adrenocorticosteroids are steroids produced by adrenal glands). Some terms are abbreviated names for the chemicals and this adds confusion to the existing disarray in the vocabulary (aspirin is the commonly used short name for acetylsalicylate) [9].

Medical diagnostic and therapeutic procedures have also added their jargon to the medical terminology. Diagnostic procedures may detect chemicals (like Glucose) or evaluate immunologic status (like Human Leukocyte Antigen for transplant organ matching and antibody titre for various diseases) or process information using electronic devices (like Electrocardiogram, Computer Aided Tomography scan, Positron Emission Tomography, Nuclear Magnetic Resonance, Echocardiography). Therapeutic procedures (like valvulotomy to repair narrowed heart valves or Percutaneous Tranluminal Coronary

Angioplasty for opening clogged heart arteries in myocardial ischemia) have further expanded the terminology [14].

2.2 Multiple Views and Relationships among Medical Concepts

Another dimension contributing to the comprehension difficulties is the semantics of the concepts. A medical vocabulary is not just a collection of terms from the medical domains but must be able to reflect multiple perspectives of medical professionals from different specialties. A clinician would like to obtain the result of the blood glucose test for a patient without worrying about the method while a lab technician would be more concerned with which tests measure glucose and what specimen is used for those tests. This requires multiple views of concepts to satisfy users from different domains [3, 6].

Besides the multiple views, each concept may relate to many other concepts. Lab tests are related to the type of specimen used and the substance they measure while disease concepts are associated with the afflicted site, the etiology and the diagnostic tests for the condition. Thus concepts with multiple views and relationships make medical terminology even more complex and difficult to model.

2.3 Current Computerized Medical Vocabularies

There have been attempts to create computerized medical vocabularies using semantic networks. The Unified Medical Language System (UMLS), that includes a medical knowledge base with a semantic network structure, has attempted to provide a common pool of terms. The purpose of the UMLS is to facilitate integration of electronic biomedical information from a variety of sources. This will help in better linking of

patient data to other databases making it useful for research and building decision support systems [4].

Another successful vocabulary is the MED that consists of concepts used at Columbia Presbyterian Medical Center (CPMC). CPMC has used this vocabulary to successfully integrate information from its major sources of medical data: patient records, labs and pharmacy. It has helped solve inter-departmental communication problems within CPMC [3].

However, both these models consider concepts at the term level and therefore suffer from comprehension problems because of their huge size and complex structure.

2.4 Complexity of Semantic Networks

The effort required to understand a semantic network depends on the number of concepts and on the inter-relationships between the concepts. In order to quantify the comprehension difficulties of a semantic network schema, its size is defined as the number of concepts and its complexity, c, is defined as the ratio of the number of relationships between the concepts to the number of concepts. For two networks of equal size i.e., with same number of concepts, a more complex network, with its greater number of relationships per concept, is more difficult to comprehend [8, 11].

CHAPTER 3

MODELING MEDICAL CONCEPTS

Medical concepts are difficult to represent with conventional data models. For modeling these concepts some sort of abstraction is needed that simplifies the concepts by focusing on the essential features and ignoring the non-essential ones. A good representation model would be one that captures all the features of the medical concepts and their relationships to other concepts. The model should also be suitable for all users of medical information. In this chapter we consider two models for representing medical concepts.

3.1 Semantic Network Model

One way to express the concepts in a medical vocabulary is by a semantic network model. In this network each concept is represented as a node. For a complete representation of the term and its semantics, each concept requires at least two types of properties:

1. Attributes - the properties of the concept that apply to the concept itself, and
2. Relationships - those that relate the concept to other concepts and capture its semantics.

3.1.1 Medical Entities Dictionary

The Medical Entities Dictionary (MED), developed by Columbia Presbyterian Medical Center (CPMC), is one such vocabulary based on a semantic network model. CPMC has

placed terms from its hospital systems (laboratory, electrocardiography, medical records coding and pharmacy) in the MED to facilitate data storage and exchange [3].

The CPMC has two data repositories:

1. Medical Entity Dictionary (MED) which is a collection of terms that serves as a common reference for users from different departments, and
2. Clinical Data Base (CDB) that stores patient's clinical information by using the codes from the MED.

The MED considers each concept to be a term that is uniquely identified by its MED-CODE. The MED-CODEs in a patient's record capture the clinical state of the patient by specifying his condition (from disease MED-CODEs), tests and their results (from lab and ECG MED-CODEs) and therapy being administered (from pharmacy domain MED-CODEs) [6, 7]. The MED-CODEs are also used while querying the patient data in the CDB for specific conditions, tests and treatments.

MED Concepts

The MED semantic network represents medical concepts as nodes with links between them. Each concept node in the MED graph can be viewed as a frame with properties that describe the characteristics of the concept. The MED uses the properties of the term to store information that describes the entities themselves (i.e., local information) in attributes and those describing how the entities are related to other entities in relationships. Any information that relates to other concepts and is not intrinsic to the concept is not stored locally because this leads to redundancy [3, 6, 7]. For example, in the pharmacy domain a chemical compound may be an ingredient of many preparations.

In an ointment form it may exist in a particular strength and in a tablet form as a different strength. If all the information pertaining to the chemical constituent is stored in the nodes of the preparations instead of relating the preparation to its chemical constituent node, then each preparation would have to store this information individually leading to redundancy and maintenance difficulties. The use of relationships allows multiple pharmacological preparations to refer to their constituent concepts and helps in maintaining the integrity of the information.

MED Relationships and Attributes

The root of the MED network is the concept Medical Entity. The IS-A hierarchy which is introduced by Medical Entity's SUBCLASS-OF (IS-A) relationship provides the inheritance path for properties of all the concepts. This hierarchy also allows multiple inheritance to accommodate multiple views for users from different medical specializations.

The IS-A hierarchy of the MED is very similar to that of the CYC project [15]. The concept Medical Entity, as the root node of the hierarchy, represents all the medical concepts in the most general form. All other concepts are immediate descendants of at least one other node. Each concept may have several parents but the IS-A relationships between the child and it's ancestors are acyclic, making the hierarchy a Directed Acyclic Graph (DAG) [3].

Each MED concept is characterized by its properties. A property is introduced at a single node in the graph and is inherited by all it's descendant nodes. There are a total

of 150 properties in the MED that are used to define all the possible features of medical concepts. These properties are of two types:

1. Attributes hold primitive values like the NAME of the concept, its MED-CODE, its code in other medical vocabularies like UMLS-CODE, its SYNONYMS etc.
2. Relationships point to other concepts and specify how the concepts relate to each other in the network. For example, the SUBCLASS-OF relationships specify the parents of the concept and the PHARMACEUTIC-COMPONENT relationship specifies the chemical ingredient(s) of the pharmacological preparation.

The domain of a concept consists of all descendants of a concept in the IS-A hierarchy because the descendants inherit the properties of it's ancestors and the ancestor concept represents the descendants in a generic form [3]. For example, the children of the concept Antibiotic Preparations include chemical families like the concepts Aminoglycoside Preparations, Penicillin Preparations and Cephalosporin Preparations. The concept Antibiotic Preparations represents these chemical families in a generic form without associating them with any specific chemical family. Within each chemical family are a number of specific compounds that are modifications of the family structure. The family root concept represents the individual structures in a generic form. For example, the concept Aminoglycoside Preparations generically represents its descendants like the concepts Neomycin Preparations and Kanamycin Preparations each of which share common family structure and properties but differ in specific functional groups that account for variations in their actions and indications for clinical usage.

Each relationship can be assigned values from a specific domain only [3]. In the pharmacy domain the relationship PHARMACEUTIC-COMPONENT (113), introduced

by the concept Pharmacy Items (Drugs and Nondrugs), is used to refer to the chemicals that form that drug. These chemicals are in the domain that is the inverse of relationship 113 i.e., PHARMACEUTIC-COMPONENT-OF (114) introduced by the concept Chemicals that relates individual chemical ingredients to the pharmacological preparations. This restriction prevents disastrous assignments like a drug concept having a disease concept as its constituent rather than a chemical.

Each term in the IS-A hierarchy has all the properties introduced by its ancestors. Since a term can be viewed as a specialization of more than one parent concept, the SUBCLASS-OF relationship may be multi-valued leading to multiple inheritance of properties. This allows the concepts to capture the features of the different domain perspectives [6, 7]. For example, the concept Neomycin Preparations inherits its basic family chemical properties from the parent concept Aminoglycoside Preparations and its DEA category from the Drug Enforcement Agency (DEA) Class 0 Drugs without Abuse Potential concept parent. Similarly other non-hierarchical relationships may also be multi-valued. Pharmacological preparations may have multiple ingredients and therefore are related to these components by multiple PHARMACEUTIC-COMPONENT relationships. This array of multi-valued relationships makes the vocabulary very complex but is essential to adequately capture the semantics of the concept and thus provide a common pool of terms to professionals from different medical disciplines.

3.1.2 Format of the MED Files

The information in the MED is held in two files, the slot file and the flat file.

Slot file

The slot file consists of tuples of seven comma separated values. Each tuple describes a slot and there are 150 slots in the MED's slot file. The format of the entries in each tuple is as follows:

1. Slot ID that is an integer
2. Unique slot name that is a string
3. MED CODE of concept where the slot is introduced
4. Directionality of link (for graphical display). The possible values are
   - no directionality, as the attribute is a literal
   - points UP to "parent" entity via the relationship
   - points DOWN to "child" entity via the relationship
5. Propagate attribute values to the descendants
   - NO
   - YES
6. ID of inverse relationship slot number
   - NULL field => no reciprocal relationship possible
   - positive integer => ID of reciprocal relationship
   - negative integer => reciprocal relationship possible but not defined (empty for attributes)
7. The data type for an attribute that can be numeric or string but only numeric for a relationship. Null field indicates that the value stored is a relationship - a link to a medical entity.

Flat File

The flat file contains triplets that describe the properties of each concept. The format of the tuples is:

1. Med-code of concept
2. Slot ID
3. Med-code of the concept related to (1) by slot (2) in case it is a relationship, otherwise it is the value of the attribute described by the slot.

The properties for each concept may be multi-valued. Then they are represented by multiple tuples, one for each distinct value for that property. The slot file and the flat file entries for the sub-net being analyzed are provided in the appendix.

3.2 Object-Oriented Model

Object-Oriented models are organized around real world concepts. These concepts are represented by objects, which combine both the data structure and the behavior in a single entity. The essence of Object-Oriented modeling is the identification and organization of application-domain concepts and their classification into class hierarchies [13].

3.2.1 Object-Oriented Model for the MED

This thesis deals with the development of the Object Model for a medical vocabulary. The source of the concepts for this model is the CPMC MED. The following sub-sections describe the components of the Object Model.

3.2.1.1 Objects: Object-Oriented modeling stresses specifying what an object is rather than how it is used. Each object is a unit of data that is encapsulated into the object. As the system requirements evolve, the features of a well defined object are much more stable than the ways it is used [13].

In the real world, all objects have an identity and are distinguishable by their inherent existence and not by their descriptive properties [13]. Therefore in the real world there may be multiple instances of the same type. For example, two patients suffering from the same type of pneumonia (Pneumococcal pneumonia) may differ in the extent of lung involvement (one lobe vs. multiple lobes) as evident in the chest X-Ray and therefore be prescribed different drug regimes (oral Ampicillin 250 mg Capsule every 6 hours vs. intravenous Ampicillin 500 mg every 6 hours). The improvements in the patient's status might be reflected in their X-Rays and may lead to changes in the drug regime.

