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Antibiotics Prescribing Patterns by UNRWA General Practitioners Primary Health Care Gaza 2006

By
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Dedication

To my father, mother, wife, sons and daughters, thanks for all for their generous support and assistance.

Isa Mohammad Saleh

Declaration:

I Certify that this thesis submitted for the degree of Master is the result of my own research, except where otherwise acknowledged, and that this thesis (or any part of the same) has not been submitted for a higher degree to any other university or institution

Signed…….

Isa Mohammad Saleh

Date: ……..

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Definitions

1-General practitioner: (GP)

A physician whose practice consists of providing ongoing care covering a variety of medical problems in patients of all ages, often including referral to appropriate specialists, also called family doctor (UNRWA, 2004).

2-Senior Medical Officer: (SMO)

A physician whose practice responsible for operation and administration of the health centre to which he/she assigned including organization of services, personnel supervision, supply management and reporting (UNRWA,2004).

3-Essential medicines:

Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness which is called EDL, (WHO, 1992).

4-local opinion leaders:

Defined as health professionals nominated by their colleagues as being educationally influential, (Management Science for Health, 1997).

5- Prescribing encounters (PE):

It is the patient encounter who is prescribed medicines, if antibiotics its called Antibiotics prescribing encounters (APE), (WHO,1993).

6-Academic detailing:

In educational outreach or "academic detailing", which is usually used to improve prescribing practices after completion of training, brief, targeted, face-to-face educational visits to clinicians, principles of communications theory and behavioural science are combined with conventional education technique, (Soumerai, and Avorn 1990).

Abstract

Antibiotics therapy is considered to be a major component of patient management in primary health care, despite this recognition, unnecessary antibiotic prescribing remains common. To evaluate the general practitioners prescribing patterns in UNRWA health centers in Gaza strip, 1080 prescriptions were collected retrospectively from all the 15 health centers, 72 from each clinic and studied using WHO indicators, in addition to structured questionnaire to evaluate knowledge, attitude, and practices of the general practitioners. The study revealed over consumption of antibiotics as the percentage of encounters receiving antibiotics was 55.4%, percentage of encounters receiving antibiotics injection 2.2%, percentage of antibiotics prescribed by generic names 4.5%, percentage of antibiotics from UNRWA Formulary 99.7%, and average number of drugs per encounter was 2. Also 14.6% of prescription were with no diagnosis mainly in the family files , the commonest diagnosis reported was URTI (37.1%) and (82.8%) of them were provided antibiotics. The study showed the importance of training and experience as a sources of information. Also physicians interest in clinical guidelines has never been great, only 9.5% of UNRWA Formularies available in front of general practitioners. General practitioners attitude toward antibiotics prescription was generally good, but their interest was high to prescribe antibiotics in case of fever 65.1%, time pressure 72.6%, treatment uncertainty 28.6%. 96.4% of respondents agree that antibiotics are over prescribed, the most important factors for overuse was over-crowding 65%, clients pressure 55.7%, antibiotics prescribed without examination and diagnosis 36% and lack of knowledge 31%. And the most important general practitioners initiatives for promotion of prudent use of antibiotics were health educations of consumers 48.7%, training 47.4%, reducing overcrowding 33% and improving knowledge 29.4%. The study concluded that rational use of antibiotics needs to be emphasized through multi-faceted interventions as informational, educational, measures. The key elements should include updating knowledge for the providers, clinic based patient education and community outreach activities, in addition to regulatory and managerial policies as establishment of "UNRWA Therapeutic Committee", active dissemination of UNRWA Drug Formulary, training and supervision.

ملخص الدراسة

أنماط وصف المضادات الحيوية من قبل الأطباء العاميون في عيادات الوكالة غزة 2006

يعتبر العلاج بالمضادات الحيوية من المكونات الأساسية في برنامج الرعاية الأولية وعلى الرغم من ذلك فإن الوصف الغير ضروري يعتبر شائعا, ولتقييم أنماط وصف المضادات الحيوية من قبل الأطباء العاميون في عيادات الوكالة في قطاع غزة قام الباحث بأخذ عينة عشوائية مكونة من 1080 وصفة طبية تمت في الأشهر الستة السابقة من شهر يوليو حتى ديسمبر 2006 من كل المراكز, 72 وصفة من كل مركز باستخدام مؤشرات منظمة الصحة العالمية بالإضافة إلى استبيان قدم للأطباء لتقييم معرفتهم ,توجههم وكذلك ممارستهم فيما يخص المضادات الحيوية . لقد أوضحت الدراسة أن هناك زيادة في استهلاك المضادات الحيوية حيث أن مؤشر الصرف للمرضى كان 55.4% ونسبة الحقن للمضادات الحيوية 2.2% والصرف باستخدام الاسم العلمي 4.5% ونسبة المضادات الموصوفة من القائمة الأساسية لأدوية الوكالة 99.7% ومتوسط عدد الأدوية الموصوفة في الوصفة الواحدة هو 2. بالإضافة إلى 14.6% من الوصفات بدون تشخيص خصوصا في ملفات العائلة وكان التشخيص الأكثر شيوعا هو التهاب الجهاز التنفسي العلوي (37.1%) ونسبة 82.8% من هذه الحالات قد تم وصف مضادات حيوية لها . كما أوضحت الدراسة أهمية التدريب والخبرة كمصدر للمعلومات, لكن اهتمام الأطباء بالدليل الدوائي ليس كبيرا حيث أن نسبة الموجود منها أمام الأطباء هو 9.5% , أما التوجه للأطباء بخصوص صرف المضادات الحيوية فقد كان جيدا لكنهم يحبذون الوصف في حالة وجود الحمى 65.1% وضغط الوقت 72.6% وفي حالة التشخيص الغير واضح 28.6%. غالبية الأطباء 96.4% تؤكد على وجود زيادة في صرف المضادات وأهم العوامل التي تؤدي إلى الإفراط في صرف المضادات هي ازدحام العيادة 65% وضغط المريض 55.7% ووصف المضادات بدون تشخيص 36% ونقص المعرفة 31% . كما أن أهم الاقتراحات لتحسين وصف المضادات الحيوية هي زيادة الوعي الصحي للمراجعين 48.7%, تدريب العاملين 47.4% ,تقليل الازدحام 33% وتحسين المعرفة للأطباء 29.4% . خلصت الدراسة على ضرورة تأكيد ترشيد استخدام المضادات الحيوية من خلال إجراءات متعددة الجوانب, حيث كانت العناصر الرئيسية هي تحديث المعلومات لمزودي الخدمة وتوعية المراجعين في المراكز الصحية وكذلك عمل أنشطة مجتمعية بالإضافة لتنفيذ سياسات تنظيمية وإدارية مثل تأسيس لجنة دوائية , التوزيع النشط لدليل الوكالة الدوائي ,التدريب والرقابة.

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List of Abbreviations

ASEAN Association of South-East Asian Nations

CFHP Chief Field Health Programme

DRA Drug regulatory authority

EDL Essential Drug List

EDM Department of Essential Drugs and Medicines Policy

EMR Eastern Mediterranean Region

IEC Information, Education and Communication

EU European Union

GMP Good manufacturing practices

GPs General Practitioners

HIC Health Insurance Commission

HIV Human immunodeficiency virus

ICIUM International Conference for Improving the Use of Medicines

INRUD International Network for Rational Use of Drugs

LRTI Lower Respiratory Tract Infection

MOH Ministry of Health

MSF Médecins Sans Frontières

MSH Management Sciences for Health

NDP National drug policy

NGOs Non Governmental Organizations

OTC Over-the-counter (drug)

PCBS Palestinian Central Bureau of Statistic

PHC Primary Health Care

PNA Palestinian National Authority

PRDU Promoting Rational Drug Use

RDU Rational drug use component

SMO Senior Medical Officer

STD Sexual Transmitted Disease

STG Standard Treatment Guidelines

UNAIDS Joint United Nations Programme on HIV/AIDS

UNFPA United Nations Population Fund

UNICEF United Nations International Children's Emergency Funds

UNRWA United Nations Relief and Work Agency

URTI Upper Respiratory Tract Infection

USAID United States Agency for International Development

WHA World Health Assembly

WHO World Health Organization

WTO World Trade Organization

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Chapter 1

Introduction

Chapter 1: Introduction

1.1 Background

Drug therapy is considered to be a major component of patient management in health care settings, including primary health care. Although the benefits gained by patients from pharmacological interventions are valuable, the risks of drugs *per se* and the consequences of inappropriate use cannot be overlooked. Additionally, the cost of medicine is a matter of great concern in both developing and industrialized countries. Of the various classes of drugs, *antibiotics* receive special attention as more money is spent on them than many

