Brief History of Antibiotics Example

CHAPTER 1

1.0 Introduction

In Yemen as well as in many other developing countries the quality of health services which constitute social indicators of justice and equity is far from being satisfactory. Inappropriate, ineffective, and inefficient use of drugs commonly occurs at different health facilities (Abdo-Rabbo, 1993; Abdo-Rabbo, 1997). Irrational prescribing is a habit, which is difficult to cure. This may lead to ineffective treatment, health risks, patient non-compliance, drug wastage, wasteful of resources and needless expenditure. According to the Yemeni constitution, “patients have the right to health care and treatment” i.e. appropriate care, consent to treatment and acceptable safety. Therefore, health workers should concentrate on making patients better and patients should concentrate on geting better. Health care in general and particularly the drug situation in any country is influenced by the availability, affordability, and accessibility of drugs as well as the prescribing practices. There are many individuals or factors influence the irrational prescribing such as patients, prescribers, workplace environment, the supply system, including industry influences, government's regulations, drug information and misinformation (Geest S. V.

et al, 1991; Hogerzeil H. V., 1995).Improving rational use of drugs (RUD) is a very complex task worldwide because changing behavior is very difficult. The 1985 Nairobi conference on the rational use of drugs marked the start of a global effort to promote rational prescribing (WHO,1987). In 1989, an overview of the subject concluded that very few interventions to promote rational drug use had been properly tested in developing countries (Laing et al., 2001). The selection of drugs to satisfy the health needs of the population is an important component of a national drug policy. The selected drugs are called "essential drugs" which are the most needed for the health care of the majority of the population in a given locality, and in a proper dosage forms. The national list of essential drugs (NEDL) is based on prevailing health conditions, drug efficacy, safety, and quality, cost-effectiveness and allocated financial resources. WHO's mission in essential drugs and medicines policy is to help save lives and improve health by closing the huge gap between the potential that essential drugs have to offer and the reality that for millions of people particularly the poor and disadvantaged medicines are unavailable, unaffordable, unsafe or improperly used. The organization works to fulfill its mission in essential drugs and medicines policy by providing global guidance on essential drugs and medicines, and working with countries to implement national drug policies to ensure equity of access to essential drugs, drug quality and safety, and rational use of drugs. Development and implementation of national drug policies are carried out within the overall national health policy context, with care taken to ensure that their goals are consistent with broader health objectives. All these activities ultimately contribute to all four WHO strategic directions to:

- reduce the excess mortality of poor and marginalized populations
- reduce the leading risk factors to human health
- develop sustainable health systems,and
- develop an enabling policy and institutional environment for securing health gains.

The greatest impact of WHO medicines activities is, and will continue to be, on reducing excess mortality and morbidity from diseases of poverty, and on developing sustainable health systems. "The people of our world do not need to bear the present burden of illness. Most of the severe illness that affects the health and well-being of the poorer people of our world could be prevented. But first, those at risk need to be able to access health care —

including essential medicines, vaccines and technologies. Millions cannot — they cannot get the help they need, when they need it. As a result they suffer unnecessarily, become poorer and may die young. A country's health service cannot respond to people's needs unless it enables people to access essential drugs of assured quality. Indeed, this access represents a very important measure of the quality of the health service. It is one of the key indicators of equity and social justice." (Dr Gro Harlem Brundtland, Director-General, World Health Organization Opening remarks, Parliamentary Commission on Investigation of Medicines, Brasilia, 4 April 2000).

1.1 Background

1.1.1 Brief history of antibiotics

According to the original definition by Waksman, antibiotics substances which are produced by microorganisms and which exhibit either an inhibitory or destructive effect on other microorganisms. In a wider, though not universally accepted definition; antibiotics are substances of biological origin, which without possessing enzyme character, in low concentrations inhibit cell growth processes (Reiner, 1982). Up to now, more than 4,000 antibiotics have been isolated from microbial sources and reported in the literature, and more than 30000 semi-synthetic antibiotics have been prepared. Of these, only about 100 are used clinically as the therapeutic utility not only depends on a high antibiotic activity but also on other important properties such as good tolerance, favorable pharmacokinetics etc. These antibiotics are today among the most efficient weapons in the armoury of the physician in his fight against infectious diseases. They are therefore used a large extent and constitute the largest class of medicaments with respect to turnover value. Today, antibiotics are also used in veterinary medicine and as additives to animal feed. In the past they were used addition, as plant protection agents and as food preservatives. In this review we have confined ourselves to a brief description clinicallyuseful antibiotics. These belong to various classes of chemical compounds, differ in origin, mechanism of action and spectrum activity, and are thus important and representative examples of known antibiotics.

1.1.2 Problem Statement

This study examines drug use in Yemen and factors leading to inappropriate use of medicines particularly antibiotics and the prescribing pattern. It defines rational drug use and describes policy developments, which aim to encourage appropriate use. In Yemen, as well as in many developing countries, the quality of health services is far from being achieved. Therefore, doctors should concentrate on making patients better and patients should concentrate on getting better. The rational use of drugs requires that patients received medications in appropriate to their clinical needs, in doses that meets their own requirements for an adequate period of time and at the lowest cost to them and their community (Bapna et al, 1994). This means deciding on the correct treatment for an individual patient based on good scientific reasons. It involves making an accurate diagnosis, selecting the most appropriate drug from these available, prescribing this drug in adequate doses for a sufficient length of time according to standard treatment. Furthermore, it involves monitoring the effect of the drug both on the patient and on the illness. There is plentiful evidence of the inappropriate use of drugs, not through self-medication or unauthorized prescribing, but inadequate medical prescribing and dispensing. Normally, patients in Yemen enter health facilities with a set of symmetrical complaints, and with expectations about the care they typically receive; they typically leave with a package of drugs or with a prescription to obtain them in a private market. In previous study in Yemen (misuse of antibiotics in Yemen, a pilot study in Aden) (Abdo-Rabbo, 1997) showed that imported quantity and total consumption of antibiotics is increasing. There is a lack of information about the problems created from antibiotics among the community and about the proper efficacy, safety, and rational use of antibiotics among health authority and workers. No supervision or strict rules are applied in the use of antibiotics. They are easily obtained without prescription and available in some shops. The percentage of prescriptions containing antibiotics was more than a quarter of the total prescriptions contained antibiotics, also antibiotics constituted about 25% of all prescribed drugs.

1.1.2.1 Inappropriate Drug Use

Increasing use of medicines may lead to an increase in the problems associated with medication use. The use of

medicines, as well as improving health, can lead to undesirable medical, social, economic and environmental consequences. Aspects of drug use, which lead to such undesirable consequences, have been called inappropriate drug use (DHHCS, 1992; WHO, 1988). Inappropriate drug use may include under-use, over-use, over-supply, non-compliance, adverse drug reactions and accidental and therapeutic poisoning (DHHCS, 1992). It also includes medicating where there is no need for drug use, the use of newer, more expensive drugs when lower cost, equally effective drugs are available (WHO, 1988) and drug use for problems which are essentially social or personal (Frauenfelder and Bungey, 1985).