In the MED, on the other hand, the concepts are defined by their properties and therefore no two concepts can have the same properties with the same assigned values. We need only one term for a particular disease (Pneumococcal Pneumonia) or drug (Ampicillin 500 mg Capsule) or test (Chest X-Ray) and no user modifies it. Since the terms are used only as reference objects and are not modified by the applications, they can be shared and there is no need for separate copies for each application. If the terms differ only in name, with all properties having identical values, then they are considered to be synonyms unless specified by a domain expert as distinct [3].

Attributes of the Objects

An attribute is a data value held by the objects in a class. Each attribute has a value for each object instance and this is a pure data value.

The attributes of the objects in the Object Model are the mapping of attributes of the MED concepts.

Relationships of the Objects

Relationships are the means for establishing links among objects and classes. Relationships in the MED are unidirectional because the reverse relationship always expresses different semantics. For example, a chemical compound may be PHARMACEUTIC-COMPONENT-OF a pharmacological preparation but the inverse relationship, PHARMACEUTIC-COMPONENT, implies that the preparation contains the chemical identified in the relationship.

In the MED a relationship is defined by a tuple in the flat file. The MED relationships are mapped to obtain the relationships for objects in the Object Model.

Multiplicity of Relationships

Multiplicity specifies how many instances of one class may relate to a single instance of an associated class. All the relationships in the MED are potentially multi-valued. This is helpful for the SUBCLASS-OF relationships in providing multiple views of the concepts in a IS-A hierarchy. For example, in the pharmacy domain a drug may be viewed by its functional classification (or actions), its DEA or its allergic categorization. Besides the IS-A relationship, other relationships can also be multi-valued and this allows

a concept to be associated with many other concepts. For example, a pharmacological preparation may be composed of many chemicals and a lab test panel may consist of many tests.

3.2.1.2 Classes: A class is an abstraction that describes the common properties of the objects. These classes are built around contexts that are shared by the concepts. The objects in a class therefore have the same data structure and behavior. Partitioning the concepts in a system like MED, will help in identifying the contexts for building object classes. This will provide a macro (class) view with reduced complexity and a micro (instance) view if detailed information is required.

The contexts in a system are not always easy to determine especially in medicine where concepts occur under multiple classifications to accommodate experts from differing specializations. At the present time, the computer systems are not sophisticated enough to determine the contexts and for a medical vocabulary there is a need for a domain expert to identify the contexts. In the pharmacy domain, the chemical constituents are the primary and determining features of drugs. For example, the concepts Neomycin Preparations and Kanamycin Preparations are SUBCLASS-OF the concept Aminoglycoside Preparations. The aminoglycoside family represents these preparations in a generic form by a class abstraction.

3.2.2 Advantages of an Object-Oriented Model for Medical Vocabulary

An Object Model will classify concepts into classes that represent concepts in the same context. By representing many individual concepts by a far smaller number of contexts,

the object class abstraction reduces the volume of information presented to the user and thereby enhances comprehension. The class model would provide a macro view of the domain in terms of classes representing objects in the same context and a micro view in terms of concepts within each class. Thus the Object Model can help in creating a successful computerized medical vocabulary.

In chapter 6 we will apply object-oriented modeling techniques to a well-defined sub-schema of the MED medical vocabulary.

CHAPTER 4

INTRODUCTION TO PHARMACOLOGY

In our analysis of a MED sub-net we will make extensive use of the knowledge of a medical expert. In order to get a window at the kind of reasoning performed by this expert, we need to give a comprehensive introduction to the fundamental principles of pharmacology and the basic pharmacological concepts that appear in the MED sub-schema.

4.1 General Principles of Pharmacology

One of the major domains of medicine is the field of pharmacology that studies substances that interact with living organisms. These interactions may be due to [9]:

1. Physical properties of substances. For example, Glycerol has hygroscopic (water retaining) properties and is therefore used in many lotions as an emollient, or
2. Chemical interactions especially by binding to regulatory molecules. In most cases certain pathological bio-processes are responsible for the manifestations of a disease. Medicinal substances may activate or inhibit biological chemical reactions leading to resolution of the pathological process. For example, fever is usually produced by certain prostaglandins that act on the thermoregulatory center in the hypothalamus. Aspirin inhibits the synthesis of these prostaglandins and is therefore used as an anti-pyretic agent.

4.1.1 Drug Body Interaction

The interactions between a drug and the body are of two types [5, 9] :

1. Pharmacodynamics - the actions of the drug on the body. These properties determine the actions of the drugs and therefore the functional classification of the drugs.
2. Pharmacokinetics - the action of the body on the drug. These properties govern the absorption, distribution and elimination of the drugs. These aspects are important for determining whether and how a drug can be used in a particular patient:
   a) Absorption of a drug determines the best route for its administration. Aminoglycosides cannot be absorbed from the gastro-intestinal tract (GIT) and therefore are injected into the body rather than being administered orally. Due to the same reason aminoglycosides are used for intestinal antisepsis before bowel surgery to reduce the chance of postsurgical infection. On the other hand, adrenal steroids are absorbed freely from all surfaces and mucus membranes and hence even topical application may lead to systemic side effects that are undesirable.
   b) Distribution of the drug determines whether it reaches the diseased site. For example, aminoglycoside cannot cross the blood brain barrier (a biological barrier that selectively shields the brain from chemicals in the blood) because of its chemical nature and therefore if it is required for treating brain infection, it has to be introduced directly into the meninges covering the brain or the ventricles.

c) Drug elimination is important because it determines the dosage schedules and whether the patient can tolerate the drug. If a drug is eliminated by kidneys (like aminoglycosides), it would be avoided if renal function is compromised or at least the dose would be reduced to avoid accumulation of drugs to toxic levels. Long acting drugs are eliminated slowly and require less frequent administration.

4.1.2 General Properties of Drugs

In general, a drug is any substance that brings about a change in biologic function. In most cases, the drug molecule interacts with specific molecules, called receptors, in the biologic system that regulates a physiologic process. In order to interact chemically with its receptor, a drug molecule must have the appropriate properties so it can reach its site of action and be recognized by the receptors [9]. These properties depend on the chemical structure of the drug. Some important features of the drugs are:

1. Molecular Size: Most of the drugs have molecular weights between 100 and 1000. In order to have specific actions, a drug molecule must be sufficiently unique in shape and charge to bind to only one type of receptor and avoid binding to other receptors. The lower size limit is dictated by the need for a drug molecule to be recognized as distinct from other molecules. Also the drug may not be administered directly at the site of action and in that case must be able to reach the desired site. This limits the size of the drugs as very large molecules are difficult to transport between body compartments.

2. Drug Reactivity: Drugs interact with receptors by means of chemical forces or bonds. There are many types of bonds between the drug and the receptor but the weaker ones lead to more specific interaction with receptors. This is because weak bonds require a precise fit of the drug to its receptor. Only a few receptor types are likely to provide such a precise fit for a particular drug molecule having a specific chemical structure.
3. Drug Shape: The shape of a drug molecule must permit binding to its receptor site. In the optimal case, the drug's shape is complementary to that of the receptor site. Some of these compounds may even have the same chemical structure but still differ in 3-D shape (phenomenon of chirality or sterioisomerism). The chiral pairs which have the same chemical structure but different 3-D orientation are called enantiomeric pairs. One of these enantiomers will be much more effective, have different side effects and duration of action reflecting a better fit for the receptor molecule.

So the major features of drugs depend on the family chemical structure that determines the size and shape of the drug molecule. Minor variations in the specific side chain chemical group and the 3-D orientation of the molecules further give the drug its specific properties within that chemical family.

4.2 Pharmacology of Drug Concepts in the Sub-net

4.2.1 Adrenocorticosteroids

The natural adrenocortical hormones are steroid molecules produced and released by the adrenal cortex.

Chemical Structure

The basic family structure of the steroid hormones consists of the cyclopentenoperhydrophenanthrane or pregnane nucleus [5, 9, 12]. The adrenal cortex synthesizes two classes of steroids:

1. the corticosteroids (glucocorticoids with main effect on intermediate metabolism and inflammation and mineralocorticoids with salt retaining properties) having 21 carbon atoms, and
2. the androgens having 19 carbon atoms.

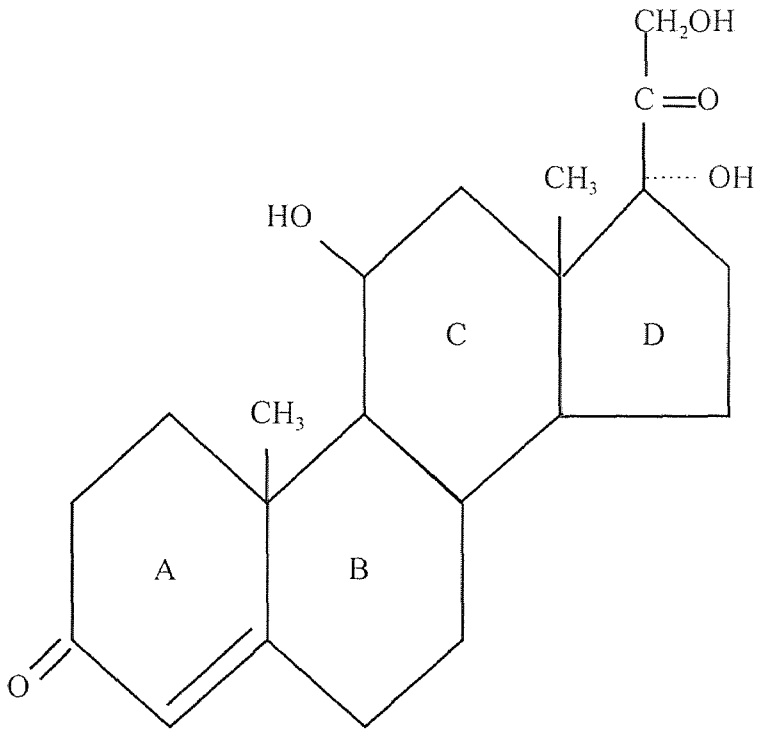

Figure 1 Structure of Adrenocorticosteroids (Hydrocortisone)

Structure-Activity Relationship

Modifications in the chemical structure of a corticosteroid may effect its affinity for glucocorticoid and mineralocorticoid receptors, its duration of action and transport to various sites. The following alterations of the pregnane nucleus demonstrate the importance of the chemical structure of glucocorticoids [5]:

1. Ring A: A 4,5 double bond and the 3-ketone are both necessary for typical adrenocorticosteroid activity. Introduction of a 1,2 double bond, as in prednisone or prednisolone, enhances glucocorticoid potency more than the mineralocorticoid. In addition, prednisolone is metabolized slowly and therefore has a prolonged effects on the body.
2. Ring B: 6∝-Methylation in cortisol increases glucocorticoid effects and fluorination in the 9∝ position enhances all biological activities of the corticosteroids.
3. Ring C: The presence of an oxygen function at C-11 is indispensable for significant anti-inflammatory and carbohydrate-regulating ability.
4. Ring D: 16-Methylation or hydroxylation selectively eliminates the mineralocorticoid effect of the drug.

These variations are useful in creating drugs for specific purposes. A corticosteroid with minimal mineralocorticoid effect would be less likely to cause hypertension as its side effect. A long acting preparation like prednisolone would have simpler dosage schedules for patients and would improve compliance. A short acting

formulation like hydrocortisone, on the other hand, would be useful in emergencies where its effect is brief and its dose can be easily titrated to achieve the precise response.