other drugs (Guglielmo, and Brooks, 1989). Some antibiotics also have specific side-effects and extensive antibiotic use can lead to the development of resistant microorganisms (Farrar, 1985). Hans Hogerzeil, Director *ad interim* of Essential Drugs and Medicines Policy at WHO (2004a) says that "Most people see a lack of access to medicines as the main problem," "Unfortunately, the irrational use of available medicines is also a major threat to health and leads to considerable waste." (Hogerzeil, 2004)."Irrational use of medicines includes: over-treatment of a mild illness; inadequate treatment of a serious illness; misuse of anti-infective drugs; over-use of injections; self-medication of prescription drugs; premature interruption of treatment. Several country figures show that such practices are frequent, and not exclusively in developing countries" (WHO,2004b). Overuse of most medicines contributes to drug resistance. For example, overuse of chloroquine, the traditional remedy for malaria, has led to resistance which has been recorded in over 80 countries. Resistance to penicillin, used to treat gonorrhea, is present in as many as 98% of patients in certain regions (WHO, 2004b). According to figures gathered by surveys presented to WHO, in 2000, about 60% of antibiotics in Nigeria were prescribed unnecessarily. In Nepal, over 50% of antibiotics prescribed in 1996 were not needed and 40% of medicines expenditure in the same year was wasted due to inappropriate prescriptions (WHO, 2001). *Globally*, the figure for unwarranted antibiotics prescriptions stands at roughly 50%. "Misuse of antibiotics, overuse of injections, and under-use of life-extending drugs for illnesses such as HIV/AIDS, heart disease, and other chronic illnesses together constitute a global epidemic of irrational use of medicines," explains Jonathan Quick, incoming president and CEO of Management Sciences for Health. "This epidemic results in untold needless suffering and costs millions of lives each year." (WHO, 2004b). The judicious use of antibiotics: The dictionary meaning of judicious is "having or showing reason and good judgment in making

decisions". With reference to antibiotics, judicious use implies using an antibiotic only *when indicated*, choosing a cost-effective agent which provides *appropriate antimicrobial coverage* for the diagnosis that is suspected and prescribing the *optimal dose and duration* of the antimicrobial. The WHO Global Strategy for Containment of Antimicrobial Resistance (2001) *defines the appropriate use of antimicrobials as the cost-effective use which maximizes clinical therapeutic effect while minimizing both drug-related toxicity and the development of antimicrobial resistance. Injudicious use of antibiotics* for both humans and animals (Shea, 2003) has long been recognized as a global problem. While over the counter access to antibiotics is mentioned as an important contributor towards injudicious antibiotic use in developing nations, as shown in a number of studies there are many provider, practice and patient characteristics which drive antibiotic overuse in developed nations such as the. United States numerous approaches have been proposed as a solution to this complex, multi-factorial problem. While some countries have shown a striking improvement in antibiotic use, in some cases associated with a drop in the problem of antimicrobial resistance, (Seppala, et al, 1997) there is abundant opportunity for improvement in most of the world. UNRWA assessment on 2003/2004 of health expenditure on medical supplies revealed that about of 15% of the total drugs supplies was allocated for antimicrobial drugs. The rate of irrational use of antibiotic identified by the study on prescription practice of antimicrobial drugs conducted in 2003/2004 at UNRWA Gaza Field was 58.2% which has signal effect on health status of the population as well as on the cost of the health care. More over study on antimicrobial resistance in 2003 to commonly isolated microorganisms at UNRWA laboratories Gaza Field showed alarming rates of resistance of microorganisms to commonly used antibiotics, so there is a great need to replace these medicine by new generation which will increase the load on the budget. Therefore it is necessary to improve the rational antibiotic use, exploring the

factors of irrational antibiotic use and to put a plan for regulating antibiotics auditing practice.

1.2 The aim of the study

To evaluate the current prescribing pattern by the physicians and to identify the potential factors of irrational use of antibiotics in UNRWA health centers Gaza Strip.

1.3 Objectives

General

To evaluate current prescribing pattern of antibiotics by UNRWA general practitioners primary health care Gaza, 2006.

Specific

1-To identify the prescribing pattern of antibiotics in relation to percentage of encounters with an antibiotics prescribed.

2-To determine the percentage of antibiotics prescription with generic name.

3-To outline the availability and use of information in UNRWA Health centers as clinical guideline about the use of antibiotics in management of infectious diseases and UNRWA drugs Formulary.

4-To highlight the potential factors of irrational use of antibiotics.

5-To evaluate knowledge attitude and practice of general practitioners about antibiotics prescribing pattern at UNRWA Health Facilities.

1.4 Research questions

1-Is there a relationship between irrational prescription and lack of UNRWA drugs Formulary (EDL)?

2-What is the percentage of encounter with an antibiotics prescribed (PEA)?

3-What are the potential factors that lead to poor prescribing patterns?

4-What are the sources of antibiotics prescribing information ?

5-Are the UNRWA drugs Formulary (EDL) available and used at the health facility?

6-What is the percentage of antibiotics prescribed by generic name?

7-Are the antibiotics prescribed from UNRWA drugs Formulary (EDL)?

8-What is the most common antibiotic prescribed?

9-Are the general practitioners having good knowledge and information about antibiotics?

10-Are the general practitioners receiving in service training related to antibiotics?

1.5 Demographic characteristics

Background

Geographically, the Strip forms the westernmost portion of the Palestinian territories in Southwest Asia, having land borders with Egypt on the south-west and (occupied land 1948) on the north and east. On the west, it is bounded by the Mediterranean Sea. The Gaza Strip is a narrow coastal strip of land along the Mediterranean, in the Middle East. It takes its name from Gaza, its main city, and has about 1,428757 (July 2006 est.) residents, mostly Palestinians, in an area of just 360 km², population density (the number of persons per unit of area) is 3,823/km² (July 2005 est.). The Strip itself and its population is under the jurisdiction of the Palestinian Authority, which also operates the Strip's Rafah border crossing into Egypt under European Union supervision **(**The World Fact book for Gaza Strip, 2007).

Demographics of the Gaza Strip

The majority of the Palestinians are direct descendants of refugees who fled or were expelled from their land in Palestine during the 1948 Arab-Israeli War. By 1967, the population had grown about six-fold, and the Strip's population has continued to increase since that time. Poverty, unemployment, and poor living conditions are widespread, and their causes have been attributed to the extremely high birth rate, disruptions to the economy due to Israeli closure policies since the first intifada. 2006 estimation by International Market Research, World Fact Book for Gaza Strip,2007 revealed that: The total population of Gaza Strip were : 1,428,757, and the age structure is as follow : *0-14 years:* 48.1% (male 351,642; female 335,060) , *15-64 years:* 49.4% (male 360,147; female 345,318) and *65 years and over:* 2.6% (male 15,231; female 21,359) (World Fact Book for Gaza Strip,2007).

Also birth rate is 39.45 births/1,000 population, death rate is 3.8 deaths/1,000 population and net migration rate is 1.48 migrant(s)/1,000 population , so the population growth rate is 3.71% and is characterized by *Demographic gap* as a Gaza's population is constantly growing extremely rapidly due to *high birth rates and low death rates*., quality of health has improved enough that death rates fall into the "accepted" range, which is usually well below 10 per 1000 people. However, birth rates remain high, and the country becomes "trapped" in a self-perpetuating cycle. The sex ratio: *At birth:* 1.05 male(s)/female, *under 15 years:* 1.05 male(s)/female, *15-64 years:* 1.04 male(s)/female, *65 years and over:* 0.71 male(s)/female and *total population:* 1.04 male(s)/female. Infant mortality rate: *total population:* 22.4/1,000 live births, *male:* 23.48/1,000 live births, and *female:* 21.27/1,000 live births. Life expectancy at birth: *total population:* 71.97 years, *male:* 70.67 years and *female:* 73.34 years. Total fertility rate: 5.78 children born/woman. Literacy is *defined* as age 15 and over can read and write ,percent of the *total population:* are 91.9%, *male:* 96.3% and *female:* 87.4% (World Fact Book for Gaza Strip,2007).

1.6 Geography

Gaza Strip is located in the Middle East (at 31°25′N 34°20′E). It has a 51km border with the (occupied land 1948), and an 11km border with Egypt, near the city of Rafah. Khan Yunis is located 7km northeast of Rafah, and several towns are located along the coast between it and Gaza City. Beit Lahia and Beit Hanoun are located to the north and northeast of Gaza City, respectively. The Gaza Strip has a temperate climate, with mild winters, and dry, hot summers subject to drought. The terrain is flat or rolling, with dunes near the coast. The highest point is Abu 'Awdah (Joz Abu 'Auda), at 105 meters above sea level. Natural resources include arable land (about a third of the strip is irrigated), and recently discovered natural gas. Environmental issues include desertification; salination of fresh water; sewage treatment; water-borne disease; soil degradation; and depletion and contamination of underground water resources. (World Fact Book for Gaza Strip, 2007).

1.7 Economy

Economic output in the Gaza Strip declined by about one-third between 1992 and 1996. This downturn has been variously attributed to Israeli closure policies the imposition of generalized border closures which disrupted previously established labor and commodity market relationships between occupied land 1948(Israel) and the Strip. The most serious negative social effect of this downturn was the emergence of high unemployment. The unemployment rate is 20.3% (includes West Bank) (2005). 63.1% of the Gaza strip population is under the poverty line (2005). The World Bank has compared the 2001-2002 recession brought about by the Second Intifada and the blockade of access points by Israel to the 1929 economic crisis. The UN institution in 2006 underlines that unemployment,

which was estimated to 23% in 2005, would increase to 39% in 2006, while poverty, estimated at 44%, would increase to 67% in 2006. (World Fact Book for Gaza Strip,2007).