1.1.2.2 Quality Use of Medicines

In an attempt to encourage the appropriate use of medicinal drugs and to reduce the level of inappropriate use in Yemen, a policy was developed on the quality use of medicines. The stated aim of the policy is: "to optimise medicinal drug use (both prescription and OTC) to improve healthoutcomes for all Yemenis". The policy endorses the definition of quality drug use as stated by the World Health Organisation, "Drugs are often required for prevention, control and treatment of illness". When a drug is required, the rational use of drugs demands that the appropriate drug be prescribed, that it be available at the right time at a price people can afford, that it be dispensed correctly, and that it be taken in the right dose at the right intervals and for the right length of time. The appropriate drug must be effective, and of acceptable quality and safety. The formulation and implementation by governments of a national drug policy are fundamental to ensure rational drug use (WHO, 1987; DHHCS, 1992). The rational use of drugs can be impeded by the inappropriate selection of management options, the inappropriate selection of a drug when a drug is required, the inappropriate dosage and duration of drug therapy and the inadequate review of drug therapy once it has been initiated.

1.1.2.3 The Requirement of Drug Information for Quality Use of Medicines

"A medicine has been described as an active substance plus information." (WHO, 1994). Education, together with, objective and appropriate drug information have been two of the factors consistently identified as necessary for rational drug use (Naismith, 1988; Soumerai, 1988; Carson et al, 1991; Dowden, 1991; Henry and Bochner, 1991;

Tomson and Diwan, 1991). The WHO guidelines for developing national drug policies also identify the importance of information provision for facilitating drug use: "Information on and promotion of drugs may greatly influence their supply and use. Monitoring and control of both activities are essential parts of any national drug policy" (WHO, 1988). Objective and appropriate drug information is a necessary factor for quality drug use. It is the basis for appropriate prescribing decisions by medical practitioners. Medical practitioners require objective product, specific drug information and comparative prescribing information. Objective drug information is available to medical practitioners through continuing education programs co-ordinated by professional bodies, medical and scientific journal articles, drug information services and drug formularies and guidelines.

1.1.2.4 Problem with antibiotic use

The concerns regarding inappropriate antibiotic use can be divided into four areas: efficacy, toxicity, cost, and resistance. Inappropriate use of antibiotic can be due to: -

i. Antibiotic use where no infection is present, e.g. continuation of peri-operative prophylaxis for more than 24 hours after clean surgery.
ii. Infection, which is not amenable to antibiotic therapy, e.g. antibiotics prescribed for viral upper respiratory infection.
iii. The wrong drug for the causative organism, e.g. the use of broad anti-Gram negative agents for community acquired pneumonia.
iv. The wrong dose or duration of therapy.

Such inappropriate use has a measurable effect on therapeutic efficacy. For example, one study showed that mortality in gram-negative septicemia is doubled when inappropriate empiric agents were used (Kreger et al., 1980). Since most initial antibiotic therapy is empiric, any attempt at improving use must tackle prescribing habits, with particular emphasis on guidelines for therapy based on clinical criteria. Inappropriate antibiotic use exposes patients to the risk of drug toxicity, while giving little or no therapeutic advantage, antibiotics are often considered relatively safe drugs and yet direct and indirect side effects of their use are frequent and may be life-threatening,

allergic reactions, particularly to beta-lactam agents are well recognized and have been described in reaction to antibiotic residues in food (Barragry, 1994). Life threatening side effects may be occur from the use of antibiotics for apparently simple infections, it is estimated, for example, that eight people per year in UK die from side effects of co-trimoxazole usage in the community (Robert and Edmond, 1998). Indirect side effects are often overlooked: especially as may occur sometime after the antibiotic has been given. These include drug interactions (such as interference of antibiotic with anti-coagulant therapy and erythromycin with antihistamine) (BNF, 1998), side effects associated with the administration of antibiotics (such as intravenous cannula infection) and super-infection (such as candidiasis and pseudomembranous colitis). Each of these may have a greater morbidity, and indeed mortality, than the initial infection for which the antibiotic was prescribed (Kunin et al., 1993). The medical benefit of antibiotics does not come cheap. In the hospital setting, up to fifty percent of population receive one antibiotic during their hospital stay, with surgical prophylaxis accounting for thirty percent of this (Robert and Edmond, 1998). The first penicillin resistant isolate of Staphylococcus aureus was described only two years after the introduction of penicillin. Within a decade, 90% of isolates were penicillin resistant. This pattern of antibiotic discovery and introduction, followedby exuberant use and rapid emergence of resistance has subsequently been repeated witheach new class of antibiotics introduced. Bacteria can so rapidly develop resistance due to two major evolutionary advantages. Firstly, bacteria have been in existence for some 3.8 billion years and resistance mechanisms have evolved over this time as a protective mechanism against naturally occurring compounds produced by other microorganisms. In addition, they have an extremely rapid generation time and can freely exchange genetic material encoding resistance, not only between other species but also between genera. The vast quantities of antibiotics used in both human and veterinary medicine, as a result present in the environment, have lead to emergence of infection due to virtually untreatable bacteria. Multiply drug resistant tuberculosis is already widespread in parts of Southern Europe and has recently caused outbreaks in hospitals in London (Hiramatsu et al., 1997). Anti-infective are vital drugs, but they are over prescribed and overused in treatment of minor disorder such as simple diarrhea, coughs, and colds. When antibiotics are too often used in sub-optimal dosages, bacteria become resistant to them. The result is treatment failure where patient continue to suffer from serious infections despite taking the medication (Mohamed, 1999). Drugs prescribed are in no way beneficial to the patient' s management if there are some negative interactions among the various agent prescribed, over

prescribed, under prescribed or prescribed in the wrong dosage schedule.

- How does one ensure that good drug are not badly used, misused, or even abused?
- How can drugs be used rationally as intended?
- What is rational use of drugs? What does rational mean?

1.1.3 Rational Use of Drug

"Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, and the lowest cost to them and their community" (Bapna et al., 1994). These requirements will be fulfilled if the process of prescribing is appropriately followed. This will include steps in defining patient's problems (or diagnosis); in defining effective and safe treatments (drugs and non-drugs); in selecting appropriate drugs, dosage, and duration; in writing a prescription; in giving patients adequate information; and in planning to evaluate treatment responses. The definition implies that rational use of drugs; especially rational prescribing should meet certain criteria as follows (Ross et al., 1992):

- Appropriate indication. The decision to prescribe drug(s) is entirely based on medical rationale and that drug therapy is an effective and safe treatment.
- Appropriate drug.The selection of drugs is based on efficacy, safety, suitability, and considerations.
- Appropriate patient. No contraindications exist and the likelihood of adverse reactions is minimal, and the drug is acceptable to the patient.
- Appropriate information. Patients should be provided with relevant, accurate, important, and clear information regarding his or her condition and the medication(s) that are prescribed.

Appropriate monitoring. The anticipated and unexpected effects of medications should be: appropriately monitored (Vance and Millington, 1986).