Mechanism of Action

Glucocorticoids diffuse or are transported through cell membrane and enter the cell where they bind to the cytoplasmic glucocorticoid receptor-heat-shock protein complex. The heat shock protein is released and the hormone receptor complex is then transported into the nucleus, where it interacts with glucocorticoid response elements (GREs) on various genes and other regulatory proteins (which may be cell specific). This interaction may stimulate or inhibit the expression of the gene resulting in the manifestations of its effects [9].

Pharmacokinetics

The adrenal steroids are absorbed from all surfaces because the cell membranes themselves have a steroid structure that allows these chemicals to diffuse easily. They are inactivated by reduction of the 4,5 double bond that occurs in the liver as well as extrahepatic sites [5].

4.2.1.1 Hydrocortisone: Hydrocortisone is a glucocorticoid and shares all the features discussed above.

4.2.2 Aminoglycosides

Aminoglycosides are a group of bactericidal drugs originally obtained from various *Streptomyces* species. They share chemical, antimicrobial, pharmacologic, and toxic characteristics. Some of the members of this family includes streptomycin, neomycin, kanamycin, amikacin, gentamicin, tobramycin, sisomicin and netilimicin.

Chemical Structure

Aminoglycosides have a hexose nucleus, either streptidine (in streptomycin) or deoxystreptamine (in other aminoglycosides), to which amino sugars are attached by glycosidic linkages. Each drug is characterized by the number and kind of amino sugars [5, 9].

Mechanism of Action

Aminoglycosides are bactericidal for susceptible organisms due to inhibition of protein synthesis. An aminoglycoside enters the bacterial cell and binds to receptors on the 30S subunit of the bacterial ribosome. Ribosomal protein synthesis is then inhibited and the bacteria is killed [9].

Pharmacokinetics

Aminoglycosides are absorbed poorly from the intact gastro-intestinal tract. They can be given by intramuscular or occasionally intravenous injection. Being highly polar compounds, unlike glucocorticoids, aminoglycosides do not enter cells readily and are largely excluded from the central nervous system and the eye. Excretion of

aminoglycosides takes place mainly by glomerular filtration in the kidneys and therefore dosage adjustments are required in patients with renal impairment [9].

4.2.2.1 Neomycin: Neomycin is an aminoglycoside antibiotic and therefore shares the features of the family.

Chemical Structure

In the neomycin family, there are three amino sugars attached to the central 2-deoxystreptamine [5].

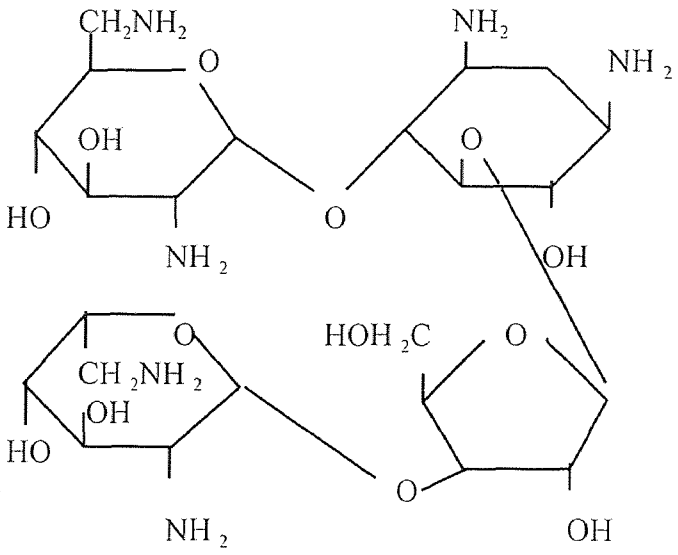

Figure 2 Structure of Neomycin

Pharmacokinetics

Neomycin shares the properties of its parent chemical family aminoglycosides.

4.2.3 Polymyxins

Polymyxins are a group of antibiotic substances produced by *Bacillus polymyxa* [5]. They are active against gram negative bacteria.

Chemical Structure

Polymyxins are cationic, basic polypeptides with molecular weights of about 1400. All contain the fatty acid D-6-methyloctan-1-oic acid and amino acids L-threonine and L-diaminobutyric acid (DAB) [5, 9].

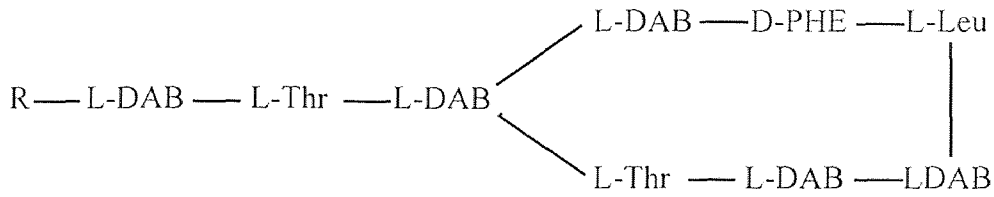

Figure 3 Structure of Polymyxins
Polymyxin B_1: R = (+)-6-Methyloctanoyl
Polymyxin B_2: R = 6-Methylheptanoyl
DAB = α, γ-Diaminobutyric Acid

Mechanism of Action

Polymyxins attach to cell membranes of bacteria that are rich in phosphatidylethanolamine and disrupt the osmotic properties and transport mechanisms of the membrane. Thus, polymyxins act like cationic detergents [5, 9].

Pharmacokinetics

Polymyxin B is not absorbed from the GIT or mucous membranes. At present, it is primarily used for topical application.

4.2.4 Bacitracin

Bacitracin is an antibiotic produced by Tracy-I strain of *Bacillis subtilis* [5] and thus its name, Baci-tracin.

Chemical Structure

Bacitracin is a cyclic polypeptide [5].

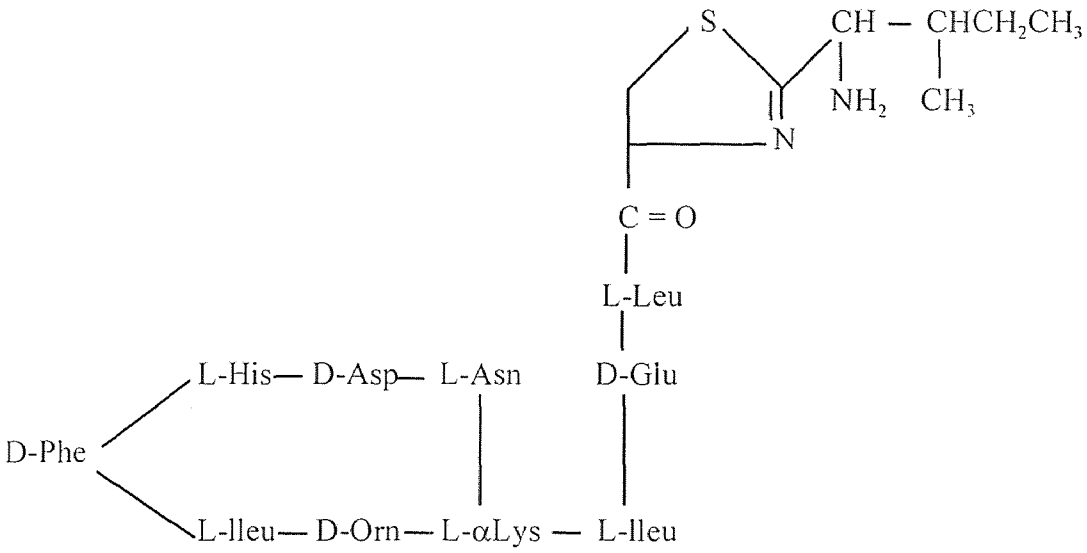

Figure 4 Structure of Bacitracin

Mechanism of Action

Bacitracin interferes with the final dephosphorylation in cycling the isoprenylphosphate carrier that transfers mucopeptide to the growing cell wall [9].

Pharmacokinetics

Bacitracin is currently used only for topical application.

4.3 Summary

From the above discussion on the drug concepts, the importance of the chemical structure of the drugs is apparent. Glucocorticoids have a pregnane ring and completely different properties and interactions with human bodies than aminoglycosides that contain amino sugar linked by glycoside bonds to hexose nucleus. Thus drugs belonging to the same chemical family share actions, side effects and clinical usage. Modifications in the chemical structure not only change how the body acts on the drug i.e., its absorption, transport and elimination but also its actions on the body or other organisms. Minor changes in the chemical structure usually change the pharmacokinetics of the drug like duration of action. However, major differences in the chemical structure indicate distinct actions. Therefore common chemical structure among pharmacological preparations will be the key consideration in determining context while partitioning these concepts in the MED sub-net.

CHAPTER 5

ANALYSIS RULES

5.1 Complexity of Class Hierarchy vs. Semantic Network Hierarchy

At a schema level, complexity was defined in [11] as the ratio of the number of relationships to the number of classes. The higher the complexity of a schema the more difficult it is to comprehend. It has also been shown in [11] that in a class specialization hierarchy, partitioning the classes into contexts and considering the inter-context relationships separately from the intra-context relationships (between classes within a context), helps in achieving a better understanding of the schema.

In semantic networks with a concept specialization hierarchy a similar situation exists with the difference that the hierarchy nodes do not represent classes but express individual concepts with no instances. At the concept level the same quantification of complexity i.e., ratio of the number of relationships to the number of concepts, also holds true. In the MED, the concepts or terms are considered to be individual objects. Just as in the class hierarchy, partitioning applied to a MED sub-net will help in grouping concepts into contexts that are easier to comprehend and create object class hierarchies on the basis of the emerging contexts.

5.2 A Methodology for Classifying Concepts in a Semantic Network

Semantic network vocabularies are difficult to comprehend because they consider each term and its associated terms individually without grouping them into logical units. A semantic network with a DAG specialization hierarchy structure and superfluous

information associated with the concepts makes it even more difficult to understand. It is therefore important to provide a means for reducing the information overload in the vocabulary network by partitioning the terms into logical units on the basis of context and thereby enabling comprehension.

The method utilized to simplify a complex semantic network schema involves two techniques described in more detail in sections 5.2.1 and 5.2.2 [8, 11]:

1. Informational thinning which removes the information that is not essential to the analysis, and
2. Partitioning which classifies the SUBCLASS-OF relationship into two types so that the semantic network DAG is divided into trees. These trees consist of concepts in the same context and therefore are more comprehensible. Thus turning the original network into a collection of such trees provides greater understanding of the whole network.

5.2.1 Informational Thinning

A vocabulary semantic network like MED, that contains a vast number of objects, relationships and attributes, is difficult to comprehend. The difficulties in understanding a vocabulary system arise mainly from the number of relationships associated with the concepts.

In the MED, at the time of this writing, there are 42,744 concepts, 54,547 IS-A relationships that connect the concepts to form a DAG and 199,693 other relationships used to capture the semantics of the terms. The complexity of the MED is c = (54547 + 199693) / 42744 = 5.95.

Informational thinning allows us to eliminate non-essential information from the network by displaying only the properties essential for the analysis. The analysis of the MED sub-net, introduced in section 6.1, is based on the IS-A hierarchy only and therefore uses this simplified hierarchy with all other attributes and relationships removed from the view. This abstraction helps to provide a model of the network that is easier to comprehend and is amenable to the partitioning analysis. The complexity of the IS-A hierarchy of the MED is 54547/42744 = 1.28.