1.8 Health care providers

There are four different types of health providers in the West Bank and Gaza Strip. The most important is the Ministry of Health. The other three are UNRWA, national and international NGOs and the private sector. MOH primary health care centres provide free services to individuals who subscribe to the government health insurance scheme. Services for pregnant women, children below three years of age and individuals with certain infectious diseases or suffering from mental illness are also provided free of charge at government facilities. UNRWA clinics provide free primary health care to registered refugees, while NGO clinics provide care at subsidized rates or cost . Hundreds of private settings (profit) are operated by private individual medical specialists, physicians, dentists, pharmacists, lab technicians and X-ray technicians, it provides services for fees paid either by private insurance or by the patient MOH hospitals assist members of insured households, provided that appropriate referral has been obtained. The non-insured pay for services at rates fixed by the MOH, which at the time of writing were about US$ 100 for each day spent in hospital. Services for individuals involved in automobile accidents and admitted to government hospitals are covered by insurance companies. NGO hospitals charge fees for their services. Admissions to them are subsidized by UNRWA or the MOH if the referral has been duly authorized. Private maternity hospitals provide obstetric services and are paid for by private insurance or by the patient. Treatment abroad, that is treatment in health institutions not belonging to the Government whether in or outside the West Bank and Gaza Strip, is available to insured household members, provided that the appropriate referral has been obtained. Co-payments are required for such treatments;

exemption is granted to social security cases and for expensive treatments. The non-insured must pay for their treatment themselves (Obeidallah, et al,2000).

1.9 Primary health care Facilities by level in Gaza

1. UNRWA primary health care services run by 18 centers three of them are sub centers.

2. MOH owns and operates 56 PHC centers out of which 29 level (II), 19 level (III) and 7 of level (IV). In addition to, one specialized mental health clinic in Khan Younis. In general, there are 10 centers working 3 shifts (24 hours, emergency services), 9 centers working 2 shifts and the rest of centers working only one shift, one of which has a delivery unite in Gaza city . The PHC centers provide special health care services in different aspects, 44 centers provide antenatal care and family planning services, in addition to 100 specialized clinics and 25 dental and oral clinics. About 34 centers have laboratories and 12 centers have x-Ray units (MOH,2004).

3. Non-governmental Organizations, (NGOs) Clinics (Non profit), in 2004, the health sector in NGOs owns and operates 51 PHC centers in Gaza. Some centers include medical laboratories to perform simple investigations, and many pharmacies that provide the attendants with low cost medications (MOH, 2004).

1.10 UNRWA Health Services

UNRWA owns and operates 18 centers in Gaza three of them are sub-centers. The number of registered refugees was 1016964 in Gaza; therefore, the ratio of refugees per center was 56,498 . The UNRWA offered comprehensive primary health services free of charge for all refugees and plays a noticeable role in the vaccination program in cooperation with the MOH, in addition to curative services, as provision of outpatient medical care including issue of medicines, laboratory, radiological, oral health services,

physiotherapy, antenatal and postnatal care and other specialized services. Furthermore, all refugees have the right of accessibility to the governmental health care services. In UNRWA Gaza Field there were 3,069462 subtotal visits seen by physicians with ratio of repeat visit to first visit 4.3. The workload in Gaza was decreased from 137 in 2005 to 95 by the end of 2006 after recruitment of additional medical officer through job creation program. (UNRWA, 2006).

1.11 UNRWA Expenditure on Medical Supplies

According to UNRWA report in 2005 the spend on medical supplies and equipment represented the second highest line of expenditure in health after staff costs . Total expenditure on medical supplies and equipment from all funds (regular cash budget in kind contributions and emergency appeals) in 2005 was approximately USD 14.62 million with an increase by 29 per cent from the rate of expenditure in 2004 . That increase was due to the introduction of *new groups of antibacterial medicines* and the increased demand on the medicines that are used for the treatment of non-communicable diseases, however the spend on medical supplies and equipment represented approximately 21 per cent of total expenditure on medical care services during 2005 and the same percent in 2006. Medical supplies and equipment distributed as follow 82% for drugs and 18% for equipments, antibiotics represented 14% of drugs expenditure(UNRWA,2006). Also the annual study of the trends of utilization of medical supplies was carried out during 2005, analysis of data on expenditure on medical supplies revealed the following: Average expenditure on medical supplies per outpatient medical consultation was USD 1.8 , Agency- wide , the highest rate of USD 3.2 per medical consultation was from Lebanon field followed by Syria and Gaza (USD 1.7), the lowest rates were observed in Jordan & West Bank (USD 1.5) . The high rate of expenditure in Lebanon is due to the in kind

donation received from Ameri cares in the from medications and disposable medical supplies . Average expenditure on medical supplies per registered refugee was USD 3.4, Agency wide. The highest rate of USD 7.2 per registered refugee was from Lebanon due to the in kind donation received , followed by USD 4.9 in Gaza , USD 3.7 in Syria and USD 3.0 in west bank . The lowest rate was USD 1.8 in Jordan . Expenditure on *antibacterial medicines* represented 15 per cent of total expenditure on drugs (UNRWA,2005) with a slight reduction from that of 2004 due to improved prescribing practices of antibacterial medicines, in spite of the introduction of the new expensive antibacterial medicines. Follow up measures have been introduced in order to improve rational antibacterial prescribing practices Agency wide during 2005. The measures included a follow up study on prescribing rates of antibacterial medicines ,preparation of clinical guidelines and the updated UNRWA model Formulary. The follow up study revealed reduction in the rates of prescribing of antibacterial medicines Agency wide from 53 per cent in 2004 to 28 per cent in 2005, increased to 31% in 2006. In 2005 the lowest rate was 15 per cent in Lebanon and the highest rate was 36 per cent in Gaza , 24 per cent in Jordan , 33 per cent and 34 per cent in Syria and West Bank respectively (UNRWA, 2005), while in 2006 the lowest rate was 20% in Lebanon and the highest was in Gaza Field 39%.

1.12 UNRWA model formulary "of essential medicines"

The first edition of UNRWA model formulary of essential medicines was prepared in 1991 in order to provide a ready guidance on use of essential medicines programmed by the Agency. Since then, the formulary went through several revisions in order to reflect the numerous additions, deletions and changes in specifications of essential medicines used in the program consistent with WHO recommended list of essential medicines and recent advances in pharmacology. The fifth edition 2005 of the formulary comprises a section

providing guidance on prescribing medicine, as well as fourteen chapters on medicines acting on the various systems and three annexes on drug interactions and use of medicines during pregnancy and breast feeding. It was updated and distributed to all fields of UNRWA. Adequate copies were made available to every medical officer and specialist aiming at providing a ready reference to assist UNRWA medical personnel in selection of appropriate medicines for treatment of patients. The Formulary was presented in a *user friendly* format for easy handling aiming at promoting rational prescribing practices consistent with WHO recommendations and recent advances in pharmacology (UNRWA, 2005).

1.13 Justification of the study

Antibiotics save lives! We must save antibiotics!

Inappropriate use of antibiotics has often been identified as a problem in effective health care delivery and results in wastage of scarce resources and widespread health hazard (WHO,2006). High level of antibiotic use, often clinically unnecessary, have led to steady increase in drug resistance (Radyowijai and Haak, 2003). Previous studies of UNRWA revealed irrational use of antibiotics in Gaza Field characterized by high prescribing rate about 53% (UNRWA ,1999) . Also another study on 2004 /UNRWA Health Centers revealed that the rate of prescribing antibiotics was 58.2% .The above results are considered high compared with the ideal values of WHO 20.0 % - 26. 8% ,(WHO,1993). Total expenditure on medical supplies in 2005 was approximately USD 14.62 million with an increase 29% from the rate of expenditure in 2004 . Indiscriminate and unconcerned use of antibiotics has led to development of antimicrobial resistance making the misused drugs inefficacious . Consequently, newer groups of antibacterial medicine was introduced (UNRWA, 2005). Also expenditure on antibacterial medicates represented 15% of the

drugs expenditure which represent the second biggest budget line in the health system, after salaries. (UNRWA ,2005). The indiscriminate use of antibiotics can have significant adverse effects on the health status of the population as well as on the cost of health care. It influence the outcome of treatment and increase the risk of developing adverse reactions of antibiotics including rapid emergence of resistance strains (UNRWA,1999). Follow up measures have been introduced in order to improve rational antibiotic prescribing practices during 2005, these measures include preparation of clinical guidlines and updated UNRWA model formulary "of Essential medicine". So since the introduction of the UNRWA Formulary there is a need to evaluate antibiotics prescribing patterns , the attitude and practice of general practitioner toward antibiotic prescription and illustration of many aspects related to the possible factors of irrational use of antibiotics specifically the compliance of general practitioners with the UNRWA model formulary .

Chapter 2

Literature Review

Chapter 2: Literature Review

Almost half of all medicines globally are used irrationally. This say medicines experts at the World Health Organization (WHO,2004b), and can have severe consequences : adverse drug reactions, drug resistance, protracted illness and even death. In addition, the financial cost incurred by individuals and governments due to irrational use is unnecessary and often extremely high, particularly in developing countries where patients often pay for medicines out of pocket (WHO,2004a). "Most people see a lack of access to medicines as the main problem," says Hans Hogerzeil, Director *ad interim* of Essential Drugs and Medicines Policy at WHO. "Unfortunately, the irrational use of available medicines is also a major

threat to health and leads to considerable waste" (WHO,2004a). Irrational use of medicines includes: over-treatment of a mild illness; inadequate treatment of a serious illness; misuse of anti-infective drugs; over-use of injections; self-medication of prescription drugs; premature interruption of treatment. Several country figures show that such practices are frequent, and not exclusively in developing countries (WHO,2004a). The inappropriate use of antibiotics has often been identified as a problem in effective health care delivery and results in wastage of scarce resources and widespread health hazards (WHO,2006). Also high levels of consumption of antibiotics, often clinically unnecessary, have led to steady increase in drug resistance, the effectiveness of many antibiotics is lost almost as quickly as scientists discover them (Radyowijati and Haak ,2002). Low-income countries , whom the majority of the world's population belong, believed to have an important role in this phenomena, where on averages, 35% of total health budget is spent on antibiotics in these countries (Isturis and Carbon ,2000). According to National Ambulatory Medical Care Survey , developed countries, also play a role in the abuse of antibiotics as 110 million prescription of oral antibiotics were written in 1992 in USA many of them have been given unnecessarily (Mc Caig and Hugles ,1995).