Unfortunately, in the real world, prescribing patterns do not always conform to these criteria and can be classified

as inappropriate or irrational prescribing. Irrational prescribing may be regarded as "pathological" prescribing, where the above- mentioned criteria are not fulfilled. Common patterns of irrational prescribing, may, therefore be manifested in the following forms:

1. The use of drugs when no drug therapy is indicated, e.g., antibiotics for viral upper respiratory infections,
2. The use of the wrong drug for a specific condition requiring drug therapy, e.g., tetracycline in childhood diarrhea requiring ORS,
3. The use of drugs with doubtful/unproven efficacy, e.g., the use of antimotility agents in acute diarrhea,
4. The use of drugs of uncertain safety status, e.g., use of dipyrone,
5. Failure to provide available, safe, and effective drugs, e.g., failure to vaccinate against measles or tetanus, failure to prescribe ORS for acute diarrhea,
6. The use of correct drugs with incorrect administration, dosages, and duration, e.g., the use of IV metronidazole when suppositories or oral formulations would be appropriate.
7. The use of unnecessarily expensive drugs, e.g., the use of a third generation, broad spectrum antimicrobial when a first-line, narrow spectrum, agent is indicated.

Some examples of commonly encountered inappropriate prescribing practices in many health care settings include: (Avorn et al., 1982).

1. Overuse of antibiotics and antidiarrheals for non-specific childhood diarrhea,
2. Multiple drug prescriptions, prescribe unnecessary drugs to counteract or augment,
3. Drugs already prescribed, and
4. Excessive use of antibiotics in treating minor respiratory tract infection.

The drug use system is complex and varies from country to country. Drugs may be imported or manufactured locally. The drugs may be used in hospitals or health centers, by private practitioners and often in a pharmacy or drug shop where OTC preparations are sold. In some countries, all drugs are available over the counter. Another problem among the public includes a very wide range of people with differing knowledge, beliefs and attitudes

about medicines.

1.1.3.1 Factors Underlying Irrational Use of Drugs

There are many different factors that affect the irrational use of drugs. In addition, different cultures view drugs in different ways, and this can affect the way drugs are used. The major forces can be categorized as those deriving from patients, prescribers, the workplace, the supply system including industry influences, regulation, druginformation and misinformation, and combinations of these factors (Table 1.1) (Ross et al., 1992). Table 1.1: Factors affecting irrational use of drug

1- Patients: drug misinformation	Due to the misleading beliefs of patient and patient demands/expectations
2- Prescribers: lack of education and training	Due to inappropriate role models, lack of objective drug information, generalization of limited experience and misleading beliefs about drugs efficacy
3- Workplace: heavy patient load	Due to pressure to prescribe, lack of adequate lab capacity and insufficient staffing
4- Drug Supply System: unreliable	Due to drug shortages and expired suppliers drugs supplied
5- Drug Regulation: non-essential drugs available	Due to non-formal prescribers and lack of regulation enforcement
6- Industry: promotional activities	Due to misleading claims

Impact of Inappropriate Use of Drugs

The impact of this irrational use of drugs can be seen in many ways: (Avorn et al., 1982).

1. Reduction in the quality of drug therapy leading to increased morbidity and mortality,
2. Waste of resources leading to reduced availability of other vital drugs and increased costs,
3. Increased risk of unwanted effects such as adverse drug reactions and the emergence of drug resistance, e.g., malaria or multiple drugs resistant tuberculosis,

4. Psychosocial impacts, such as when patients come to believe that there is "a pill for every ill". This may cause an apparent increased demand for drugs.

1.1.3.2 The Rational Prescription (i.e. the right to prescribe)

The rights to prescription writing must be ensuring the patient's five rights: the right drug, the right dose, by the right route, to the right patient, at the right time. Illegible handwriting and misinterpretation of prescriptions and medication orders are widely recognized causes of prescription error. The medicines should be prescribed only when they are necessary, should be written legibly in ink or, other wise, should be led, and should be signed in ink by the prescriber, The patients full name and address, diagnosis should be written clearly, the name of drugs and formulations should be written clearly and not abbreviated, using approved titles only. Dose and dose frequency should be stated; in the cases of formulations to be taken as required, a minimum dose should be specified (British National Formulary, 1998).

1.2 Overview on Essential Drug Concept (EDC)

Essential drugs relate to an international concept proposed by the World Health Organization (WHO) in 1977. WHO in that year published the first model list of essential drug and WHO has put in enormous resources into the campaign to promote the concept of essential drugs (EDL). Essential drugs were defined as a limited number of drugs that should be available at any time to the majority of population in appropriate dosage forms and at affordable prices. In other words, it meets the criteria generally abbreviated as SANE [that mean safety , availability, need efficacy] (John, 1997). The essential drug concept is important in ensuring that the vast majority of the population is accessible to drugs of high quality, safety and efficacy relevant to their health care needs, and at reasonable cost (New Straits Times, 1997a). In support of this concept, the WHOissued a model drug list that provided examples of essential drugs. The list is drawn up by a group of experts based on clinical scientific merits, and provides an economical basis of drug use. This list is regularly, revised and, since 1997, eight editions have been published. This ensures that the need for essential drugs is always kept up-to-date with additions and deletions. Despite such rigorous revision, the number of drugs in the list remains at about 300, although the initial

list comprised less. Most of the drugs are no longer protected by patents and can therefore be produced in quantity at a lower cost without comprising standards (WHO, 1995). This is indeed important for countries like Yemen not only because health care are rapidly escalating, but also because the country is still very dependent on imports of strategic commodities like drugs. The EDC will enable Yemen to focus on becoming self-reliant where generic equivalents of essential drugs can be manufactured and popularized to meet the health needs of the majority of the people. The limited number of drugs regarded as essential on the list offers a useful guide for practitioners as well as consumers. It underscores the general principle thata majority of diseases can be treated by similar drugs regardless of national boundaries and geographical locations (New Straits Times, 2000) Moreover, certain self-limiting diseases may not need "drug treatment" as such. For example, in the case of diarrhea, certain so-called potent anti-diarrhoeal drugs (including antibiotics) are not generally recommended. The more preferred treatment is oral rehydration salt that could easily be obtained or prepared at a fraction of the cost while giving the most optimum outcome. The goal of the Yemen Drug Policy was to:

1. Prepare a list of essential drugs to meet the health of needs of the people.
2. Assure that the essential drugs made available to the public are of good quality
3. Improve prescribing and dispensing practices
4. Promote rational use of drug by the public
5. Lower cost of the drugs to the government and public
6. Reduce foreign exchange expenditure

1.3 Yemen Essential Drug List and Drug Policy in Yemen

The Concept of Essential Drugs (EDC) developed by World Health Organization (WHO) in 1977 has provided a rational basis, not only for drug procurement at national level but also for establishing drug requirements at various levels within the health care system. The WHO's Action Program on Essential Drugs (DAP) aimed to improve health care. It was established in order to provide operational support in the development of National Drug Policies (NDP), to improve the availability of essential drugs to the whole population and to work towards the rational use of drugs and consequently the patient care. The program seeks to ensure that all people,