The sub-net with the leaf concept CPMC Drug: Cortisporin Opth Oint (=opthalmic ointment, an eye ointment) has the most ancestors, 39 (figure 7), of any concept in the MED. In this sub-net there are 821 attributes, 62 IS-A relationships and 157 other relationships. Thus the complexity c = (62 + 157) / (39 + 1) = 5.5. All the relationships and attributes with the exception of the IS-A relationship are not required for the analysis. Informational thinning allows us to create a simplified hierarchy that has the same size (number of concepts) as the original network but fewer relationships because only IS-A relationships are represented for the analysis. The complexity of this IS-A sub-net is 62/40 = 1.55. Thus the selected sub-net (with complexity 1.55) is more complex than any average IS-A sub-net in the MED (with complexity 1.28) and therefore partitioning other sub-nets of the MED will be simpler than the current one.

5.2.2 Partitioning

Informational thinning removes all the attributes and relationships except the IS-A relationship from the sub-net. But still the network is difficult to comprehend due to multiple inheritance. Partitioning is used to obtain a set of simple and disjoint smaller

sub-hierarchies consisting of concepts in the same context. Partitioning also helps to minimize the number of relationships between different logical units of concepts and thus reduce the complexity of the sub-net.

5.2.2.1 Refinement of the SUBCLASS-OF Relation: In the specialization hierarchy obtained after Informational Thinning, all the SUBCLASS-OF (IS-A) relationships are of the same type. Partitioning divides the objects into logical groups in the same context such that each object has only one path in the specialization hierarchy to the root of its context. This requires the division of SUBCLASS-OF relationships into two types [11]:

1. Category-Of is a specialization relationship which relates the specialization object to the more general object where both are in the same application context. These are represented in the figures as regular arrows.
2. Role-Of is a specialization relationship which relates the specialization object to the more general object, where the two objects are in different contexts of the application. These are represented in the figures as dashed arrows.

The decision whether a given sub-object relationship in the hierarchy, shown in figure 7, is either Category-Of or Role-Of depends on whether the super-object and sub-object are in the same context or not. This decision lies with the domain expert who defines the partitioning rules for a particular domain based on an intuitive understanding of the domain.

As described in the Introduction to Pharmacology (chapter 4), the chemical structure of the pharmacological preparations is a key feature in determining the properties of a preparation. Therefore the concepts would be classified according to their

chemical families. Besides the chemical family the second priority in determining context would be given to the site of action and the third to the actions or site of productions.

Inspite of the understanding of the domain and the above mentioned simple priority guidelines some rules to resolve difficult cases and ensure consistency are required. Disciplined Modeling provides such a set of guidelines that help in the partitioning process [8, 11].

5.2.2.2 Disciplined Modeling: The partitioning paradigm is supported by the rules of Disciplined Modeling which ensure that a forest sub-hierarchy can be identified. Disciplined Modeling allows the refinement of the IS-A hierarchy according to three rules.

Rule 1: The equicontext relationship between objects is an equivalence relationship and thus partitions the objects of a hierarchy into disjoint contexts.

This forces the designer to explicitly specify the contexts in the hierarchy and leads him to resolve some ambiguous situations especially in situations where contexts overlap because a concept belongs to multiple domains.

Rule 2: Two objects which are Category-Of specializations of a super-object cannot have a common Category-Of descendant object.

This rule guarantees that when we refine a general concept represented by an object into several sub-concepts in the same context we achieve a partition into mutually exclusive concepts.

Rule 3: For each context there exists one object which is the major (or defining) object for this context such that every object in this context is a descendant of this object.

This means that each context has only one object which is a root for it i.e., there is a directed path of the Category-Of relationships from each object of the context to this root object.

In addition, it has been proved in [8,11] that using Disciplined Modeling, an object has at most one Category-Of super-object. This theorem guarantees that the Category-Of hierarchy has a forest structure. This forest structure is simpler than the original DAG and reduces the effort required to comprehend the network.

5.2.2.3 Type of Role-Of Relationships: In the original MED sub-net, all the super-object relationships are of the same type i.e., Category-Of. However, in the analysis some of these are changed to Role-Of. For most objects with multiple super-objects the determination of the defining super-object in the same context is easy yielding a Category-Of relationship directed to it. There are a few cases where the decision about a definitional super-object for a given object is difficult. In such cases, at most one of the several super-objects should have a Category-Of relationship pointing to it, based on the partial context information that has already been accumulated in a processing at that

juncture. Such a selection may occur in 3 situations resulting in three types of Role-Of: regular Role-Of , Role-Of /Intersection, and Role-Of/Category-Of [8].

Case 1: One of the super-objects is definitional while the others are functional. If the context of the sub-object is definitional, the sub-object will have a Category-Of relationship to the definitional super-object and if the context is functional, then a Category-Of relationship to the functional super-object. If there are several functional super-objects, the super-object which fits the function described in the context of the sub-object is selected. The object is Category-Of this primary super-object and Role-Of the other super-objects. This kind of Role-Of relationship is a regular Role-Of since a switch of context from a super-object to a sub-object has occurred. An example of this case will be discussed in section 6.2.1.

Case 2: All super-objects are definitional with the same importance because each of them contributes to the definition of the sub-object in an equal way. In such a situation, the object with multiple super-objects would need to be in the context of all its super-objects. However, by the rules of Disciplined Modeling it cannot belong to more than one context. Since both super-objects are of equal importance it would be incorrect to associate the object with only one context. Therefore, such an object starts a new context which represents the context obtained as an intersection of the contexts of all its super-objects. Thus, the object is Role-Of all its super-objects. This type of Role-Of is Role-Of/Intersection represented as r/i in the figures. This is not an actual case of a switch of

context but an artificial case due to the requirements of the theorem to forbid two Category-Of super-objects. An example of this case will be discussed in section 6.2.1.

Case 3: The context of the sub-object is a combination of the contexts of its multiple super-objects, but one of them contributes more to the meaning than the others. Then the Category-Of relationship should point to the preferred super-object.

5.2.2.4 Diamond Structure: The Role-Of/Intersection gives rise to another situation that needs to be resolved so that partitioning into disjoint context is consistent and complete. This is the diamond situation as shown in figure 5 where object *d* is a Role-Of/Intersection of its super-objects *b* and *c*.

Figure 5 The Diamond Structure due to Role-Of/Intersection Relationships

Since the object *d* is the intersection of two super-objects, the two super-objects *b* and *c* cannot both belong to the same context of their super-object *a*. Otherwise, because the intersection of a context with itself will result in the original context, the intersection must belong to this common context. Thus the objects *b* and *c* are also defined as separate contexts. The Category-Of relationship is changed to Role-Of. This kind of

Role-Of is described as Role-Of/Category-Of since originally this link was a Category-Of relationship but due to Rule 2 it becomes Role-Of and is represented as r/c in the figures [8].

5.2.2.5 Analysis Sequence for the Sub-net: In the semantic network sub-net from the MED, the leaf concepts represent the concepts corresponding most directly to real-world objects. A bottom-up analysis in this situation would be appropriate because the context of the objects is best evident with the distinct objects at the bottom of the sub-net. This knowledge will help to determine which of the contexts of the super-objects fits best with the already identified sub-object context especially as the super-objects become more generic higher up in the hierarchy.

CHAPTER 6

PARTITIONING ANALYSIS OF A SUB-NETWORK OF THE MED

In this chapter, partitioning along with rules of Disciplined Modeling are applied to the DAG sub-net of the MED to obtain a forest of trees. Each tree produced by the partitioning would consist of concepts in the same context.

6.1 Introduction to the MED Sub-net

The objective of this thesis is to analyze and partition the most complex hierarchical sub-net in the MED. This sub-net is the one with the leaf that has the maximum number of ancestors. This sub-net is in the pharmacy domain and consists of ancestors of the leaf concept CPMC Drug: Cortisporin Opth Oint (MED-CODE 28602). In order to enable understanding of the sub-net, figure 7 shows the sub-net after Informational Thinning has been applied leaving only the IS-A relationships in the sub-net. In the following discussion the attribute names of the objects (or concepts) are followed by their slot ID numbers in parenthesis.

The root of this sub-net is the concept Medical Entity. As we move down the hierarchy the concepts become more specific. The concept Medical Entity provides 10 basic properties that constitute the minimal set of properties describing each concept in the vocabulary. This basic set consists of the attributes MED-CODE (0), UMLS-CODE (1), NAME (2), SUBCLASS-OF (4), SYNONYM (5), PRINT-NAME (6), HAS-PART (7), PART-OF (8), MAIN-MESH (50) and SUPPLEMENTARY-MESH (51) that are common to all the MED entities.

The concepts in the pharmacy domain can be viewed from various perspectives. Each of these perspectives describes one or more specific properties of that concept and classifies them according to this property. The top level ancestors of the pharmacy concepts correspond to the various classifications of drugs.

Two major classifications in the sub-net are the concepts CPMC Formulary Drug Item and American Hospital Formulary Service (AHFS) Class. The concept AHFS Class introduces the attribute AHFS-CLASS-CODE (55) that is used to map each descendant of the concepts CPMC Formulary Drug Item to AHFS Class code. Both these formularies group drugs according to their action (like the concepts Anti-Infective Agents and Anti-Inflammatory Agents), site of action (like the concepts Eye, Ear, Nose & Throat (EENT) Preparations, Skin and Mucous Membrane Agents) or biological existence in the human body (like the concept Hormones and Synthetic Substitutes). The concept Hormones and Synthetic Substitutes further classify concepts according to their physiological source like the concept Adrenal Agents that refers to substances produced by adrenal glands.

Drugs having similar actions are further classified according to their chemical families. In the sub-net, the concept Antibiotic Preparations is sub-classified into concepts Aminoglycoside Preparations and Miscellaneous Antibiotics groups and similarly the concept Anti-Inflammatory Agents into concepts Glucocorticoids Agents and non-steroidal families (not shown in the sub-net).

Other classifications group drugs on the basis of other properties. The Drug Enforcement Agency (DEA) Controlled Substance Category concept classifies drugs according to its abuse potential and introduces attribute DEA-CODE (73). The attribute

ALLERGY-CLASS-CODE (70) is introduced by the concept Drug Allergy Class. The allergic effects are characteristics of the chemical ingredients of the preparations and therefore are classified according to the chemical families like the concepts Drug Allergy Class: Glucocorticoid and Drug Allergy Class: Aminoglycoside.

The attribute DRUG-DESCRIPTION (71) is introduced by the concept CPMC Formulary Drug Forms that specifies its form of dispensation. The actual prescribed preparations, which are the leaves in the sub-net, can be dispensed in various forms like tablets, by milligram or grams. Only the leaf nodes which are the actual real world objects or dispensed drugs can be descendants of this concept.

The concept Pharmacy Items (Drug and Nondrugs) introduces a host of properties for its descendants that define pharmaceutical preparation concepts.

The Orderable Entity concept is the ancestor of any concept that represents something that can be ordered like a drug as a descendant of the concept Pharmacy Item (Drugs or Nondrugs) or a special diet as a descendant of the concept Prescribed Diet (not shown in the sub-net).

The concepts in the middle of the sub-net describe various individual preparations that are dispensed as single component drugs like Neosporin Preparations, Bacitracin Preparations, Polymyxin B Preparations and Hydrocortisone Preparations (figure 7). These individual single drug preparations form the ancestors of drug combinations like a combination of two different antibiotics may be used to enhance the spectrum against the organism while reducing the dosage of each agent to reduce the side effects (Bacitracin/ Polymyxin B Combination Preparations). Drugs may also be combined with other drugs with different actions. An antibiotic preparation may be combined with an anti-

inflammatory one like the concept Hydrocortisone/Neomycin /Polymyxin B Combination Preparations. This combination would act against the infecting bacteria and also provides relief from inflammation induced by the infection.