2.1 UNRWA'S Antibiotics situation

UNRWA Assessment of health expenditure on medical supplies during the past several years showed that about 15% out of total expenditure of medical supplies was allocated for antibacterial drugs (UNRWA, 2005). LeGrand, et al, in 1999 reported that many studies have been done to document antibiotics use patterns and indicate that over prescribing, multi-drug prescribing, misuse of drugs and the use of unnecessary expensive drugs are the most common problems of irrational antibiotics use by prescribers as well as consumers. The International Network for the Rational use of drugs (INRUD) in collaboration with the WHO action program in 1993 on essential drugs undertook a project to develop field tests

on basic drug use indicators it was tested in the twelve developing countries: Yemen, Sudan , Malawi, Bangladesh, Indonesia, Nigeria, Uganda, Zimbabwe, Nepal, Guatemala, Tansania, and Ecuador, the results from the previous developing countries, showed that prescription of one or more antibiotics were high in Uganda & Sudan (56% & 63% respectively). (Hogerzeil, et al, 1993). Also study conducted in 100 primary health care centers in 5 provinces of the Islamic Republic of Iran using WHO indicators revealed that prescription pattern was 58% (Cheraghali , et al, 2004). As in many health sectors UNRWA has a mission to provide appropriate antibiotics therapy including efficiency, effectiveness, safety, of sufficient quantity and high quality for the whole refugee's population and free of charge. UNRWA'S 5^{th} edition of Essential drugs list formulary (EDL) and Standard Treatment Guidelines (STG) for antibiotics prescription including Sexual Transmitted Disease (STD) and management of common infectious diseases were introduced in 2005 and for most of the medical officers to be acquainted with the updated information. UNRWA Studies about prescribing antibacterial drugs in the field of Gaza in 2004 and 1999 was 58.2% and 53% respectively which mean that is increasing and has signal effect on health status of the population as well as on the cost of the health care. The inappropriate use of antibiotics contributes to: adverse clinical outcomes, spread of antimicrobial resistance, unnecessary expenditures by consumers, and heavy economic burden to health-care system. Antibiotics represented 14% of drugs expenditure (UNRWA, 2006).

Although the irrational use of antibiotics has been widely described there is a paucity of researches about the factors that influence it. There for assessment of irrational use of antibiotics will enable UNRWA to evaluate the prescribing pattern after the introduction of EDL and STG and explore the factors that influence it (UNRWA, 2005). Moreover study on antimicrobial resistance to commonly isolated microorganisms at UNRWA laboratories

was conducted in 2003 in the five fields .The findings revealed alarming rates of resistance of microorganisms against most of the commonly used antibiotics. Should this trend continue in future years, most of the commonly used antibiotics, will loose their efficacy in treatment of infective diseases. This is a major concern in term of growing risks to human life ,ethical considerations relevant to use of medicine of low or doubtful efficacy and unjustified expenditure when there is evidence of high resistance. Due to increased resistance of microorganisms to the conventional antimicrobial medicine, the agency responded to the results of the anti-microbial resistance study by deleting the antimicrobial drugs that showed high resistance and introducing new generations of antibacterial drugs of higher efficacy but at a considerable higher cost. Unless appropriately prescribed, the new generations will themselves become less effective because of resistance (UNRWA, 2004).

2.2 Definitions of an antibiotic

Antimicrobial agents are not always classified in an identical way. Sometimes drugs such as antiprotozoals, antihelminthics or antituberclosis agents are placed in a separate category from other antibiotics, while other systems may classify all these products in a single category of anti-infective or antimicrobials .The indicators of antibiotic use are quite sensitive to whether or not certain groups of drugs are included as antibiotics, especially in environments where problems such as parasitic infestation or tuberclosis are common. Another issue in the definition of antibiotics for drug use indicators is whether topical

antibiotics preparations, such as skin cream and ophthalmic ointments, should be counted as antibiotics.

Table below provides a classification scheme for the common classes of anti-infective drugs derived from the WHO model list of essential drugs. The classes which are recommended to be counted as antibiotics are marked in this table. Metronidazol used as (antiprotozoal) should in this context not counted as antibiotic . However, sulfa drugs are counted as antibiotics. Also antibiotics eye ointment and skin cream such as Neomycine sulphate and Bacitracin ointment for skin infection and Silver Sulphadiazine 1% cream for burn are counted as antibiotics under this system. The *literal definition* of Antibiotic is against (anti-) life (-biotic); Often detrimental to host, however the *old definition* of antibiotic is a chemical substance produced by various species of microorganisms that is capable, in low concentrations, of inhibiting the growth of or killing other microorganisms (Rollins and Joseph 2000). The *antibiotic* have no effect against viruses, fungi, or parasites. Antibiotics are one class of antimicrobials, a larger group which also includes anti-viral, anti-fungal, and anti-parasitic drugs. They are relatively harmless to the host, and therefore can be used to treat infections (selective toxicity). The term, coined by Selman Waksman, originally described only those formulations derived from living organisms, in contrast to "chemotherapeutic agents", which are purely synthetic.

Table (2.1) Antimicrobial classification for prescribing indicators

Count as Antibiotic	Code in WHO Model list	Class
	6.1.3	Antifilarials
	6.1.4	Antischistosomals
Yes	6.2.1	Penicillins
Yes	6.2.2	Other antibacterials
	6.2.3	Antileprosy drugs
	6.2.4	Antituberculosis drugs
	6.3	Antifungal

	6.4.1	Antiamoebic and antigiardiasis drugs
	6.4.2	Antileishmaniasis drugs
	6.4.3	Antimalarial drugs
	6.4.4	Antitrypanosomal drugs
Yes	13.2	Anti-infective dermatological drugs
Yes	21.1	Anti-infective ophthalmological agents

From WHO Model list of Essential Drugs (WHO,1993)

Nowadays the term "antibiotic" is also applied to synthetic antimicrobials, such as the sulfa drugs. Antibiotics are generally small molecules with a molecular weight less than 2000. They are not enzymes, some antibiotics have been derived from mould, for example the penicillin class (Todar, 2002).

" So the new definition of Antibiotic is a substance produced by a microorganism such as bacteria and fungi or a similar product produced wholly (synthetic) or partially (semi-synthetic) by chemical synthesis and in low concentrations inhibits the growth of (bacteriostatic) or kills (bactericidal) microorganisms "(Rollins and Joseph, 2000).

2.3 History of the Development of Antibiotics

The great modern advances in chemotherapy have come from the chance discovery that many micro-organisms synthesize and excrete compounds that are selectively toxic to other micro-organisms. These compounds are called antibiotics and have revolutionized medicine. The period since World War II has seen the establishment and extremely rapid growth of a major industry, using micro-organisms for the synthesis of, amongst other compounds, chemotherapeutic agents. The first chemotherapeutically effective antibiotic was discovered in 1929 by Alexander Fleming (1881-1955), a British bacteriologist, who had long been interested in the treatment of wound infections. He noticed among a pile of

Petri dishes on his bench one that had been streaked with a culture of *Staphyloccocus aureus* which was also contaminated by a single colony of mold. Fleming isolated the mold, which proved to be a species of *Penicillium,* and established that culture filtrates contained an antibacterial substance, which he called penicillin. Penicillin proved to be chemically unstable and Fleming was unable to purify it. Working with impure preparations, he demonstrated its remarkable effectiveness in inhibiting the growth of many Gram-positive bacteria, and he even used it with success for the local treatment of human eye infections. In the meantime, the chemotherapeutic effectiveness of other, non-antibiotic compounds such as sulphonamide had been discovered, and Fleming, discouraged by the difficulties in purifying penicillin, abandoned further work on the problem. Ten years later a group of British scientists headed by H. W. Florey (1898-1968) and E. Chain (1906-1979) resumed the study of penicillin. Clinical trials with partly purified material were dramatically successful. By this time, however, Britain was at war; and the industrial development of penicillin was undertaken in the United States, where an intensive program of research and development was begun in many laboratories. Within three years, penicillin was produced on an industrial scale. Today it remains one of the most effective chemotherapeutic agents for the treatment of many bacterial infections. The various penicillin vary with respect to the chemical composition of their side chain. The penicillin that was first isolated in Peoria, Illinois, designated penicillin G, carried a benzyl side chain. The penicillin isolated soon after in England, designated penicillin F, carried an isopentanyl side chain. Penicillin G proved the most successful and later it became possible to remove the side chain and replace it by a variety of chemical substituents, thereby producing *semisynthetic penicillins*. For example, *penicillin V is resistant to acid and therefore can be administered orally because it is not inactivated in the stomach*; ampicillin is also acid resistant and also effective against enteric bacteria; oxacillin is

resistant to the action of lactamase, the enzyme produced by certain "penicillin-resistant" strains of bacteria. The remarkable chemotherapeutic efficacy of penicillin for certain bacterial infections, primarily those caused by Gram-positive bacteria, prompted intensive research into new antibiotics. In the 1940s, a second clinically important antibiotic, streptomycin, effective against both Gram-negative bacteria and *Mycobacterium tuberculosis,* was discovered by A. Schatz and S. *Waksman*. This was the first example of a broad-spectrum antibiotic. Other antibiotics with even broader spectra of activity, such as the tetracycline, were subsequently discovered. The search for new antibiotics remains an empirical enterprise. So far, they have proved very effective as antibacterial agents, although some bacteria do acquire resistance to antibiotics, so there is a continuous search for new and effective antibacterial agents. Antibiotics have proved less effective in the treatment of fungal infections. Antifungal antibiotics, such as nystatin and amphoterecin B are considerably less successful therapeutically than their bacterial counterparts, at least in part because their toxicity is far less selective. There are no known antiviral antibiotics. Since 1945, thousands of different antibiotics produced by fungi, actinomycetes or unicellular bacteria have been isolated and characterized. A small fraction of these are of therapeutic value. Their nomenclature is complicated as one antibiotic may be sold under several different names. For example in the United States the compound, which in Europe has the generic name rifampicin, is called rifampin. Its proper chemical class name is rifamycin and it is also sold under the trade names Rifactin and Rifadin, among others (Gale, 2006). Resistance to penicillin in some strains of staphylococci was recognized almost immediately after introduction of the drug. (Resistance to penicillin today occurs in as many as 80% of all strains of *Staphylococcus aureus*). Surprisingly, *Streptococcus pyogenes* (Group A strep) have never fully developed resistance to penicillin and it remains a reasonable choice antibiotic for many types of streptococcal infections.