whenever they may be, are able to obtain the drugs they need at the lowest possible price; that these drugs are safe and effective; and that they are prescribed and used rationally. The first WHO Model List of Essential Drugs was published in 1977 (WHO, 1977). Since that time essential drugs become an important part of health policies in developing countries; but the Essential Drugs Program has been criticized because it emphasis in improving supply of drugs rather than their rational prescribing. The recent revised WHO Model List of Essential Drugs was published the 13th edition in April 2003 (WHO, 2003). Yemen was one of the first countries in the region adapted the EDC in 1984 and implemented this concept in the public sector (Hogerzeil et al., 1989). The first Yemen (National) Essential Drugs List (YEDL) was officially issued in 1987 based on the WHO List of Essential Drugs and other resources. The second edition of the Yemen Drugs list and the Yemen Standard Treatment Guidelines were published in 1996 (MoPH&P/NEDL, (1996); MoPH&P/NSTG, (1996).Recently the latest edition was published in 2001 with the Standard Treatment Guidelines (STG) in the same booklet (MoPH&P/YSTG and YEDL, 2001). The new edition of the Treatment Guidelines and the Essential Drugs List has been created through a long process of consultation of medical and pharmaceutical professionals in Yemen and abroad. Review workshops were held in Sana'a and Aden and more than 200 representatives of the health workers from different governorates including the major medical specialists participated. Essential drugs are selected to fulfil the real needs of the majority of the population in diagnostic, prophylactic, therapeutic and rehabilitative services using criteria of risk-benefit ratio, cost-effectiveness, quality, practical administration as well as patient compliance and acceptance (Budon-Jakobowiez, 1994). The YEDL was initially used for the rural health units and health centers as well as some public hospitals, but not applied for all levels of health care and the private sector. However, despite the recognition of the essential drug concept by the government of Yemen represented by the Ministry of Public Health and Population (MoPH&P), drugs remain in short supply to many of the population and irrationally used. Procurement cost is sometimes needlessly high. Knowledge of appropriate drug use and the adverse health consequences remain unacceptably low. In addition, diminished funding in the public sector resulted in shortage of pharmaceuticals. The 20th century has witnessed an explosion of pharmaceutical discovery, which has widened the therapeutic potential of medical practice. The vast increase in the number of pharmaceutical products marketed in the last decades has not made drug available to all people and neither has resulted in the expected health improvement. While some of the newly invented drugs are significant advance in therapy, the majorities of

drugs marketed as “new” are minor variations of existing drug preparations and do not always represent a significant treatment improvement. In addition, the vast number "brand names" products for the same drug increases the total number of products of this particular drug resulting in an unjustified large range of drug preparations marketed throughout the world. The regular supply of drugs to treat the most common diseases was a major problem for governments in low-income countries. The WHO recommends that activities to strengthen the pharmaceutical sector be organized under the umbrella of the national drug policy (WHO, 1988). In 1995, over 50 of these countries has formulated National Drug Policies (NDP). The NDP is a guide for action, containing the goals set by the government for the pharmaceutical sector and the main strategies and approaches for attaining them. It provides a framework to co-ordinate activities of patients involved in pharmaceutical sector, the public sector, the private sector, non-governmental organizations (NGOs), donors and other interested parties. A NDP will therefore, indicate the various courses of action to be in relation to medicines within a country. The Yemen National Drug Policy was developed since 1993 with the objectives of ensuring availability of essential drugs through equitable distribution, ensuring drugs efficacy and safety, as well as promoting the rational use of drugs. Unfortunately, it has not been systemically implemented(Abdo-Rabbo, 2001a). During the last years efforts have been increased to improve drug practices in the country. National and international programs as well as donor organizations established in the country concentrated mainly on improving the availability of essential drugs as well as promoting the rational use of drugs. The government should endeavour to make essential drugs of acceptable quality in sufficient quantities available to all who need them at lowest possible cost. Health Sector Reform (HSR) is a process aimed to improve equity, quality, and efficacy in the health sector through changes in the organization and financing of health services. One of the HSR components is the Drug Financing Reforms (DFR). The type of arrangement arranged by the government is the Revolving Drug Fund (RDF). In a RDF, a sum or money contributed by the government, donors, or the community is used to purchase an initial stock of drugs and ensure a continuous supply. The Drug Fund (DF) for Medical Supply which is recently established in Yemen aimed to increase availability of drugs, ensure more affordable drugs, make low-cost essential drugs more accessible, improve patient adherence to treatment, and increase price awareness by prescribers and patients, and improve rational use of drugs. Normally patients enter health facilities with a set of symptoms and complaints, and with expectations about the care they will receive. They

typically leave with a package of drugs or with a prescription to obtain them in a private market. WHO promotes the use of generic names of drugs. Most of the essential drugs are now no longer patent products and can in principle be manufactured under their International Non-proprietary Names (INN) or generic names. The adequacy of patient care is measured by different parameters. International health organizations interested in the subject particularly WHO Action Program on Essential Drugs (WHO/DAP),the International Network for Rational Use of Drugs (INRUD) and other organizations have made serious attempts to examine drug use rationality and developed indicators for assessment. The developed drug use indicators to measure the prescribing performance in health facilities were used in this study (WHO, 1993).

1.4 Treatment Guideline

Some physicians inappropriately prescribe expensive antibiotics, which are countering productive to patient (e.g. fungal infection linked to overuse of cephalosporins (WHO, 1993a). WHO recommends research by educational institutions on the rational prescription of drug by physicians, which can become the basis of regulatory legislation (WHO, 1993a). Monitoring of the duration of antibiotic therapy poses a problem for evaluators since it varies on criteria that are more subjective than objective. Standard medical references allow one an enormous leeway in deciding the length of therapy for infections (Farber et al., 1995). Even then prescription audit, drug utilization studies, reviewing drug expenditure trends and patterns are certainly of immense value in faming policy and initiating corrective measures for appropriate usage of antibiotics. Generally, drug utilization study is important in establishing the status of drug use in particular country; the goal of drug utilization review has been to increase the appropriateness of drug therapy by focusing on whether a drug is being effectively used [e.g., appropriate dose, duration of therapy, etc]. To influencing future prescribing and dispensing, drug utilization review criteria may also be applied retrospectively to pharmacy claims data to identify physicians and pharmacists who need education about appropriate drug use (Edward, 2000). Drug therapy is considered to be a major component of patient management in health care settings, including primary health care. The risks of drugs per use and the consequences of inappropriate use cannot be over looked. Additionally, the cost of medicine is a matter of great concern in both developing and industrialized countries. Among the various classes of drugs,

antibiotics receive special attention as more money is spent on them other than many other drugs (Gugliemo and Brooks, 1989). Some antibiotics also have specific side effects and extensive antibiotic use lead to the development of resistant microorganisms (Farrar, 1985).

The guidelines emphasized the following:

- The presence of up-to-date information about all antibiotics in each primary health care center and hospital.
- Methods and strategies for choosing appropriate antibiotics for a specific disease condition.
- The establishment of antibiotics subcommittees in each health care facility for auditing antibiotics use. The information package contained articles about the use and abuse of antibiotics. Worldwide meeting were organized with the physician of the district to discuss the states of antibiotics and the details of the guidelines.

1.5 Why Antibiotics?

The detection of problems with antimicrobial drug use in hospitals is the first step in evaluating the underlying causes and taking remedial action. The management and use of antimicrobial drugs has clinical, economic, and environmental implications. In many countries, antimicrobial drugs are the most frequently prescribed therapeutic agents, accounting for 30 to 50 percent of drug prescriptions. From a clinical standpoint, there are three principal concerns surrounding the use and management of antimicrobial drugs:

1. They are necessary for treatment of most bacterial infections. If they are not available in hospital pharmacies, lives may be jeopardized.
2. They may be prescribed inappropriately by physicians and drug sellers and especially by the general public (self-prescribing) where antimicrobial drugs are sold over the counter. Inappropriate prescribing includes use of antimicrobial drugs without proof of infection or to treat viral infections or non-infectious diarrhoea. The wrong drug may be prescribed or taken for a particular infection or, if the correct drug is used, it may be prescribed or taken at the wrong dosage or by an inappropriate route of administration. Perhaps the

greatest misuse of antimicrobial drugs is shortened duration of therapy.