Finally we reach the leaves that are the actual preparations provided to the patients. These may be a single drug represented by the concept CPMC Drug: Bacitracin Oint 30 Gm or a combination like CPMC Drug: Cortisporin Opth Oint that is the focus of our analysis in this thesis.

Some of the concepts that are not ancestors of the concept CPMC Drug: Cortisporin Opth Oint like CPMC Drug: Cortisporin Otic Soln 10 ml (ear drops), CPMC Drug: Neosporin GU Irrigent 1 ml amp, CPMC Drug: Bacitracin Oint 30 Gm, CPMC Drug: Neosporin Topical Oint 30 Gm and CPMC Drug: Polymyxin B Sulf 500,000u pwd are also included in the sub-net. These concepts help in resolving the context issues in difficult cases during the analysis.

The Leaf Concept CPMC Drug: Cortisporin Opth Oint

All the features of the concept CPMC Drug: Cortisporin Opth Oint are captured in these tuples for the concept in the MED flat file as shown in figure 6.

The NAME (2) of the preparation is CPMC DRUG: CORTISPORIN OPTH OINT and its PRINT-NAME (6) is CPMC Drug: Cortisporin Opth Oint. It is SUBCLASS-OF (4) concepts Eye, Ear, Nose and Throat Antibiotic (MED-CODE 24077) indicating its site and effect, Drugs Dispensed by the Gram (MED-CODE 28308) that indicates its form of dispensation and Bacitracin/Hydrocortisone/Neomycin/Polymyxin B Combination Preparations (MED-CODE 32818) that supplies its chemical constituents.

```
28602,1,""
28602,2,"CPMC DRUG: CORTISPORIN OPTH OINT"
28602,4,24077
28602,4,28308
28602,4,32818
28602,5,""
28602,6,"CPMC Drug: Cortisporin Opth Oint"
28602,7,
28602,8,
28602,50,""
28602,51,""
28602,55,"520404"
28602,56,""
28602,57,"0.00"
28602,58,"CORTISPORIN OPTH OINT"
28602,59,"COROO"
28602,60,"00081019786"
28602,61,"CORTISPORIN"
28602,62,"NEOMYCIN/BACITRACIN/POLY/HC"
28602,63,"BURROUGHS"
28602,64,"F"
28602,65,"3"
28602,66,"N"
28602,67,"OPTH"
28602,68,"Y"
28602,69,"0"
28602,70,"02"
28602,70,"10"
28602,71,"GM"
28602,72,"0"
28602,73,"0"
28602,74,"Q6W"
28602,75,"87269"
28602,76,"819"
28602,108,30365
28602,112,30379
28602,113,30430
28602,113,30632
28602,113,30730
28602,113,30776
28602,123,"00000447"
28602,132,""
```

Figure 6 Flat File Abstract for the Concept CPMC Drug: Cortisporin Opth Oint

It has no synonyms and therefore SYNONYMS (5) is a null string. Its AHFS-CLASS-CODE (55) is 520404. Since it is an ointment it is not measured in dose and therefore its DOSE-STRENGTH-UNITS (56) is not applicable, its DOSE-STRENGTH-NUMBER (57) is 0.0 and DRUG-VOLUME (69) is 0. Its FORMULARY-NAME (58) is CORTISPORIN OPTH OINT and SHORT-FORMULARY-NAME (59) is COROO which is a concatenation of the CORtisporin Ophthalmic Ointment. It FORMULARY-CODE (60) is 00081019786 and its DRUG-TRADE-NAME (61) is CORTISPORIN. Its DRUG-GENERIC-NAME (62) is its components chemicals, NEOMYCIN / BACITRACIN / POLY / HC and DRUG-MANUFACTURER (63) is BURROUGHS. Its DRUG-ROUTE (67) i.e., route of administration, is OPTHalmic i.e., to be applied to the eye. Its DRUG-DESCRIPTION (71) indicates its is dispensed by grams and its DEA-CODE (73) indicates it belongs to DEA category 0 i.e., those drugs that have no abuse potential. Its two instances of ALLERGY-CLASS-CODE (70) indicates it can have two types of allergic reactions, one due to Aminoglycoside components and one due to Hydrocortisone. Its PHARMACEUTIC-COMPONENTs (113) are Bacitracin (MED-CODE 30430), Hydrocortisone (MED-CODE 30632), Polymyxin B (MED-CODE 30776) and Neomycin (MED-CODE 30730). The other properties are for internal use of CPMC.

Thus, the attributes and relationships for the concept CPMC Drug: Cortisporin Opth Oint capture all the essential features that might be queried by the physician, pharmacist, the DEA or any other user of medical information.

6.2 Applying Partitioning Methodology to the Complex Sub-net

In this section, partitioning along with the rules of Disciplined Modeling are applied to the DAG sub-net of the MED to obtain a forest of trees. Each tree produced by the partitioning would consist of concepts (or objects) that are in the same context. One of the concept (or object) in each tree, usually the root of that tree, defines the unifying context for all the concepts in that tree.

The partitioning will be carried out in a bottom-up manner and involves two passes:

1. Classification of the IS-A relationships, and
2. Resolution of any diamond structures that would be a contradiction for Disciplined Modeling.

6.2.1 Classification of the IS-A Relationships

The hierarchical sub-net shown in figure 7 includes all the ancestors of the object CPMC Drug: Cortisporin Opth Oint (MED-CODE 28602) in which all the super-object relationships are of the same type. In the following description the objects are followed by numbers in parentheses that identify them in the accompanying figures.

The object at the bottom of the hierarchy, CPMC Drug: Cortisporin Opth Oint (2), has three super-objects, Bacitracin / Hydrocortisone / Neomycin / Polymyxin B Combination Preparations (3), Drugs Dispensed by the Gram (23) and Eye, Ear, Nose and Throat Antibiotics (28). The super-object 3 defines the chemicals constituents of the object 2. The super-object 23 specifies the dispensation form of the drug. Other siblings of 23 are Tablets, Drugs Dispensed by the Milliliter and Drugs Dispensed by the

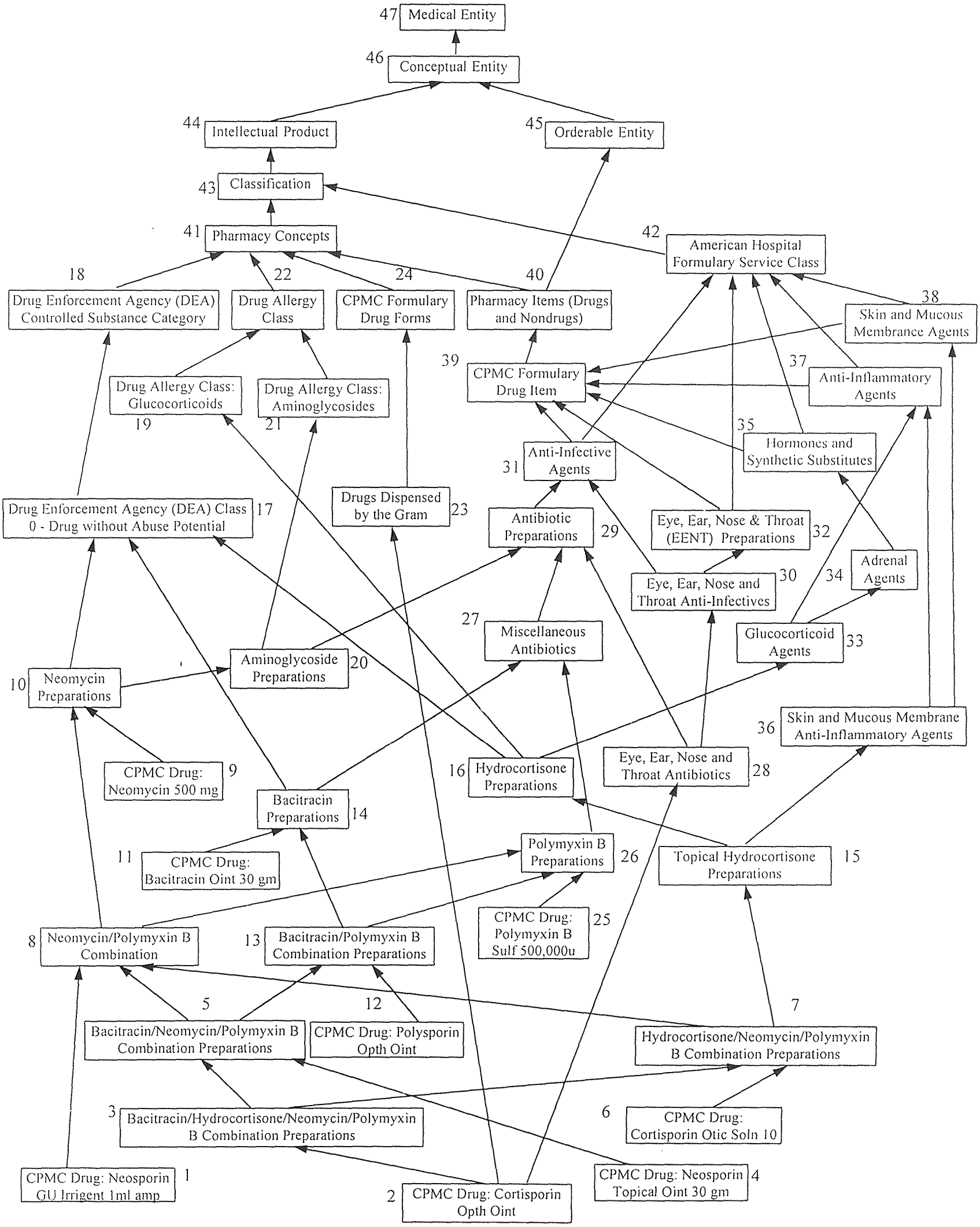

Figure 7 Most Complex Sub-net in the MED after Informational Thinning

Milliequivalents (not shown in the figures), that specify some other forms of drug dispensation. The super-object 28 specifies the site (eye, ear, nose and throat) and action (antibiotic) of the object 2. The ingredients of the ointment uniquely define the properties of the object 2. Neither super-objects, 23 or 28, define the context of object 2. Therefore by Case 1 of Disciplined Modeling, the object 3 is the primary super-object and the object 2 is Category-Of 3, Role-Of 23 and Role-Of 28.

The object Bacitracin / Hydrocortisone / Neomycin / Polymyxin B Combination Preparations (3), has two super-objects, Bacitracin / Neomycin / Polymyxin B Combination Preparations (5) and Hydrocortisone / Neomycin / Polymyxin B Combination Preparations (7). Both these super-objects contribute the properties of Neomycin Preparations and Polymyxin B Preparations to the object 3. In addition, 5 adds properties of Bacitracin Preparations and 7 adds features of Hydrocortisone Preparations. The four chemical constituents together define the object 3. Therefore by Case 2 it is not possible to associate 3 with one of the super-objects and it is a Role-Of both objects 5 and 7. This Role-Of is a result of intersection of the properties of the super-objects and is of type Role-Of/Intersection.

A similar analysis can be applied to all objects that are roots of drug combinations like Bacitracin / Neomycin / Polymyxin B Combination Preparations (5) that is Role-Of both Bacitracin / Polymyxin B Combination Preparations (13) and Neomycin / Polymyxin B Combination Preparations (8). Similarly, Hydrocortisone / Neomycin / Polymyxin B Combination Preparations (7) becomes Role-Of its super-objects Neomycin / Polymyxin B Combination Preparations (8) and Topical Hydrocortisone Preparations (15), while Bacitracin / Polymyxin B Combination Preparations (13) is Role-Of both

Bacitracin Preparations (14) and Polymyxin B Preparations (26). Finally, the object Neomycin / Polymyxin B Combination Preparations (8) becomes Role-Of both its super-objects Neomycin Preparations (10) and Polymyxin B Preparations (26).