Interestingly, penicillin has never been effective against most Gram-negative pathogens (e.g. *Salmonella*, *Shigella*, *Bordetella pertussis*, *Yersinia pestis*, *Pseudomonas*) with the notable exception of *Neisseria gonorrhoeae*. Gram-negative bacteria are inherently resistant to penicillin because their vulnerable cell wall is protected by an outer membrane that prevents permeation of the penicillin molecule (Todar, 2002).

2.4 Micro-organisms that produce antibiotics

Penicillium and Cephalosporium produce Beta-lactam antibiotics, penicillin, cephalosporin, and their relatives. Actinomycetes, mainly Streptomyces species produce tetracyclines, aminoglycosides (streptomycin and its relatives), macrolides (erythromycin and its relatives), chloramphenicol, rifamycins, and most other clinically-useful antibiotics that are not beta-lactams. Bacillus species, such as B. polymyxa and Bacillus subtilis produce polypeptide antibiotics (e.g. polymyxin and bacitracin), and B. cereus produces zwittermicin. These organisms all have in common that they live in a soil habitat and they form some sort of a spore or resting structure. It is not known why these microorganisms produce antibiotics but it may rest in the obvious: affording them some nutritional advantage in their habitat by antagonizing the competition; or the subtle: acting as some sort of hormone or signal molecule associated with sporulation or dormancy or germination. Antibiotics are secondary metabolites of microorganisms and they are produced at the same time that the cells begin sporulation processes. Most of the microorganisms that produce antibiotics are resistant to the action of their own antibiotic, although the organisms are affected by other antibiotics (Todar, 2002).

2.5 Indications for antibacterial therapy

Kakkilaya in 2002 stated that antibiotics are the most important weapons in our hands. Each one of them have been invented after spending considerable amount of time, energy and money. Therefore, we cannot afford to lose them. He also emphasized the importance of exertion considerable restraint in prescribing antibacterial and restrict the use of antibacterial to only certain definite indications as follow:

1-Definitive therapy: This is for proven bacterial infections, antibiotics (read antibacterial) are drugs to tackle bacteria and hence should be restricted for the treatment of bacterial infections only. This may sound silly, but most doctors seem to forget this simple fact. Attempts should be made to confirm the bacterial infection by means of staining of secretions/fluids /exudates, culture and sensitivity, serological tests and other tests. Based on the reports, a narrow spectrum, least toxic, easy to administer and cheap drug should be prescribed.

2-Empirical therapy: Empirical antibacterial therapy should be restricted to critical cases, when time is inadequate for identification and isolation of the bacteria and reasonably strong doubt of bacterial infection exists: Septicemic shock/ sepsis syndrome, immune-compromised patients with severe systemic infection, hectic temperature, neutrophilic leukocytosis, raised ESR etc. In such situations, drugs that cover the most probable infective agent/s should be used.

3-Prophylactic therapy: Antimicrobial prophylaxis is administered to *susceptible patients* to prevent *specific infections* that can cause *definite* detrimental effect. These include anti-tubercular prophylaxis, anti-rheumatic prophylaxis, anti-endocarditis prophylaxis and prophylactic use of antimicrobials in invasive medical procedures etc. In all these

situations, only narrow spectrum and specific drugs are used. It should be remembered that there is no single prophylaxis to 'prevent' all possible bacterial infections. There are more than 100 antibacterial available today, and each one has its own spectrum of activity, adverse effect profile and cost. The doctor should consider many factors before prescribing an antibacterial agent so as to make the treatment most effective with least adverse effects and cost. Also Kakkilaya in 2002 highlighted *the factors that should be considered while prescribing an antibacterial agent which are as follow:* Site of infection**,** type of infection, severity of infection, isolate and its sensitivity, source of infection, host factors and drug related factors (Kakkilaya, 2002).

2.6 Medicines prescription by generic name

According to Huss in 2003 there are at least four important issues behind the concept of generic drugs :

1-*Communication:* The use of international nonproprietary names facilitates communication among health professionals and citizens as we all use the same terminology for certain drugs.

2-*Avoidance of manipulation:* The ultimate success of marketing is to brand the drug name of a certain company into every body mind. When one ask about a good analgesic drug, every body mention aspirin, but nobody proposes acetysalicylic acid. The same phenomenon can be observed in other area of marketing the brand name.

3-*Economic production of drugs:* The aim of any economy should be the avoidance of waste, not the establishment of monopolies. This can be best achieved through multiple providers that compete for the most economic way of production.

4-*Unrestricted research and knowledge generation*: Human creativity and ingenuity should not be restricted by commercial interest (Huss, 2003).

2.7 Appropriate or (Rational) Prescribing of an antibiotics

Definition of rational use of antibiotics : means based on logic, it reflects the mindset of the person prescribing antibiotics. Therefore rational antibiotic therapy would mean antibiotic therapy given by physician with a rational mindset. WHO, in 2002 stated that *"Rational drug use involves: the correct drug, administered by the best route, in the right amount, at optimum intervals, for the appropriate period, and after an accurate diagnosis"*.

The terms *"appropriate" and "rational"* use of drugs are used interchangeably. The Conference of Experts on the Rational Use of Drugs, convened by the World Health Organization in Nairobi in 1985 defined that: *"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."* The definition implies that rational use of drugs, especially rational prescribing should meet certain criteria as follows:

- *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 cost considerations.
- *Appropriate patient:* No contra-indications 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 *(Laing , and Ross-Degnan,1992).*

Since the introduction of antimicrobial agents, there has been an association between antibiotic use and the development of antimicrobial resistance. Antibiotic therapy eradicates not only pathogenic organisms but also the protective normal flora. This so called "selective pressure" results in colonization with bacteria that are resistant to the original therapy. The result has been an increase over the past two decades in antibiotic resistance among common bacterial causes of outpatient infections. *The appropriate use of antibiotics is vital for two main reasons. Firstly, to ensure the best possible clinical outcome in treating a patient; and secondly, to reduce the development of further antibiotic resistance.* Several studies have demonstrated that a substantial portion of the antibiotics prescribed in the outpatient setting are given for viral illnesses or bacterial diseases where the benefit of antibacterial therapy is marginal. The reasons for prescribing antibiotics in these situations are related to medical and social factors. Physicians should be familiar with the clinical situations in which they should provide antibiotics and those in which they may safely be withheld. Physicians should understand the motivations of patients who are seeking antibiotics and provide education, empathy and alternative treatments (Colgan, and Powers ,2001).

Study in West-Bank and Gaza by Obeidallah, et al, 2000 revealed that there is a general tendency to over-prescribe drugs. This is particularly true and of great concern in relation to antibiotics and injections. However, there are indicators that the problem is significant and costly. There is also widespread prescription of fixed-dose combination drugs. With a

few notable exceptions, prescription of such drugs is not recommended. Doctors tend also to prescribe more expensive brand name drugs; current legislation does not allow generic name drug substitution. Public service doctors are not aware of the costs of the drugs they prescribe and there is no mechanism to monitor on a regular basis drug prescriptions and consumption patterns. Lack of budget ceilings on drug consumption in health institutions also contributes to over-prescribing. Therapeutic protocols do not form part of the guidelines used by the Public Health Department or in hospitals. The United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) and some nongovernmental organizations (NGOs) have developed their own guidelines based on internationally accepted standards, but adjusted to the local situation. The preparation and adoption of therapeutic protocols together with an Essential Drugs List and in-service training could improve the situation and the quality of care. This would also alleviate the psychological pressure exerted on doctors by patients requesting drugs and would provide the basis for patient's education about this issue (Obeidallah, etal,2000).

The bottom line for increasing rational use of medicines is the improvement of health systems, which can only be achieved through multilateral partnerships concretely promoting development, WHO and other agencies have worked to promote rational use of medicines through advocacy and education programmes for health providers, prescribers and consumers. Further steps to be promoted in the future are: advice to policy makers on market and price controls and limiting the medicines options for a country to those that are strictly necessary for the public health priority concerns (WHO, 2004a).

In 2006 WHO advocates 12 key interventions to promote more rational use:

1. Establishment of a multidisciplinary national body to coordinate policies on medicine use.
2. Use of clinical guidelines.

3. Development and use of national essential medicines list.
4. Establishment of drug and therapeutics committees in districts and hospitals.
5. Inclusion of problem-based pharmacotherapy training in undergraduate curricula.
6. Continuing in-service medical education as a licensure requirement.
7. Supervision, audit and feedback.
8. Use of independent information on medicines.
9. Public education about medicines.
10. Avoidance of perverse financial incentives.
11. Use of appropriate and enforced regulation.
12. Sufficient government expenditure to ensure availability of medicines and staff.