3. Adverse drug reactions (ADRs) constitute the third critical area of antimicrobial drug use. Such reactions include nephrotoxicity and allergic reactions as well as antibiotic associated diarrhoea. It is estimated that 25 percent of ADRs are caused by antimicrobial drugs (Beringer et al.,1998).

In conclusion, hospitals must ensure availability of antimicrobial drugs while at the same time controlling and improving prescribing practices of physicians and minimizing untoward side effects. In economic terms, expenditures on antimicrobial drugs in the year 2000 are projected at $40 billion with about one-third of that in developing countries. Worldwide, antimicrobial drugs accounted for 12 percent of all pharmaceutical sales in 1990 while in developing countries they accounted for 19 percent; this proportion was projected to increase to 34 percent in 2000 (Liss, RH, and FR Batchelor, 1987). Thus, antimicrobial drugs are a large and growing component of pharmaceutical expenditures in developing countries and must be managed effectively in the face of limited financial resources. Finally, cases of antimicrobial drug resistance have drawn public attention to the public health and ecologic implications of drug-resistant microorganisms in the environment. The very ubiquity of antimicrobial drugs and their frequent over- and under-use are associated with the appearance of antimicrobial drug-resistant strains of major pathogens such as Staphylococcus aureus and Pseudomonas spp. (Urassa et al., 1997; Centres for Disease Control, 1997). Highest levels of resistance to antimicrobial drugs occur in countries with highest levels of antimicrobial drug use (WHO, 1984; Levy etal., 1987; Kunin, 1993). It has been estimated that hospital-acquired infections due to drug-resistant organisms cost the United States $4 billion in 1990 (Institute of Medicine, 1998). The high cost of treating drug-resistant infections may exceed the financial capacity of many patients and hospitals in developing countries. Thus, managers must monitor and minimize antibacterial resistance in their hospitals.

1.5.1 How to Investigate Antimicrobial Drug Use in Hospitals?

The Rational Pharmaceutical Management (RPM) Project of the U.S. Agency for International Development (USAID) has produced two drug assessment manuals based on indicators (Rapid Pharmaceutical Management Assessment: An Indicator-Based Approach and Drug Management for Childhood Illness Manual). Both of these

manuals were aimed at assessing outpatient drug use as opposed to hospital inpatient use and were directed at a broad range of pharmaceutical products, not specifically antimicrobial drugs (also referred to in this document as antimicrobials or AMDs). In 1993, the World Health Organization (WHO) published "How to investigate drug use in health facilities": selected drug use indicators. Only 2 of the 19 indicators in that publication specifically referred to antibiotic use or management. In response to antimicrobial drug resistance legislation by the U.S. Congress, RPM proposed to USAID to development of a manual for assessment of antimicrobial drug use in hospitals. Such a manual would be a tool for hospital managers to assess antimicrobial drug management and use and thus contribute to reducing antibiotic misuse, a congressionally mandated objective for USAID worldwide. The present manual is intended for use by hospital drug and therapeutics committees (DTCs), physicians, pharmacists, and managers, as well as drug use researchers who wish to evaluate and improve antimicrobial drug use in hospitals. It will allow basic comparisons of antimicrobial drug use in a hospital over time and between hospitals (RPMPP, 2001).

1.5.2 Objectives of a Hospital Antimicrobial Use Study

Hospital administrators, researchers, and DTCs will want to study antimicrobial drug use in order to:

1. Describe antimicrobial drug prescribing practices
2. Compare performance among hospitals or prescribers
3. Monitor performance and orient supervision
4. Assess changes resulting from interventions

Once problems have been detected, investigators will decide whether further study is warranted to explore causes of the problems detected in the first round. These additional studies will explore areas such as:

- Antimicrobial drug selection procedures and criteria
- Antimicrobial use in specific wards or specialties or by individual prescribers
- Purchasing and financing of drugs and antimicrobial drugs

- Impediments to patient compliance with antimicrobial drug prescriptions.
- Comparison of antimicrobial drug use among hospitals

Investigators should clearly state why the study is needed and what is expected as the outcome. For example, hospital management may want to use the following wording: “Undertake a rapid, hospital- wide review of antimicrobial drug use and management to detect problem areas and assign responsibility for correction to the respective departments”.

1.5.3 Antibiotic prescribing and bacterial resistance

Increasing bacterial resistance to antibiotics is becoming a significant issue, both in primary and secondary care. The Standing Medical Advisory Committee (SMAC) report ‘The path of least resistance' points out that some 50 million prescriptions for antibiotics are dispensed each year in England alone; 80% of this activity occurs in primary care (SMAC, 1998). A twofold variation exists in levels of antibiotic usage between the areas of highest and lowest prescribing, for which there is no apparent explanation. Although antibiotic resistance is a worldwide problem, there is evidence that local antibiotic prescribing practices can affect local resistance patterns. A study in Wales investigated antibiotic prescribing in general practitioners' surgeries and resistance to antibiotics over the period from March 1996 to April 1998. Rates of prescribing for urinary tract infections and resistance rates in coliform organisms were examined (Magee et al., 1999). A correlation between the rate of prescribing of an antibiotic and the rate of resistance to that agent was demonstrated. A cross-sectional survey in Iceland also found that carriage of penicillin resistant pneumococci was strongly associated with both individual and community-wide levels of antibiotic use (Arason et al., 1996). In Finland, the incidence of erythromycin resistance in group A streptococcus reduced by half over three years following a campaign to reduce the use of macrolide antibiotics (Seppala et al., 1997).

1.5.4 Disadvantages of antibiotic prescribing

Antibiotics are associated with several well-documented common side effects, including diarrhoea and rashes, as

well as rare, but potentially life-threatening, anaphylactic reactions. The risk of side effects should always be considered before prescribing any medication. Prescribing antibiotics can also have other, perhaps unforeseen, consequences. In the open study comparing three approaches to the management of sore throat, patients who received an immediate prescription for antibiotics were more likely to believe that antibiotics were effective in this condition (Little et al., 1997a). They were also more likely than other patients to intend consulting a GP in future episodes. In a follow-up study, a higher reconsultation rate in those patients who had been given immediate antibiotic treatment was demonstrated (Little et al., 1997).