The object Topical Hydrocortisone Preparations (15) has two super-objects, Hydrocortisone Preparations (16) and Skin and Mucous Membrane Anti-inflammatory Agents (36). The super-object 16, an adrenal steroid having a cyclopentenoperhydrophenanthrane ring structure, defines the chemical structure for 15 while super-object 36 defines the action (anti-inflammatory) and the site of the action (skin and mucous membrane or topical). Thus the structural definition for 15 is provided by the super-object 16 and the object 15 is Category-Of 16 and Role-Of 36.

The object Neomycin Preparations (10) also has two super-objects, Aminoglycoside Preparations (20) and Drug Enforcement Agency (DEA) Class 0-Drug without Abuse Potential (17). The object 10 is one of the aminoglycoside antibiotics that are characterized chemically by amino sugars linked by a glycoside bond to an aminocyclitol ring [5, 12]. The super-object 17 indicates a grouping used by the DEA to identify preparations like 10 that do not have abuse potential but this does not add to the properties of 10. Therefore 10 is Category-Of 20 and Role-Of 17.

The object Bacitracin Preparations (14) has two super-objects, Miscellaneous Antibiotics (27) and Drug Enforcement Agency (DEA) Class 0-Drug without Abuse Potential (17). The 27 group is a heterogeneous group of antibiotics that have chemical structures that do not fall into the major antibiotic families represented by objects like Penicillin Preparations or Aminoglycoside Preparations. Some of the sub-objects of Miscellaneous Antibiotics are Vancomycin Preparations (a glycopeptide), Polymyxin B

Preparations (26) (a basic polypeptide) and Clindamycin Preparations (a lincosamide) and Bacitracin Preparations (a cyclic polypeptide) (14) [5, 9, 12]. The super-object 17, like in the case of object 10, does not provide any definitional property to object 14. Therefore 14 is Category-Of 27 and Role-Of 17. On a similar note Polymyxin B Preparations (26) (another sibling of Bacitracin Preparation) is also Category-Of 27.

The object Hydrocortisone Preparations (16) has three super-objects, Glucocorticoid Agents (33), Drug Enforcement Agency (DEA) Class 0-Drug without Abuse Potential (17) and Drug Allergy Class: Glucocorticoids (19). All glucocorticoids have a cyclopentenoperhydrophenanthrane ring structure that is responsible for their common family properties. The super-object 33 defines the chemical structure for 16. Some other glucocorticoid agents in the MED that share the structure and properties of 16 are objects like Prednisolone Preparations, Methyl-prednisolone Preparations, Triamcinolone Preparations, Betamethasone Preparations and Dexamethasone Preparations (not shown in the figures). The super-objects 17 (that groups drugs according to abuse potential) and 19 (that groups the drugs according to its allergic potential) do not define any structural feature of 16. Hence, 16 is Category-Of 33, Role-Of 17 and Role-Of 19.

The object Aminoglycoside Preparations (20), has super-objects Antibiotic Preparations (29) and Drug Allergy Class: Aminoglycosides (21). The object 29 is a heterogeneous concept that defines the action (antibiotic) of object 20 rather than its chemical structure. The object 20 is a major antibiotic chemical family among others like Penicillin Preparations and Cephalosporin Preparations (not shown in the figures). The object 21 indicates the allergic effects of preparations belonging to domain of object 20.

Hence 20 is not in the same context with either of the super-objects 21 or 29. It defines a new context for its descendants and is therefore Role-Of both 21 and 29.

The object Miscellaneous Antibiotics (27) has one super-object, Antibiotic Preparations (29). The super-object 29 defines the group of drugs that have antibiotic effects and does not define any chemical structure for 27. Other siblings of 27 in the MED include the major antibiotic families like the objects Penicillin Preparations, Aminoglycoside Preparations and Tetracycline Preparations each defining the basic chemical structure for their descendant objects. Similarly, the object 27 also defines a group of antibiotics without any specifying their chemical structure. Therefore the object 27 is Category-Of 29.

The object Eye, Ear, Nose and Throat Antibiotics (28) has super-objects Antibiotic Preparations (29) and Eye, Ear, Nose and Throat Anti-Infectives (30). The object 28 defines the site (eye, ear, nose and throat) and the type of action (antibiotic) for its descendants. The super-object 29 indicates only the type of action (antibiotic) where the super-object 30 indicates both the site and action. Therefore 28 is Role-Of 29 and Category-Of 30.

The object Eye, Ear, Nose and Throat Anti-Infectives (30) has two super-objects, Anti-Infective Agents (31) and Eye, Ear, Nose and Throat Preparations (32). The super-object 31 defines the actions of 30 and super-object 32 identifies its site. As discussed previously, site of action is given a higher preference in deciding the context of an object and therefore 30 is Category-Of 32 and Role-Of 31.

The object Glucocorticoid Agents (33) has two super-objects, Adrenal Agents (34) and Anti-Inflammatory Agents (37). Glucocorticoids are chemicals that are secreted

by adrenal glands and super-object 34 indicates the physiological source for 33. Another type of adrenal agents are mineralocorticoids which are functionally distinct from glucocorticoids. The super-object 37 is a heterogeneous set of concepts that includes steroidal anti-inflammatory drugs like Glucocorticoid Agents and non-steroidal anti-inflammatory agents like the objects Aspirin Preparations, Ibuprofen Preparations or Phenylbutazone Preparations (not shown in the figures). Therefore neither of the super-objects define the properties for object 33 and so it is a Role-Of both 34 and 37. The object 33 defines a new context consisting of objects Hydrocortisone Preparations, Betamethasone Preparations and Dexamethasone Preparations (not shown in the figures) that belong to the same chemical family.

The object Adrenal Agents (34) had one super-object Hormones and Synthetic Substitutes (35). Adrenal Agents are hormones that are produced by adrenal glands and therefore the object 34 is Category-Of 35.

The object Skin and Mucous Membrane Anti-Inflammatory Agents (36) has two super-objects, Skin and Mucous Membrane Agents (38) and Anti-Inflammatory Agents (37). The object 36 indicates a site (skin and mucous membrane) and an action (anti-inflammatory). The super-object 38 defines the site while 37 defines the action. The super-object 37 has children which define different types of chemicals having anti-inflammatory properties or different sites where anti-inflammatory agents can be applied. Here, once again, the site is considered more important in determining the context of the object. Therefore 36 is Category-Of 38 and Role-Of 37.

The object Antibiotic Preparations (29) has one super-object, Anti-Infective Agents (31). Since antibiotic substances are a type of anti-infective agents that are produced by living organisms, 29 is a Category-Of 31.

The object Anti-Infective Agents (31) has two super-objects, CPMC Formulary Drug Item (39) and American Hospital Formulary Service Class (42). Both 42 and 39 define formulations of various pharmacological preparations according to the action or site of application or physiological existence in the body. Therefore 31, which specifies a particular action of its domain objects, is not in the same context with any of the formularies. Hence 31 is Role-Of both 39 and 42. The objects Eye, Ear, Nose and Throat Preparations (32), Hormones and Synthetic Substitutes (35), Anti-Inflammatory Agents (37) and Skin and Mucous Membrane Agents (38) all have the two super-objects 39 and 42. All of these, like 31, are Role-Of their super-objects.

The object Drug Enforcement Agency (DEA) Class 0-Drugs without Abuse Potential (17) has one super-object, Drug Enforcement Agency Controlled Substance Category (18). The super-object 18 is in the same context as the object 17 i.e., a classification of the drugs according to DEA. Therefore 17 is a Category-Of 18. On a parallel analysis object Drug Allergy Class: Glucocorticoid (19) is a Category-Of Drug Allergy Class (22) and so is object Drug Allergy Class: Aminoglycoside (21).

The object Drugs Dispensed by the Gram (23) has one super-object, CPMC Formulary Drug Form (24). The object 24 defines all the forms in which a drug may be dispensed. The object 23 is one of the forms of drug dispensation along with other forms like the concept Dispensed by the Milligrams etc. Therefore the object 23 is Category-Of 24.

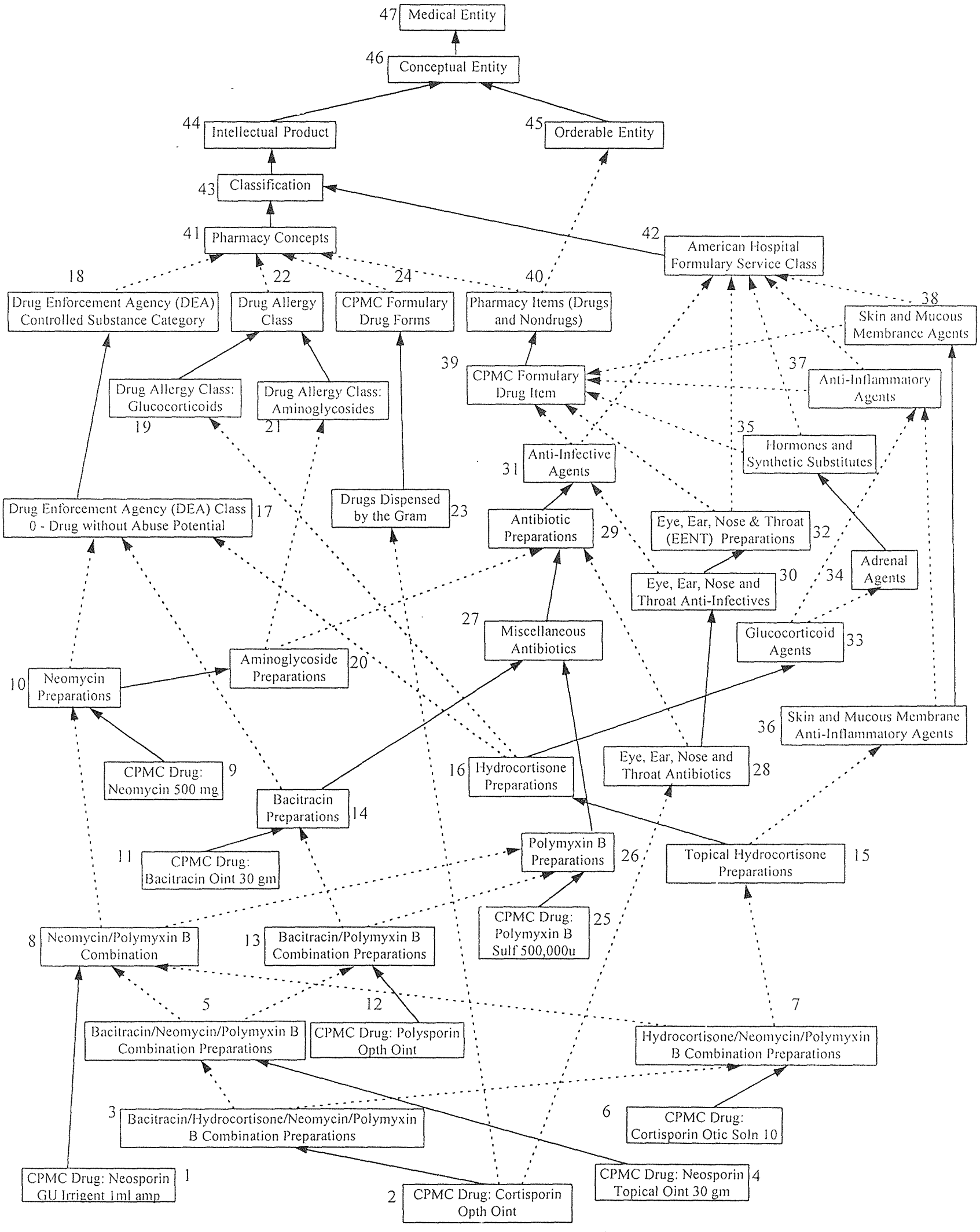

Figure 8 Sub-net after Classifying IS-A Relationships

The object CPMC Formulary Drug Item (39) has one super-object, Pharmacy Items (Drugs and Nondrugs) (40). The objects 39 and 40 are in the same context because CPMC Formulary Drug Item is one of the Pharmacy Items.