(WHO,2006).

2.8 Inappropriate or (Irrational) prescribing of an antibiotics

Unfortunately, in the real world, prescribing patterns do not always conform to the above 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. In 2002, WHO define *inappropriate prescribing* when antimicrobials are: not equitably available, used by too many people, to treat the wrong disease, in the wrong dosage, for the wrong period of time, and/or not in the correct formulation or strength. Similarly WHO in 2004 described the common patterns of irrational prescribing, which may be manifested in the following forms:

The use of drugs when no drug therapy is indicated, e.g., antibiotics for viral upper respiratory infections, the use of the wrong drug for a specific condition requiring drug

therapy, e.g., tetracycline in childhood diarrhea requiring ORS, the use of drugs with doubtful/unproven efficacy, e.g., the use of antimotility agents in acute diarrhea, the use of drugs of uncertain safety status, e.g., use of dipyrone (Baralgan, etc.), failure to provide available, safe, and effective drugs, e.g., failure to vaccinate against measles or tetanus, failure to prescribe ORS for acute diarrhea, 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, 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: Overuse of antibiotics and antidiarrheals for non specific childhood diarrhea, indiscriminate use of injections, e.g., in malaria treatment, multiple drug prescriptions, excessive use of antibiotics for treating minor ARI., minerals and tonics for malnutrition *(Laing , and Ross-Degnan,1992)*.

There is a wide variation in the prescribing of antibiotics. In primary health care 30%–60% of patients receive antibiotics, perhaps *twice* the number of patients with real clinical need. Misuse is common and may take the form of incorrect dosage or inappropriate prescription. For instance, studies from various parts of the world report that over 80% of patients with viral respiratory tract infections receive antibiotics, as is the case for childhood diarrhoea when the appropriate treatment would be oral rehydration salts (ORS). Irrational, or inappropriate, use of antimicrobials is a global problem affecting all countries and health systems and ultimately all consumers and patients (WHO, 2002).

A multitude of factors affect the use of antimicrobial medicines. Some of the more pertinent include the following: Education on prudent use of, and resistance to antimicrobials is lacking among dispensers and prescribers. It is thus not surprising that

drugs are frequently used in inappropriate doses and combinations. Empiric treatment predominates because of the widespread lack of diagnostic services. Drug sales may constitute a significant portion of prescribers' income. Antimicrobials are available over-the-counter (OTC) in many countries and may be purchased without prescription. Inefficient regulatory mechanisms or poor enforcement thereof, with lack of quality assurance and with marketing of substandard drugs, are important contributory factors. Marketing of antimicrobials by the pharmaceutical industry influences prescribing behaviour and use patterns. And for veterinary drugs: antimicrobial growth promoters are often not considered drugs and are licensed, if at all, as feed additives (WHO, 2002).

Ozkurt, et al, in 2005 grouped the irrational use of antibiotics in to eight categories:

1- No indication.

2- Improper dosage or dosage interval.

3- Unnecessary or improper combination.

4- Reserve or broad spectrum antibiotic.

5- Improper beginning time for prophylactic use or improper duration of treatment.

6- Incorrect choice of antibiotic (antibiotic is not appropriate for diagnosis or disease).

7- More expensive and toxic drugs.

8- Any combinations of the above (Ozkurt, et al, 2005).

2.9 Factors Underlying Irrational Use of Drugs

There are many different factors which 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, drug information and misinformation, and combinations of these factors as below Table (2.2). All of these factors are affected by changes in national and global practices. For example, the frequent use of injections is declining in many African countries because of the fear of AIDS. In some countries, however, the use of injectibles remains high due to false assumption of prescribers that injections will improve patient satisfaction and that they are always expected by the patients. (Laing , and Ross-Degnan,1992).

Table (2.2). ***Driving forces which affect the irrational use of drugs.***

Driving forces which affect the irrational use of drugs	
-Patients , drug misinformation.	-Misleading beliefs -Patient demands/expectations
-Prescribers , lack of education and training	-Inappropriate role models -Lack of objective drug information -Generalization of limited experience -Misleading beliefs about drugs efficacy
-Workplace , heavy patient load	- Pressure to prescribe - Lack of adequate lab. capacity - Insufficient staffing

-Drug Supply System , unreliable suppliers	-Drug shortages -Expired drugs supplied
-Drug Regulation, non-essential drugs available	-Non-formal prescribers -Lack of regulation enforcement
-Industry , promotional activities	-Misleading claims

(Laing , and Ross-Degnan,1992).

A local study was conducted on 2000 by Obeidallah , et al clarified a need to *establish and implement a drug policy* aimed at ensuring not only that effective and safe drugs of good quality are available at affordable prices, but also that drugs are rationally prescribed and used. He summarized the Causes of irrational use of drugs in PNA health institutions as follows:

No national formulary has been published and made available to medical practitioners, there is no control over medical schools; prescribers have graduated from different countries with different training in the rational prescribing of drugs, there are no therapeutic protocols, there is no formal in-service training programme for practitioners, prescribers have few opportunities to access non-biased drug information, and there is no manual on prescribing essential drugs. Also he stated that there are no drug review bodies at various levels of health care to:

Monitor the supply and use of drugs ensure the economic use of drugs, and adequate supplies of critical essential drugs in institutions. Currently, the public sector in the West Bank and Gaza Strip does not have policies to deal with irrational use of drugs. The issue is scarcely addressed. The need to establish and implement a national policy dealing with it is therefore urgent. Several measures could and should be taken in the short run in order to

improve the rational use of drugs while a coherent drug policy is developed (Obeidallah,etal,2000).

2.10 Magnitude of the problem

1-Locally in Palestine

In 2002 by El Khoudary clarified that there was an over use and misuse of antibiotics in treating pediatric acute respiratory infection 77.8% of study children were prescribed antibiotics, and 77.7% of these antibiotics were unnecessary. Amoxicilline trihydrate was the antibiotics of choice for treating acute upper and lower respiratory infection. Antibiotics were prescribed more to older children, high income families, town's children, children with fever, those who had diffuse redness of tonsils and children with wheezes. Both acute lower respiratory infections and tonsillitis cases received more antibiotics than other cases.(El Khoudary ,2002). In the same year another study have been carried out by WHO to determine the magnitude of the problem of irrational drug use and when ,113 isolates of *Streptococcus pneumoniae* from children with acute lower respiratory tract infections were tested for drug resistance. Resistance rates were: penicillin 88%, cefuroxime 85%, erythromycin 63%, tetracycline 45%, chloramphenicol 27% and ofloxacin 2%. Resistances to erythromycin and cefuroxime were significantly associated with penicillin resistance as were hospitalization and previous use of beta-lactam antibiotics. (WHO,2002). Also drug situation analysis study for the West Bank and Gaza Strip was conducted in 2000 by Ministry of Health in collaboration with WHO Health Coordinator in Jerusalem, Coordinator of the Drug Action Program and Essential Drugs Medicines & Policy/WHO which revealed the magnitude of problems relating to irrational prescribing of drugs, specifically:

-A liberal, sometimes arguable, use of antibiotics (40-50% of patients were prescribed antibiotics), analgesics, non-steroid anti-inflammatory drugs (NSAIDs) and steroids.

- Doctor' propensity to prescribe drugs by brand name rather than generic name.

- Questionable combination of different drugs in a single prescription.

-The large number of drugs prescribed to every patient.

The study also highlighted other issues, the most significant of which relates to the doctor-patient relationship. The average consultation time spent by doctors with each individual patient seemed to be insufficient, ranging from less than one minute to three minutes. This could be due to the large number of patients that an individual prescriber may have to see: up to 120 patients during his/her 6.5 hours' duty. Examination of patients in such a context should be considered insufficient since it often results in incorrect diagnosis and inappropriate treatment. Previously, Ross-Degnan et al in 1993 stated that the average patient contact time at health facilities in developing countries, was often only one to three minutes. This is too short for effective communication, and prescribers will not consult guidelines or other information if they are forced to see one patient a minute (Holloway, 2005). Moreover, it is clear that in such circumstances prescriber-patient communication hardly exists and presumably hinders patient's understanding of their disease and of prescriptions, and ultimately their compliance. Addressing the causes of the overcrowding of clinics will require the development of policies and interventions. But it is clear that the quality of care cannot be high when prescriber's workloads are so heavy (Obeidallah, et al,2000). There is no supervision or monitoring of drug use in health facilities. Prescribers are not trained in the application of therapeutic protocols. In-service training on rational prescribing, commonly considered an essential policy measure in efforts to ensure rational use of drugs in health institutions, is never carried out (Obeidallah, et al,2000).

2- Regional:

While the reports from different countries, were not sufficiently comprehensive to determine in detail the scale of antimicrobial drug resistance at regional level, it indicates that drug resistance as a consequence to irrational prescription of antibiotics is both widely present and increasing. Factors contributing to increasing resistance include wide availability of antimicrobial drugs in private pharmacies, often without the need for prescriptions, and unnecessary and widespread use of new generations of antibiotics for uncomplicated conditions. The following sample of studies from the region reflects the great similarity between countries in terms of scope and magnitude of the problem of antimicrobial resistance. Several of the studies listed clearly identify the link between various elements of irrational drug use and resulting drug resistance (WHO,2002).