1.6 Literature Review

Many studies have been done to document drug use pattern, and indicate that over prescribing, multi-drug prescribing, misuse of drugs, and use of unnecessary expensive drugs and over use of antibiotic and injections are the most common problems of irrational drug use by prescribers as well as benefits. Many efforts have been under taken to improve drug use. 1. Prescribing patterns of recently graduated physicians in Colombia survey during the mandatory social work period (Rodolfo et al., 1998). Objective: To quantify prescribing pattern of physicians in health centers of Bogotá, Colombia, for three tracer conditions, acute respiratory tract infection, systemic hypertension and acute diarrhoea. Design: cross-sectional survey. Finding: The information was collected on a total of 1099 patient-physician encounters. The results show that 61% of prescriptions in these setting are non-generic, and only 62% are from the Colombian essential drug list. Numbers of medication prescribed per encounter were higher with acute respiratory tract infection, as well as prescription of non-generic forms, antibiotics, and medications outside of the Colombian essential drug list. Inappropriate prescriptions were seen in 31% of all encounters. Conclusion: teaching of rational prescribing pattern should be targeted with much more emphasis in schools of medicine. 2. Survey of antibiotic prescribing pattern in government health facilities of Wassa West district of Ghana (Bosu and Adjei, 1997). Antibiotic prescribing pattern was studied from 700 retrospective outpatients clinical; records from seven government health facilities in the Wassa West of Ghana. Prescribing patterns were compared between the district hospital six-health centers. The percentage of patients receiving one or more antibiotic was significantly more at the health centers (60.7%) than at the hospital 41.2%

(chi2=13.6;p<0.001) the average number of antibiotics was 1.4 and 1.1, respectively. The commonest antibiotics prescribed were penicillin, cotrimoxazole, benzyl penicillin, metronidazole and amoxicillin. Malaria, upper respiratory tract infection, soft tissue infection and diarrhoea are the commonest indications for antibiotic use factors such as the diagnostic facilities, type of prescriber, lack of refresher training and pattern demand were considered to significantly influence antibiotic prescribing. 3. Antibiotic use in the Australian community in 1990-1995. Objective: To determine the pattern of antibiotic use in the Australian community and compare it with the pattern in the other developed countries (Peter et al., 1997). Design: survey of data from the national database on drugs dispensed in Australia (1990-1995), an international database on retail drug sales (1985-1994), and Australian prescribers surveys (1994, 1995). The main outcome measures: National and international retail sales of oral antibiotic (defined daily doses [DDDs]/1000 population/day) and antibiotic prescriptions dispensed through community pharmacies by drug type; antibiotic prescribing profiles for common conditions. Antibiotic use in Australia remained steady between 1990 and 1995, with an estimated 24.7 DDDs/1000 population/day dispensed through community pharmacies in 1990 and 24.8 DDDs/1000 population/day in 1995. Amoxycillin, although declining in use, remained the most dispensed antibiotic. Compared with the other countries surveyed, Australia had the highest percentage use of tetracycline, such as doxycycline, and the lowest percentage use of fluoroquinolones. Use of trimethoprim-sulfamethoxazole and flucloxacillin declined in Australia. In new cases of upper respiratory tract infection or pharyngitis, an antibiotic prescription was recorded for 57% of urban patient encounters and 73% of rural patient encounters. 4. Irrational and inappropriate prescribing was observed in graduate (GP) and non-graduate (NGP) medical prescribers in rural Bangladesh, 1995 (Baqui and Chowdhury, 1995). The objectiveof this study was to describe the prescribing patterns of both graduate medical physician and non-graduate medical physician for five common diseases: watery diarrhoea, dysentery, acute respiratory infection (<5 yrs), urinary tract infection and enteric fever. A cross sectional study was carried out from June 1995 to July 1996 at Sonargaon, Arihazar and Trishal Thana in rural Bangladesh. 840 prescriptions were collected, audited, and analyzed using INRUD prescribing indicators from Thana Health Complexes (THCs) and private practices (PP) of GPs and NGPs. In THCs data were collected from hospital records and by exit interviews of the patients of the GPs. In PP data were collected for both GPs and NGPs by photocopying the prescriptions from 50 drug-selling shops by shop attendants. Outcome measures: Average number of drugs per encounter, % of drugs

in generic name, % of drugs from the essential drugs list (EDL), % of antibiotics prescribed, % of drugs with an injection prescribed and % of patients treated according to standard treatment guidelines (STG). Drugs prescribed from EDL and in generic name occurred more frequently in THCs than PP due to the implementation of the 1982 Bangladesh national drug policy. Average number of drugs and % of antibiotics prescribed per encounter were higher in PP of both GPs and NGPs than in THCs by GPs. Patients treat according to STG was lower in PP of NGPs than that of GPs in THCs and PP. Injection prescribed by NGPs were higher than that of GPs in PP. 5. The prescribing pattern of outpatient polyclinic doctors (Lim and Yap, 1999). This study aims to analyze the prescribing pattern of doctors working in a government outpatient polyclinic in Singapore. Design: Retrospective study of 1 week of prescription scripts in 1996. The main outcome measurement is: Number, types and duration, drugs prescribed combination of drugs, age distribution, and bad handwriting. Two thousand six hundred and seventy-nine scripts were analyzed. The age of patients ranged from 1 to 93 years with a mean of 43.8 years. There were 44.0% males and 56.0% females. The overall mean of 'total number of drugs prescribed ` was 2.8 items. The means of 'number of drug items prescribed for more than 1 week' by age-group were: < 20 years = 0.2; 20 to < 40 years = 0.5; 40 to < 60 years = 1.3, and > 60 years = 2.4. One-way analysis of variance showed significant difference between the means of each age group. Post hoc analysis revealed that the oldest age group accounted for most of this significant result. The top 10 drugs prescribed in descending order were: antihistamines, paracetamol, throat medications (e.g. lozenges, gargles, etc), nifedipine, beta-blockers, antacids, mistbenadryl expectorant, Procodin cough syrup (containing codeine and promethazine), amoxycillin and vitamin B. Nifedipine and beta-blockers were the most commonly prescribed anti-hypertensives. Non-steroidal anti-inflammatory drugs were prescribed usually with antacids. One hundred and twenty (4.5%) scripts were illegible. 6. A study of the prescribing patterns and rational drug utilization of medical practitioner in the west of India (Kshirsagar et al., 1998), which was undertaken by analyzing their prescriptions. In 1975, the world health assembly requested the director-general to advise member states on the selection and procurement of essential drugs corresponding to their national health needs. The results indicated a lack of rational prescribing practices by a significant number of practitioners. Fixed-dose formations dominated the prescribing pattern and generic prescriptions were negligible, with prescriptions for essential drugs accounting for less than 60% of total number of drugs prescribed. More than 30% of prescriptions were irrational, with probability of such prescriptions increasing significantly with the

number of drugs per prescription. A study of sources of drug formulations available for prescription revealed significantly more fixed-dose combinations, many of which were irrational. 7. The prescribing pattern of antibacterial agents was analyzed by reviewing case notes of 407 patients discharged between October and November 1992 from teaching hospital in Gondar, northwest Ethiopia (Aseffa et al., 1995). Seventy percent had received one or more antibacterial. Most exposure was in surgical ward {84%) followed by pediatric (82%), orthopedic (78%), medical (72%), gynecologic (58%) and obstetric (20%) wards. The antibacterial most frequently prescribed were peniciliin G (25%), chloramphenicol (24%), and ampicillin (20%). The total list numbered 13 and included no cephalosporins or quinolone derivatives. The preliminary survey indicated an inappropriate use of antibacterial and suggested the need to develop a policy on hospital antibacterial use. 8. Analyzed the prescribing patterns in different patient categories within the public and private sectors in Durban metropolitan area in South Africa (Suleman et al., 1997). The study design: A descriptive cross sectional study, and collect the prescription of patient from four public hospitals (3589 prescriptions); 10 randomly chosen individual dispensing medical practices (629 prescriptions); 15 randomly chosen pharmacies (273 prescriptions) and 24 randomly chosen dispensaries from a medical aid-clearing house (212 prescriptions). Results: The hospital category had an older patient profile ($p<0.0001$); prescribed more drugs on average than the private sector ($p<0.0001$); and had a disease profile consisting of more chronic conditions. The dispensing doctor category had the highest percentage of generic prescribing (24.4%; $p<0.001$); percentage of encounters with an antibiotic prescribed (33.7%; $p<0.0001$); and percentage of encounter with an injection prescribed. 9. Drug utilization and antibiotic use in the primary health care centers IL Sharjah (United Arab Emirates) (Mohamed et al., 1997). The resultsof this study of prescribing indicators showed that the average number of drug prescribed per encounter was 2.8 before and 2.7 after interventions. All drugs were prescribed by proprietary names, although they were included in the formulary in their generic names. It was found that 92% of visits to the health centers resulted in a prescription before intervention and it dropped to 85% after intervention and the difference was statistically significant. The percentage of prescriptions of antibiotics dropped from 45% before to 35% after intervention, the percentage of encounters with an injection dropped from 16% before to 14% after intervention. The average consultation and dispensing times were similar before and after intervention. Antibiotics commonly prescribed were penicillin (most frequently amoxycillin), far a head of cephalosporins and erythromycin. The prescription of penicillin