The object Drug Enforcement Agency (DEA) Controlled Substance Category (18) has one super-object, Pharmacy Concepts (41). The super-object 41 is a generic term that has sub-objects referring to different contexts. One of the sub-objects of 41 is Drug Enforcement Agency (DEA) Controlled Substance Category (18) that defines drug concepts that are controlled by DEA. Another sub-object of 41 is Drug Allergy Class (22) that groups concepts according to its allergic properties. Still another is CPMC Formulary Drug Forms (24) that refers to the dispensation form (tablet, injectable etc). Therefore each of the sub-objects of 41 is a specialization in a different context making all its sub-objects (18, 22, 24) Role-Of 41.

The object Pharmacy Items (Drugs and Nondrugs) (40) has super-objects Pharmacy Concepts (41) and Orderable Entity (45). Based on the analysis of objects 18, 22 and 24, the object 40 is Role-Of 41. Also 45 is a heterogeneous group of objects that can be ordered that may be pharmacy or non-pharmacy concepts like Prescribed Diet (not shown in the figures). Therefore 40 is not in the same context as 45 and is a Role-Of 45.

The object American Hospital Formulary Service Class (42) has one super-object, Classification (43). AHFS Class is a type of classification and therefore Category-Of 43. Similarly, the object Pharmacy Concepts (41) has one super-object Classification (43) and is a Category-Of 43.

The objects at the top level including Classification (43), Intellectual Product (44), Conceptual Entity (46) and Orderable Entity (45) have only one super-object (44, 46, 47

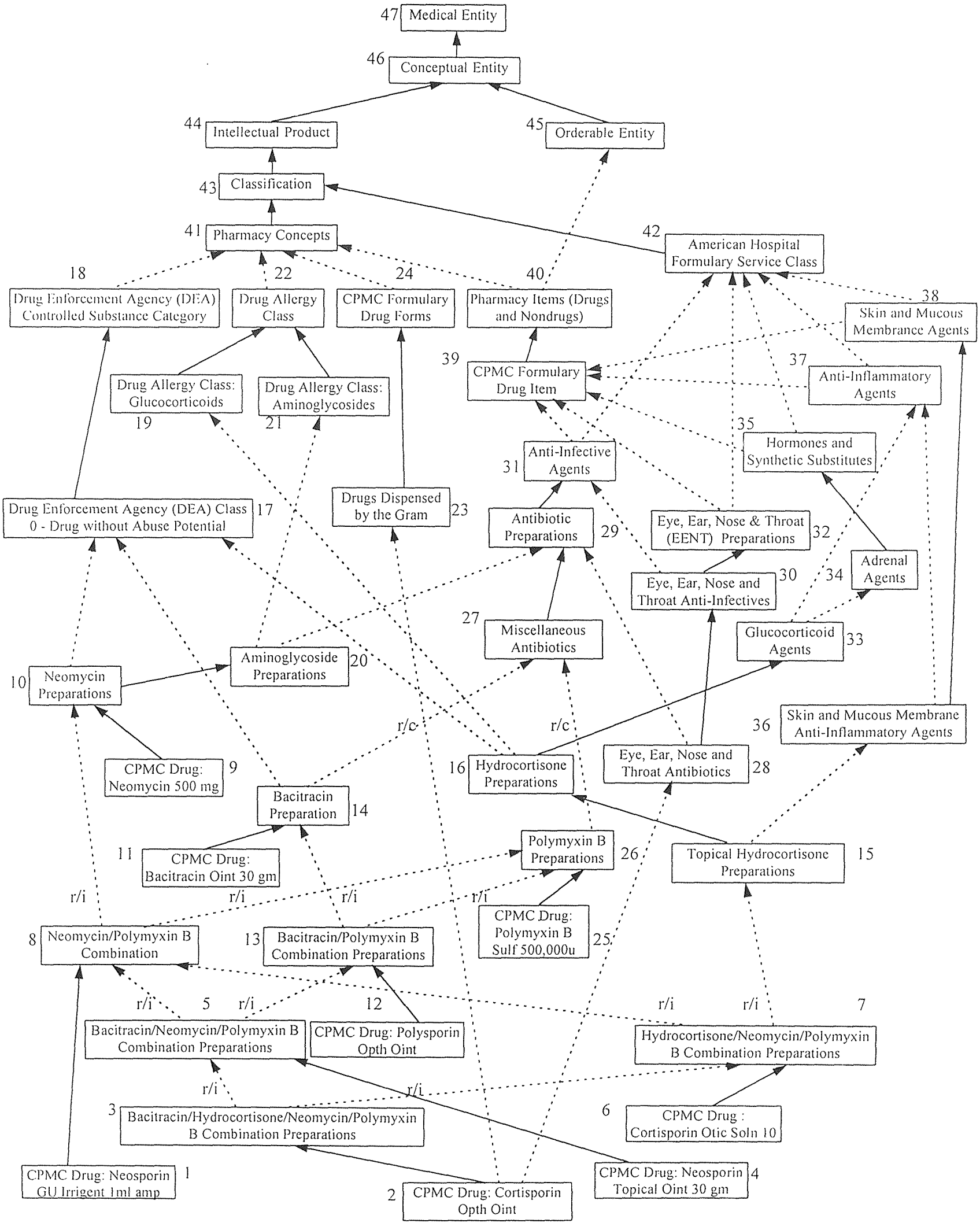

Figure 9 Sub-net after Resolving Diamond Structure

and 46 respectively). All of them are generic concepts like Medical Entity (47) and therefore are Category-Of their super-objects.

The results of the classification of IS-A relationships is shown in figure 8 with all Category-Of as solid lines and all Role-Of as dashed lines.

6.2.2 Resolving the Diamond Structure

After the first pass, the resulting partitioned contexts must be examined to determine if there are any contradictions to the rules of Disciplined Modeling produced by a diamond structure for the Role-Of/Intersection type of IS-A relationships. A diamond structure can be identified by an ordered pair <*a, b*> where *a* represents the upper vertex and *b* the lower vertex. In the figure 8 the diamond structures present are <3,8>, <7,17>, <7,39>, <7,42>, <5,26>, <8,29> and <13,27>. All of these except <13, 27> satisfy the rules of Disciplined Modeling. In the case of <13, 27> diamond, the sub-object 13 is the intersection of 14 and 26 with both contributing defining components to 13. Thus 13 is a Role-Of/Intersection of both 14 and 26. However, in the first pass of the analysis both 14 and 26 were considered to be Category-Of 27 and this contradicts the Disciplined Modeling Rule 2 and therefore both relationships are changed to Role-Of/Category-Of 27 (shown as r/c in the figure).

Figure 9 shows the sub-net after resolution of the diamond structure.

6.2.3 Results

Figure 9 presents the result of the analysis after the partitioning is complete. As can be seen in figure 10, with the removal of the Role-Of relationships, the objects are now

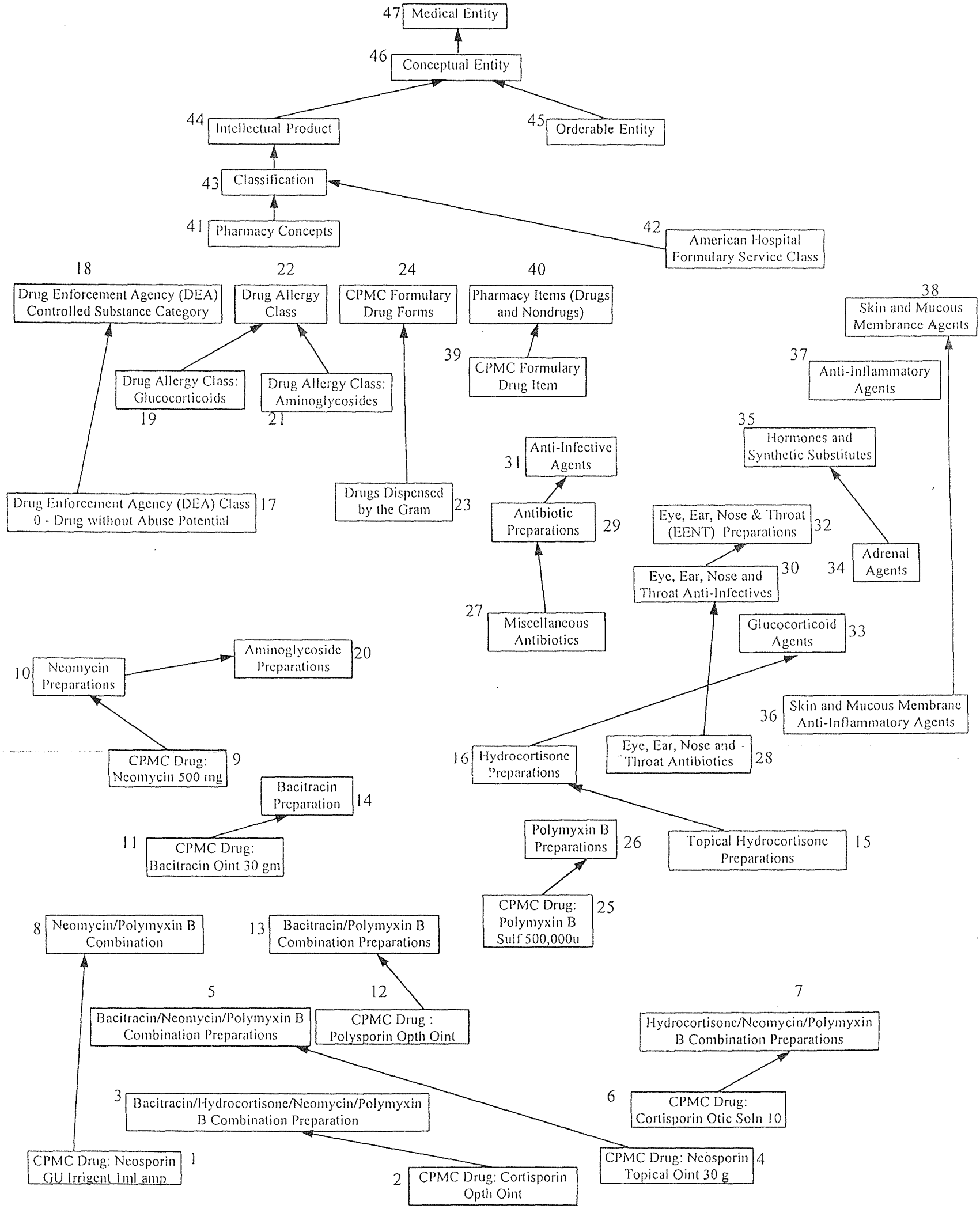

Figure 10 Partitioned Sub-net with only Category-Of Relationships

grouped into units that are in the same context. The Role-Of relationships can be utilized for inheritance of properties but for simplifying the sub-net and to enable comprehension they are removed to produce the following logical groups :