In Jordan: The percentage of encounters with antibiotics prescribed was 60.9% overall, ranging at different centers from 46.7% to 83.3% (Otoom, et al 2002). The overuse of antibiotics is still a problem in Jordan, despite the negative effects of indiscriminate prescribing and consumption (Otoom, et al 2002). Dr. Asem A. Shehabi presented local data on antibiotic resistance in workshop about Rational Use of Drugs Strategy Development, Jordan, 2004. He noted there had been a dramatic increase in penicillin resistance to Streptococcus pneumoniae (an important community pathogen causing meningitis, pneumonia, otitis media, etc) over recent years. High levels of antimicrobial resistance in urinary and faecal pathogens were also reported with similar rates of resistance occurring to antibiotics commonly used in both out-patients and in-patients (a reflection of high community use of antibiotics). There were also severe problems of antibiotic-resistant nosocomial infection in tertiary hospital neonatal and adult intensive care units. Dr. Shehabi noted that increasing antibiotic resistance required the use of newer,

more expensive and sometimes more toxic antibiotics; it also raised the real danger that physicians will run out of effective antibiotics to treat certain infections. The data highlighted the need for antibiotic control policies.

In Egypt (Assiut): In a major reference hospital 25 *Mycobacterium tuberculosis* isolates from patients who had been treated for at least 1 year for tuberculosis were evaluated. Multi-drug resistance was found among 11 (44%) of the isolates (WHO,2002).

In Iraq (Mosul): Of a total of 600 isolates of *E. coli* collected, of which over 90% were *E. coli* type 1 and 8.3% serotyped as enteropathogenic *E coli*, resistance to 11 antimicrobial agents was assessed. Over 40% were antibiotic-resistant and of these 77.1% were resistant to more than one antibiotic (WHO,2002).

In Kuwait: 1253 urinary tract isolates were analysed for sensitivity to 13 antimicrobial agents commonly used for the treatment of urinary tract infections. High resistance of *E. coli* was noticed to ampicillin, sulfonamides and trimethoprim/sulfamethoxazole. The authors concluded that the "generous policy for the prescription of especially ampicillin and other broad spectrum antibiotics in uncomplicated infections has generated this serious consequence" (WHO,2002).

In Lebanon: 153 clinical enterococcal isolates were tested against 11 antimicrobial agents. The majority of isolates were *Enterococcus faecalis* (72.5%) followed by *Enterococcus faecium* (22.9%). Resistance was found against ampicillin (0.9% and 14%), erythromycin (59% and 40%), tetracycline (72% and 34%), chloramphenicol (32% and 11%), rifampicin (36% and 57%), ciprofloxacin (23% and 34%) and norfloxacin (22% and 8%). The authors concluded that "These variable antimicrobial rates of resistance suggest a surveillance programme for antimicrobial resistance in this country would be helpful to help control

infection, guide empirical antibiotic therapy and implement a policy of antibiotic usage" (WHO,2002).

In Saudi Arabia: A review study concludes that the problem of antimicrobial resistance is widespread, that the causative factors are uncontrolled and that national strategies to address the problem are lacking. The multiplicity of factors driving antimicrobial resistance requires that solutions are built around collaboration of governmental agencies, pharmaceutical companies, health care providers and consumers. Leadership should be provided by a national steering committee on antimicrobial resistance (WHO,2002).

In Sudan (Khartoum): A study of the prevalence of resistance to six commonly used antimicrobial agents in faecal coliforms from children showed high resistance patterns ranging from 96% to ampicillin to 70% to chloramphenicol; 39% of children had isolates resistant to all six antibiotics studied and 80% against at least four. (WHO,2002).

3- Globally:

According to figures gathered by surveys presented to WHO, in 2000, about 60% of antibiotics in Nigeria were prescribed unnecessarily. In Nepal, over 50% of antibiotics prescribed in 1996 were not needed and 40% of medicines expenditure in the same year was wasted due to inappropriate prescriptions (WHO,2004b). In Pakistan (Multan): 2840 urine samples were tested to determine the frequency and antibiotic susceptibility pattern of uro-pathogens. For *E. coli* ampicillin, ceftazidime, nitrofurantoin and gentamicin sensitivity was 26%, 20%, 80% and 65% respectively. Enterococcus isolates showed 40% sensitivity to ampicillin. The authors conclude that the resistance pattern of uro-pathogens causing urinary tract infections to common antimicrobial agents is changing and must be

taken into account when selecting treatment strategies. Therefore, antibiotic policy should be set according to local survey data. (WHO,2002). Globally, the figure for unwarranted antibiotics prescriptions stands at roughly 50%. Irrational use of drugs due to inappropriate prescription can also lead to adverse drug events which cause illness or death. In the United Sates, adverse drug events represent one of the six leading causes of death (WHO,2004a).

"Misuse of antibiotics, overuse of injections, and under-use of life-extending drugs for illnesses such as HIV/AIDS, heart disease, and other chronic illnesses together constitute a global epidemic of irrational use of medicines," explains Jonathan Quick, incoming president and CEO of Management Sciences for Health. "This epidemic results in untold needless suffering and costs millions of lives each year. "Currently, about 20000 medicines are sold on the global market. *WHO's List of Essential Medicines*, which includes examples of medicines addressing all the major diseases of public health importance, contains *316 products*. The wide range of very similar medicines that exist for the same condition can lead to irrational use and all the negative consequences this brings with it (WHO,2004b).

WHO's 2002-2003 data show the following antimicrobial resistance global prevalence rates: malaria (chloroquine resistance in 81 out of 92 countries); tuberculosis (0-17% primary multi-drug resistance); HIV/AIDS (0-25% primary resistance to at least one antiretroviral drug); gonorrhoea (5-98% penicillin resistance); pneumonia and bacterial meningitis (0-70% penincillin resistance in streptococcus pneumonia); diarrhoea: shigellosis (10-90% ampicillin resistance, 5-95% cotrimoxazole resistance); hospital infections (0-70% resistance of staphy-lococcus aureus to all penicillins and

cephalosporins). “The rapid and alarming spread of antimicrobial resistance around the world has not been matched by a concerted and powerful public health response.”

2.11 The concept of essential medicines

Since the 1970s many developing countries have started national programmes for essential drugs to promote the availability, accessibility, affordability, quality, and rational use of medicines. The cornerstones of such programmes are the careful selection of essential medicines for public supply and reimbursement, based on a systematic review of comparative efficacy, safety, and value for money; evidence based national clinical guidelines as the basis for training and rational prescribing; and a national medicines policy to balance conflicting policy objectives and to express government commitment to a common goal (Hogerzeil, 2004). The concept of essential medicines was launched in 1977 with the publication of the first World Health Organization's Model List of Essential Medicines. Since then the list has been revised every two years. By the turn of the century, 156 mostly developing countries have a national list of essential medicines, two thirds of which have been updated in the past five years. Lists of essential medicines are also used by UNICEF , the United Nations high commissioner for refugees, and many non-governmental organizations. Follow up measures have been introduced by UNRWA during 2005 in order to improve rational antibiotic prescribing practices, these measures include preparation of clinical guidlines and updated the 5^{th} edition of UNRWA model formulary “ of Essential medicine “ National lists of essential medicines are used to guide the procurement and supply of medicines in the public sector, reimbursement schemes, medicine donations, and local production of medicine; they also help define the training of health workers. In short, lists of essential medicines provide the scientific and public health basis for focus and expenditure in the pharmaceutical sector.

2.12 The value of clinical guidelines and lists:

Good evidence shows that clinical guidelines and lists of essential medicines, when properly developed, introduced, and supported, improve prescribing quality and lead to better health outcomes. But there is also an economic argument. Firstly, in developing countries pharmaceuticals are the second biggest budget line in the health system, after salaries. Secondly, new essential medicines are expensive. The advantages of limited lists are therefore both medical and economical. From a medical point of view they lead to better quality of care and better health outcomes and help focus quality control, drug information, prescriber training, and medical audit. Economically they lead to better value for money, to lower costs through economies of scale, and to simplified systems of procurement, supply, distribution, and reimbursement (Hogerzeil, 2004). Also The use of clinical practice guidelines can be an effective means of changing behavior, (Grimshaw, and, Russell, 1993) such as promoting the appropriate use of antibiotics. (Cabana, Rand, and Powe,1999).

Table (2.3). Barriers to Clinician Adherence to Clinical Practice Guidelines

Barrier	**Explanation**
Lack of awareness	Clinician unaware that the guidelines exist
Lack of familiarity	Clinician aware of guidelines but unfamiliar with specifics
Lack of agreement	Clinician does not agree with a specific recommendation made in guidelines or is averse to the concept of guidelines in general
Lack of self-efficacy	Clinician doubts whether he or she can perform the behavior
Lack of outcome expectancy	Clinician believes that the recommendations will be unsuccessful
Lack of motivation	Clinician is unable/unmotivated to change previous practices

Guideline-related barriers	Guidelines are not easy or convenient to use
Patient-related barriers	Clinician may be unable to reconcile guidelines with patient preferences
Environmental-related barriers	Clinician may not have control over some changes (eg, time, resources, organizational constraints)

*Adapted from (Cabana, Rand, and Powe,1999)

Effective clinical guidelines should improve patient care while enhancing cost savings. However, cost savings should not be the primary motivating factor. The guidelines should also reflect data on resistance, recognizing that local patterns of resistance often differ across geographic regions. Hence, effective guidelines should be readily adaptable for implementation locally. A meta-analysis of relevant studies has shown that there are numerous barriers to adherence to practice guidelines as in (Table 2.3).