dropped after intervention, while erythromycin and cephalosporins increased after intervention. 10. Other study showed that out of 208 primary heaths care centers in the South Western Saudi Arabia (Ahmed et al., 1997), a stratified random sample of 23 primary health's care centers was randomly chosen. Data regarding all the medical consultations (n=66432) provided by all primary health care centers physicians (number of physician= 49) and their prescriptions were collected to study prescribing patterns. The data were collected from the health information system of the primary health care centers without the physician's knowledge. The study showed that more than two-thirds of medical consultations (71.5%, n=47494) ended by prescribing medications. The average number of drug items prescribed for the individual patient was 1.44. The leading missing items in the studied prescriptions were, for how long medication should be taken (32.9%), the patients' name (15.8%) and the family health record number (6.5%). Prescribing drug by generic name is very minimal among physicians (2.9%). The groups of drugs commonly prescribed were analgesic-antipyretics (61.9%), antibiotics (56.2%), cough medications (26.6%) and vitamins (22.7%). The observed defects identify fields to be addressed in continuing medical education programmes aimed at encouraging more rational prescribing among primary health care physicians. 11. Drug prescribing pattern for outpatients in three hospitals in northwest Ethiopia by Desta Zeruesenay, Abula Teferra, Asfawoseen, Gebre-Yohannes and Worku Alemayehu (Desta et al., 2002). Objective: To evaluate and compare patterns of drug prescribing practiced in the outpatient departments of three hospitals. Methods: Case notes of outpatients attending the Gondar teaching hospital (n=2023), Bahir Dar regional hospital (n=2597) and Debre Tabor rural hospital (n=1808) were reviewed retrospectively over one year period. Results: The leading diagnoses in the three hospitals were similar and include disease of the respiratory system, gastrointestinal tract, sexually transmitted and skin. The average number of drugs per patient was 0.98 in Gondar, 1.8 in Bahir Dar and 2.2 in Debre Tabor hospitals. Antibacterial including anti-TB drugs (40-51%) and analgesics (11-49%) were the most frequently prescribed drugs in the three hospitals. Conclusion: The average number of drugs prescribed per patient was within the acceptable range. Deviation of prescribing pattern among the outpatients possibly reflects the availability of drugs, attitude (habit) of the prescriber and diagnostic profiles and facilities. Much remains to be done to promote rational selection and use of drugs in hospitals. 12. Field tests for rational drug use in twelve developing countries (Hogerzeil, et al., 1993) by World Health Organization, Action Programme on Essential Drugs, Geneva, Switzerland. Increasing efforts are being made to improve drug-use practices and prescribing behaviour

in developing countries. An essential tool for such work is an objective and standard method of assessment. They presented there a set of drug-use indicators produced and tested in twelve developing countries. They described practical applications, which include the use of indicators to increase awareness among prescribers in Malawi and Bangladesh, to identify priorities for action (e.g., polypharmacy in Indonesia and Nigeria, overuse of injections in Uganda, Sudan, and Nigeria, and low percentage of patients who understood the dosage schedule in Malawi), and to quantify the impact of interventions in Yemen, Uganda, Sudan, and Zimbabwe. PIP: A set of drug-use indicators produced and tested in 12 developing countries and the recommended method for data collection are presented to improve drug use and prescribing behaviour. The International Network for the Rational Use of Drugs in collaboration with the WHO Action Program on Essential Drugs undertook a project to develop and field-test a set of basic drug-use indicators. The method for collecting the data was first tested in Indonesia, Bangladesh, and Nepal; other tests took place in Guatemala, Malawi, Nigeria, Tanzania, and well as in Ecuador, Sudan, and Zimbabwe. In results from 12 developing countries, drug-use patterns were ascertained. The average numbers of drugs per encounter were high in Indonesia and Nigeria (3.3 and 3.8); the prescriptions of 1 or more antibiotics were also high in Uganda and Sudan (56% and 63%), similar to injectable drugs in Uganda, Sudan, and Nigeria (36-48%); and the availability of essential drugs was low in Ecuador (38%). 94% of drugs were prescribed by generic name in Zimbabwe, whereas only 37% were in Ecuador. In Yemen, the comparison of an essential drugs project area to a control area demonstrated 1.5 and 2.4 drugs per encounter, 46% and 67% of them antibiotics and 22% and 45% of them injections, respectively. In Uganda, a study on the effect of training showed decline in the use of injections (50% to 41%), improvement in the use of oral rehydration treatment for diarrhea (52% to 89%), and reduction in antidiarrheal drug use (60% to 39%). In rural health facilities in Sudan, the drugs prescribed by generic name increased from 17% to 70% between 1989 and 1991. In 10 developing countries the average number of drugs per prescription for general outpatient encounters ranges from 1.3 to 2.2, but in Indonesia and Nigeria it is 3.3 and 3.8. The median of 41% of antibiotics prescribed in the 12 countries reflects actual prescribing, not optimum values. 13. Survey of drug use practices and antibiotic prescribing pattern at a general hospital in Nigeria (Chukwuani et al.,2002). Objective: To describe the current drug use practices at theinstitution, and gather baseline data, which can serve as a basis for designing an appropriate intervention to improve the drug use profile. Method: A retrospective audit of in-patient and out-patient prescriptions, generated during the period