1. Bacitracin/Hydrocortisone/Neomycin/Polymyxin B Combination Preparations group that consists of 3 and 2.
2. Hydrocortisone/Neomycin/Polymyxin B Combination Preparations group consists of objects 7 and 6 (not an ancestor of 2).
3. Bacitracin/Neomycin/Polymyxin B Combination Preparations group consisting of 5 and 4 (not ancestor of 2).
4. Bacitracin/Polymyxin B Combination Preparations group consisting of 13 and 12 (not ancestor of 2)
5. Neomycin/Polymyxin B Combination Preparations group consisting of 8 and 1 (not ancestor of 2)
6. Polymyxin B Preparations group consisting of 26 and 25 (not ancestor of 2)
7. Bacitracin Preparations group consisting of 14 and 11 (not ancestor of 2)
8. Glucocorticoid Agents group consisting of 33, 16 and 15
9. Aminoglycoside Preparations group consisting of 20, 10 and 9 (not ancestor of 2)
10. Anti-Infective Agents group consisting of 31, 29 and 27
11. EENT Preparations group consisting of 32, 30 and 28
12. Hormones and Synthetic Substitutes group consisting of 35 and 34
13. Anti-Inflammatory Agents group consisting of 37
14. Skin and Mucous Membrane Agents group consisting of 38 and 36

15. DEA Controlled Substance Category group consisting of 18 and 17

16. Drug Allergy Class group consisting of 22, 19 and 21

17. CPMC Formulary Drug Forms group consisting of 24 and 23

18. Pharmacy Items group consisting of 40 and 39

19. Medical Entity group consisting of 47, 46, 45, 44, 43, 42 and 41

The size of the sub-net remains 40 while the number of relationships (Category-Of) is now 21 (not including the objects that are not ancestors of the leaf CPMC Drug: Cortisporin Opth Oint). Therefore the complexity is reduced from 1.55 to 0.525 i.e., a much simpler hierarchy. In fact with the emergence of the forest structure, the maximum complexity would be 39/40 if it were a spanning tree.

Also the number of contexts will not increase dramatically if more objects are added to the sub-net but remains quite stable. The concept Aminoglycoside Preparations generically represents objects like Streptomycin Preparations, Kanamycin Preparations and Amikacin Preparations (which are not shown in the sub-net) and even when these objects are added as children of the object Aminoglycoside Preparations the number of contexts remains unchanged. Similarly, adding siblings to the object Hydrocortisone Preparations like the objects Prednisolone Preparations and Triamcinolone Preparations, they will once again be absorbed in the group Glucocorticoid Agents with no additional comprehension effort required.

Hence, partitioning is a powerful tool that reduces the DAG specialization hierarchy to a more comprehensible forest of trees.

CHAPTER 7

CONCLUSIONS

From the experience gained in the partitioning of the most complex sub-net of the MED, it is apparent that context partitioning of the DAG sub-net into tree sub-hierarchies reduces the complexity of the sub-net and aids comprehension. In the pharmacy domain the chemical structure was deemed to be the most important feature for identifying objects in the same context. This methodology can be extended to other domains of medicine by identifying the respective context defining features. In the disease domain the etiology and site of disease can uniquely identify the disease and in the lab domain the substance being detected and the test specimen can identify the tests that are in the same context. In this way partitioning can be applied to the complete the MED network resulting in class hierarchies that simplify the network and help in comprehension and management of information.

APPENDIX A

MED SLOT FILE

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APPENDIX B

MED FLAT FILE ABSTRACT

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23954,6,"Miscellaneous Antibiotics"
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24104,4,41225
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24104,6,"Hormones and Synthetic Substitutes"
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28102,123,""
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28103,1,""
28103,2,"PHARMACY ITEMS (DRUGS AND NONDRUGS)"
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28103,4,41152
28103,5,""
28103,6,"Pharmacy Items (Drugs and Nondrugs)"
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28103,69,""
28103,72,""
28103,74,""
28103,75,""
28103,76,""
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28103,113,
28103,123,""
28103,132,""

28104,1,""
28104,2,"DRUG ENFORCEMENT AGENCY (DEA) CONTROLLED SUBSTANCE CATEGORY"
28104,4,41152
28104,5,""
28104,6,"Drug Enforcement Agency (DEA) Controlled Substance Category"
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28104,50,""
28104,51,""
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28109,1,""
28109,2,"DRUG ALLERGY CLASS"
28109,4,41152
28109,5,""
28109,6,"Drug Allergy Class"
28109,7,
28109,8,
28109,50,""
28109,51,""
28109,70,""
28109,112,30379

28112,1,""
28112,2,"DRUG ALLERGY CLASS: GLUCOCORTICOIDS"
28112,4,28109
28112,5,""
28112,6,"Drug Allergy Class: Glucocorticoids"
28112,7,
28112,8,
28112,50,""
28112,51,""
28112,70,"02"
28112,112,30379

28120,1,""
28120,2,"DRUG ALLERGY CLASS: AMINOGLYCOSIDES"
28120,4,28109
28120,5,""
28120,6,"Drug Allergy Class: Aminoglycosides"
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28120,8,
28120,50,""
28120,51,""

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28202,4,41152
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28202,6,"CPMC Formulary Drug Forms"
28202,7,
28202,8,
28202,50,""
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28202,71,""

28308,1,""
28308,2,"DRUGS DISPENSED BY THE GRAM"
28308,4,28202
28308,5,""
28308,6,"Drugs Dispensed by the Gram"
28308,7,
28308,8,
28308,50,""
28308,51,""
28308,71,"GM"

28385,1,""
28385,2,"CPMC DRUG: BACITRACIN OINT 30 GM"
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28385,4,28110
28385,4,28308
28385,4,31586
28385,5,""
28385,6,"CPMC Drug: Bacitracin Oint 30 Gm"
28385,7,
28385,8,
28385,50,""
28385,51,""
28385,55,"840404"
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28385,57,"500.00"
28385,58,"BACITRACIN OINT 30 GM"
28385,59,"_BACXO"
28385,60,"00168001131"
28385,61,"_BACIGUENT"
28385,62,"BACITRAIN"
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28385,63,"FOUGERA"
28385,64,"O"
28385,65,"3"
28385,66,"N"
28385,67,"TOPI"
28385,68,"Y"
28385,69,"1"
28385,70,"00"
28385,71,"GM"
28385,72,"0"
28385,73,"0"
28385,74,"Q5W"
28385,75,"31812"
28385,76,""
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28385,112,30379
28385,113,30430
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28602,1,""
28602,2,"CPMC DRUG: CORTISPORIN OPTH OINT"
28602,4,24077
28602,4,28308
28602,4,32818
28602,5,""
28602,6,"CPMC Drug: Cortisporin Opth Oint"
28602,7,
28602,8,
28602,50,""
28602,51,""
28602,55,"520404"
28602,56,""
28602,57,"0.00"
28602,58,"CORTISPORIN OPTH OINT"
28602,59,"COROO"
28602,60,"00081019786"
28602,61,"CORTISPORIN"
28602,62,"NEOMYCIN/BACITRACIN/POLY/HC"
28602,63,"BURROUGHS"
28602,64,"F"
28602,65,"3"
28602,66,"N"
28602,67,"OPTH"
28602,68,"Y"

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28602,70,"10"
28602,71,"GM"
28602,72,"0"
28602,73,"0"
28602,74,"Q6W"
28602,75,"87269"
28602,76,"819"
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28602,112,30379
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28602,113,30632
28602,113,30730
28602,113,30776
28602,123,"00000447"
28602,132,""

28604,1,""
28604,2,"CPMC DRUG: CORTISPORIN OTIC SOLN 10 ML"
28604,4,24077
28604,4,28204
28604,4,32819
28604,5,""
28604,6,"CPMC Drug: Cortisporin Otic Soln 10 Ml"
28604,7,
28604,8,
28604,50,""
28604,51,""
28604,55,"520404"
28604,56,""
28604,57,"0.00"
28604,58,"CORTISPORIN OTIC SOLN 10 ML"
28604,59,"COROTA"
28604,60,"00405616110"
28604,61,"CORTISPORIN"
28604,62,"NEOMYCIN SULFATE/POLYMYXIN/HC"
28604,63,"SCHEIN"
28604,64,"F"
28604,65,"3"
28604,66,"N"
28604,67,"OTIC"
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28604,69,"0"
28604,70,"02"

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28604,71,"ML"
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28604,73,"0"
28604,74,"Q8W"
28604,75,"88370"
28604,76,"819"
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28604,113,30632
28604,113,30730
28604,113,30776
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28604,132,""

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29308,4,31614
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29308,6,"CPMC Drug: Neomycin 500 Mg Tab"
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29308,8,
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29308,58,"NEOMYCIN 500 MG TAB"
29308,59,"BNEO500"
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29308,62,"NEOMYCIN"
29308,63,"PHARMA TEK"
29308,64,"F"
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29308,74,"W1F"

29308,75,"41072"
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29312,4,24068
29312,4,32796
29312,4,34549
29312,5,""
29312,6,"CPMC Drug: Neosporin Gu Irrigant 1 Ml Amp"
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29312,8,
29312,50,""
29312,51,""
29312,55,"403600"
29312,56,""
29312,57,"0.00"
29312,58,"NEOSPORIN GU IRRIGANT 1 ML AMP"
29312,59,"NEOGU"
29312,60,"00081074815"
29312,61,"NEOSPORIN"
29312,62,"NEOMYCIN /POLYMYXIN B SO4"
29312,63,"BURROUGHS"
29312,64,"F"
29312,65,"1"
29312,66,"N"
29312,67,"IRRI"
29312,68,"Y"
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29312,71,"AMP"
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29312,76,"819"

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29315,4,28308
29315,4,32817
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29315,51,""
29315,55,"840404"
29315,56,""
29315,57,"0.00"
29315,58,"NEOSPORIN TOPICAL OINT 30 GM"
29315,59,"NEOXO"
29315,60,"00168001231"
29315,61,"NEOSPORIN"
29315,62,"NEOMYCIN/BACITRA/POLYMYXIN"
29315,63,"E.FOUGERA"
29315,64,"O"
29315,65,"3"
29315,66,"N"
29315,67,"TOPI"
29315,68,"Y"
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29315,71,"GM"
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29315,113,30776

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29478,4,31622
29478,4,33921
29478,4,34573
29478,5,""
29478,6,"CPMC Drug: Polymyxin B Sulf 500,000u Pwd"
29478,7,
29478,8,
29478,50,""
29478,51,""
29478,55,"081228"
29478,56,"U"
29478,57,"500000.00"
29478,58,"POLYMYXIN B SULF 500,000U PWD"
29478,59,"NAPOL5I"
29478,60,"00081003510"
29478,61,"_AEROSPORIN"
29478,62,"POLYMYXIN B SULFATE"
29478,63,"BURROUGHS"
29478,64,"F"
29478,65,"1"
29478,66,"N"
29478,67,"IM/I"
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29478,73,"0"
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29479,4,28110
29479,4,28308
29479,4,32794
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29479,59,"POLOO"
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29479,61,"POLYSPORIN"
29479,62,"BACITRACIN/POLYMYXIN B SULFATE"
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31604,4,33921
31604,4,34162
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31604,61,""
31604,62,"HYDROCORTISONE"
31604,62,"HYDROCORTISONE ACETATE"
31604,62,"HYDROCORTISONE SOD SUCCINATE"
31604,62,"HYDROCORTISONE CREAM"
31604,62,"HYDROCORTISONE SODIUM SUCCINAT"
31604,62,"HYDROCORTISONE CYPIONATE"
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