January–March 1999. Indicators of drug use pattern include: average number of drugs prescribed per encounter (ANDPE), average number of antibiotics prescribed per encounter (ANAPE), % encounter with antibiotics (PEA), percent of antibiotic prescriptions based on microbial sensitivity test results (MCST). Additionally, a knowledge, attitude and practice" (KAP) survey of prescribers and dispensers was performed. Indicators of prescribing anddispensing quality include: sources of drug/prescribing information, availability and use of the hospital formulary, knowledge of the prescribing process and the adequacy of the drug supply management system. Results: A total of 9984 outpatient prescriptions and 127 in-patient case notes were audited. The total number of prescribers and dispensers surveyed were 88 and 13, respectively. The ANDPE was found to be 3.16 for outpatients and 9.7 for in-patients; ANAPE was1.1 and 2.4 for outpatients and inpatients, respectively. The PEA was 50.3% for outpatients and 96.7% for in-patients. Only 4.2% of in-patient antibiotic prescriptions were based on MCST and percent encounter with switches in antimicrobial therapy was 52.1% while the average number of switches per encounter was 1.35. In 18.5% of the in-patient encounters there was evidence of drug incompatibilities. The KAP survey revealed that prescribers and dispensers in the hospital rely on different sources for their drug information needs (MIMS vs. Martindale Extrapharmacoepia). None of the prescribers surveyed was able to correctly enumerate all the 4 steps involved in the prescribing process, about 25% got at least 2 steps correctly, and only 9.1% of thedispensers surveyed could accurately define a hospital formulary. The drug supply management system was found to be inadequate. Conclusion: The survey revealed that appreciable gaps in knowledge with respect to rational drug use, still exists among these cadre of healthcare professionals. The foregoing suggests an urgent need forreview of current policies and systems in the hospital with the view of enhancing the drug use practices of the health providers. Specifically, it is recommended that there should be an intervention program involving concerted continuing education (to influence the KAP of the various cadres of healthcare providers) and the establishment of a hospital formulary / standard treatment guidelines. 14. Evaluation of rational drug prescribing in Democratic Yemen by Walker GJ, Hogerzeil HV, Sallami AO, Alwan AA, Fernando G, Kassem FA. (Walker et al., 1990). The government of Democratic Yemen started an essential drugs programme in 1984. Every month quantities of 30 drugs are delivered in prepacked kits to health units and standard treatment schedules have been agreed. The quantities of each drug were estimated by applying the standard treatment schedules to the typical morbidity patterns seen at these facilities. Most health workers

attended a training course on the correct use of the standard treatment schedules. Hospital and health centres have been included in the programme to a more limited extent. In March 1988 an evaluation of the programme was carried out. Comparisons were made between random samples of health units included in the programme and those where it had not yet been implemented. The adequacy of knowledge necessary for reasonable use of drugs was assessed by interviewing health workers. Actual drug prescription was studied by means of quantitative indicators. A more qualitative insight was obtained by reviewing drug prescriptions for four tracer diseases at a sample of health centre and hospital outpatient departments. Health workers at units included in the programme had significantly (p less than 0.05) higher levels of rational drug knowledge and 'better' actual drug prescription in terms of proportions of patients receiving injections (25% vs. 58%), antibiotics (45% vs. 67%) and the average number of drugs per patient (1.5 vs. 2.4), all p less than 0.001. Many patients treated at health centres and hospitals were receiving irrational drug treatment for the tracer conditions. It is suggested that the methods used in this evaluation to measure rational drug prescription could be appropriate in the assessment of other essential drugs programmes.

1.7 Country Profile

Yemen is situated in the southwest corner of the Arabian Peninsula. Saudi Arabia borders the country in the north, the Arabian Sea and Gulf of Aden in the south and Sultanate of Oman in the east, and the Red sea from the west it is comprised of 19 governorates (Yemen Map as in the Appendix No. 1). Land area is approximately 550,000 sq km. The political capital is Sana'a. The GNI per capita (formerly GNP per capita): 473 US$ and the Ministry of Public Health, Budget from the total Government Budget was 4.5% in year 2001 (CSO, 2001;Yemen in figures booklet, 2002).The Resident population of the Republic of Yemen according to population projection for 2003 in the Republic of Yemen was 19.2 millions. These populations are distributed among 19 governorates in addition to Sana'a City, the metropolis. The population has increased at an average growth rate of about 3.0 % in year 2003.(World Bank, 2005).

1.8 Rationale of study

Despite the growing volume of drug utilization studies in developed and developing countries that have been used to assess and quantify the magnitude of the problem of inappropriate drug use, there are very few studies have taken place in Yemen. In addition, no structured study has been conducted to date in the prescribing patterns of antibiotics in Yemen. Therefore, this area need to be investigated, as irrational prescribing of antibiotics is wasteful of money, increases the likelihood of hazards to the patients and the development of resistance. It is therefore, important to conduct a study in outpatient public hospitals for logistic reasons, time and cost. Sana'a is the most highly populated area in Yemen. In addition, many patients from areas near to Sana'a as well as from other governorates come to Sana'a public hospitals seeking for medical care. It is therefore important to study the antibiotic use practices and quantify the magnitude and severity of irrational practices.

1.9 Research Questions

Every ill does not require a pill. Drugs are not substitute for preventive measures. Injudicious use may lead to premature obliteration of highly efficacious and life saving antibiotics. Therefore, this study was design to determine and evaluate the prescribing pattern of Sana`a government hospitals when prescribing antibiotics. The following research will be answered in this particular study. 1. Is the prescription written in an appropriate way (i.e. in rational way)?

i. How many drugs per prescription?

- Do the prescriptions contain antibiotics?
- Do the prescriptions contain injections?
- Do the prescriptions contain vitamins and tonic preparations?
- Do the prescriptions contain more than 2 drugs?
- Are the drugs prescribed listed in the Yemen Essential Drug List?
- Are the drugs prescribed by the generic name?2. Is the antibiotic prescriptions written in an appropriate

way (i.e. in rational way)?

i. Is the age of the patient written in the prescription?
ii. Are the name, gender and address of patient written in the prescription?
iii. Are the strength, dosage form, dose, frequency, and duration of antibiotics written in the prescription?
iv. Is the diagnosis written in the prescription?
3. Is the antibiotic prescribed in generic name or brand name?
4. Is the antibiotic prescribed listed in the Yemen Essential Drug List?
5. What is the extent of the antibiotic expenditure and what is the mean cost of antibiotics prescribed?
6. Which is the most frequent type of antibiotic written in the prescrioptions?
7. Are the YEDL and YSTG and the other prescibing information resourses available in these health facilities?
8. Is there a suitable stock of essential antibiotics in these health facilities?

In addition to the above, this study also need results for all indicators selected to evaluate and compare the antibiotics prescribing pattern in the four hospitals studied.

1.10 Study Objective

Aim and objectives of the study are as follows:- AIM : the aim of this study is to evaluate and improve antibiotics use in hospitals.

OBJECTIVES:

In it attempts to answer the research questions, this study has the following important objectives:

1. To review generally the prescriptions written by doctors in the four government hospitals.
2. To conduct drug utilization review on the prescriptions specifically on antibiotics.
3. To evaluate the prescribing pattern of antibiotics comparing to Yemen Essential Drug List.
4. To evaluate and compare the differences in terms of the prescribing pattern of antibiotics between the four hospitals.

5. To determine the availability of Yemen standard treatment guidelines and Essential drug list in the hospitals.

1.11 Significance of study

The current study is aimed to assess the current prescribing of antibiotics, correlate it with specific variable and provide the baseline data for further investigations or qualitative research in order to determine the main factors which contribute to inappropriate prescribing behaviour and for targeting future interventions, i.e. this study would serve as the basis for follow up intervention. It is also timely to know whether health facilities are above or below the WHO/INRUD standards of prescribing practices and to investigate the differences in prescribing practices between the studied health facilities. From the measurement of performance in antibiotics prescribing practices by health providers particularly the use of NSTG and NEDL in their treatment with antibiotics, this study in addition to other similar studies will help in developing strategies for rational use of drugs in terms of more appropriate prescribing and use of antibiotics by dissemination of the results to health authorities and policy makers. Overall, this study will be an attempt to strengthen Yemen National Medicine Policy.