2.13 Impact of Inappropriate Use of Drugs

The impact of this irrational use of drugs can be seen in many ways: reduction in the quality of drug therapy leading to increased morbidity and mortality, waste of resources leading to reduced availability of other vital drugs and increased costs, increased risk of unwanted affects such as adverse drug reactions and the emergence of drug resistance, e.g., malaria or multiple drug resistant tuberculosis, 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 (Laing , and Ross-Degnan , 1992).

Medicines becoming useless due to overuse:

On June 2005 World Health Assembly highlighted a major global health problem: that many medicines are becoming ineffective because their overuse or wrong use have enabled life-threatening microbes to become resistant to antibiotics and other drugs. Action to curb irrational drug use is now urgent, yet not much has been done until now. Both the irrational use of drugs, and the anti-microbial resistance have reached alarming proportions. The World Health Organization says that antimicrobial resistance is one of the world's most *serious public health problems*. A major cause is the wrong use of medicines, worldwide, more than 50% of all medicines are prescribed, dispensed or sold inappropriately, and 50% of patients fail to take them correctly. These startling facts were presented by WHO officials at a briefing for World Health Assembly (WHA, 2005) participants on *"Irrational use of medicines damages health and wastes resources."*

Holloway, K. in 2005 reported that: "Only two thirds of the world's population have regular access to medicines, and of the people who do receive medicines, more than half of those people are prescribed medicines incorrectly," "And of the people that are prescribed medicines, more than half of those people fail to take them correctly." Arithmetically, that would mean that *less than a quarter of medicines* prescribed are used appropriately. Holloway also gave some data on adverse consequences of irrational drug use:

- 2.3 to 4.7 million new cases of hepatitis B and C and 160,000 new cases of HIV per year, resulting from 15 billion injections per year, *half of which are non-sterile.*

- 4 to 10 percent of hospital inpatients suffer an adverse drug reaction in developed countries. This is the fourth to sixth leading cause of death in the US and costs $130 billion in the US and 466 million pounds sterling in the UK yearly.

- There is increasing antimicrobial resistance, with resistance of up to 70-90 percent to original first-line antibiotics for dysentery (shigella), pneumonia (pneumococcal), gonorrhoea, and hospital infections (staph. Aureus).

"Irrational drug use is a very serious global public health problem and much more action is needed at national level," she concluded (WHA, 2005).

2.14 Factors contributing to antibiotics overuse:

In addition to the prescription of antibiotics for viral infections, a variety of factors contribute to the inappropriate use of these agents, such as patient expectations, time constraints imposed on the clinician, and the practice of defensive medicine (Schwartz, Bell , and Hughes 1997). Many patients who consult clinicians expect an antibiotic to be prescribed; as a result, clinicians may feel pressured to write antibiotic drug prescriptions to satisfy patients and to maintain good physician- patient relationships. Receiving an antibiotic reinforces the patient's perception that antibiotics are warranted in similar situations. Thus, patients may continue to consult clinicians each time similar symptoms occur, expecting that antibiotics are again needed. Clinicians also may prescribe antibiotics as a rapid means of treating patients' symptoms rather than taking the time to educate patients that antibiotics are not always necessary, especially if a viral infection is suspected. Moreover, clinicians may prescribe antibiotics as part of a defensive approach to avoid the potential sequelae of not prescribing for patients with bacterial infection. However, clinicians should recognize that patient satisfaction is not compromised by the

absence of an antibiotic prescription provided that patients understand the reasons (Hamm, Hicks, and Bemben,1996). Hamm, Hicks, and Bemben have demonstrated that patient satisfaction was affected by patient perceptions that the clinician spent enough time discussing the illness and by patient knowledge about the treatment choice. Decreasing excess antibiotic use is an important strategy for combating the increase in community-acquired antibiotic-resistant infections (Guillemot, Courvalin, and the Working Party,2001). A WHO, 2005 policy paper on "Containing antimicrobial resistance" says that many of the microbes that cause infectious disease no longer respond to common antimicrobial drugs such as antibiotics, antiviral and antiprotozoal drugs. "The problem is so serious that unless concerted action is taken worldwide, we run the risk of returning to the *pre-antibiotic era* when many more children than now died of infectious diseases and major surgery was impossible due to the risk of infection." "Countries should consider regulating and monitoring the quality of drug advertising and of the pharmaceutical industry's promotional practices, and enforcing sanctions for violations "(WHO , 2005).

2.15 Global Strategy for Containment of Antimicrobial Resistance

Antimicrobial resistance is a natural biological phenomenon of response of microbes to the selective pressure of an antimicrobial drug. Resistance may be inherent, which explains the phenomenon of opportunistic infection or acquired.The introduction of every antimicrobial agent into clinical practice has been followed by the detection in the laboratory of strains of micro-organisms that are resistant. Such resistance may either be a characteristic

associated with the entire species or emerge in strains of a normally susceptible species through mutation or gene transfer. With the widespread use of antimicrobials, the prevalence of resistance to each new drug has increased. The prevalence of resistance varies between geographical regions and over time, but sooner or later resistance emerges to every antimicrobial. While much evidence supports the view that the total consumption of antimicrobials is the critical factor in selecting resistance, the relationship between use and resistance is not a simple correlation. In particular, the relative contribution of mode of use (dose, duration of therapy, route of administration, dosage interval) as opposed to total consumption is poorly understood. Paradoxically, under use through lack of access, inadequate dosing, poor adherence and sub-standard antimicrobials may play as important a role as overuse. There is consensus, however, that the inappropriate use of antimicrobial agents does not achieve the desired therapeutic outcomes and is associated with the emergence of resistance. For this reason, improving use is a priority if the emergence and spread of resistance is to be controlled (WHO,2001).

The development of antibiotic-resistant

The development of antibiotic-resistant bacteria seems to be an inevitable consequence of using antimicrobial drugs. Antimicrobial resistance has increased since the introduction of antibiotics. Penicillin was first used in the early 1940s and by 1950, most *Staphylococcus aureus* organisms were resistant to the drug by virtue of elaboration of a penicillinase enzyme. Concern about the resistance increased in the late 1990's since then, many governmental and agency reports have been published regarding the agricultural use of antibacterials, advising less use of antibacterials, appropriate choice of antibacterials and regimens, prevention of cross-infection and development of new antibacterials.

Antimicrobial drug resistance (AMR) jeopardizes the effectiveness of the treatment of bacterial, viral, fungal and parasitic infections worldwide (Cosgrove, and Carmeli ,2003). Also in 2003 Radyowijati and Haak stated that high levels of antibiotics use, often clinically unnecessary, have led to steady increase in drug resistance. Low-income countries, whom the majority of the world's population belong, believed to have an important role in this phenomena, where on averages, 35% of total health budget is spent on antibiotics in these countries (Isturis and Carbon ,2000). The emergence of a resistant population of bacteria in a patient as a result of antibiotic use generally occurs through a process termed *"selective pressure."* Studies using special culture techniques show that healthy persons normally harbor small numbers of bacteria that are intrinsically resistant to antibiotics (Olson , et al, 1984).

A survey gathered by Doern , et al, 1996 from 30 U.S. medical centers in 1994 and 1995, of clinically significant outpatient isolates of *Streptococcus pneumoniae*, the most common bacterial cause of most respiratory tract infections, revealed that 23.6 percent of strains were not susceptible to penicillin. Intermediate resistance was detected in about 14.1 percent of isolates, while about 9.6 percent of strains demonstrated high-level resistance. (Doern ,et al,1996). *Appropriate prescribing of antibiotics* may slow the rate at which resistance becomes widespread throughout the community. A study in Finland demonstrated that erythromycin resistance among group A streptococci decreased from 16.5 to 8.6 percent over a four-year period during a nationwide program relying on national guidelines to limit the use of erythromycin (Seppala, et al ,1997). According to the Centers for Disease Control and Prevention, in approximately 50 percent of the antibiotic prescriptions written by office-based physicians are unnecessary (CDC,2001). Also developed countries play a role in the abuse of antibiotics as 110 million prescription of oral antibiotics were written in 1992 in USA many of them have been given unnecessarily

(Mc Caig and Hugles ,1995). A good portion of antibiotic use appears to be for viral or spontaneously resolving bacterial infections. The Centers for Disease Control and Prevention (CDC) estimates that about 100 million courses of antibiotics are prescribed by office-based physicians each year, and that approximately one half of those prescriptions are unnecessary.(Principles of judicious use of antimicrobial agents for pediatric upper respiratory tract infections. Pediatrics 1998). Studies evaluating physicians' prescribing patterns have found that almost 50 percent of office visits for colds and upper respiratory tract infections (URTI), and 80 percent of visits for acute bronchitis are treated with antibacterial agents. (McCaig, and Hughes,1995). This prescribing pattern persists despite the fact that antibacterial agents have no effect against a viral disease such as the common cold. Data from numerous studies show that antibacterial agents do not significantly shorten the duration of illness in acute bronchitis (Fahey, Stocks, and Thomas,1998).

Physicians continue to prescribe antibiotics despite acknowledging the association of antimicrobial use and bacterial resistance. In one study 97 percent of surveyed physicians agreed that overuse of antibiotics is a major factor contributing to antimicrobial resistance. (Watson, et al,1999). However, an evaluation of the practice patterns of these same physicians revealed continued prescribing of antimicrobials for viral illnesses. Other potential harms of indiscriminate antibiotic prescribing include allergic reactions, adverse reactions and drug-drug interactions (Gonzalez, et al , 2001).

The WHO Global Strategy for Containment of Antimicrobial Resistance, addresses this challenge. It provides a framework of interventions to slow the emergence and reduce the spread of antimicrobial-resistant micro-organisms through:

— Reducing the disease burden and the spread of infection.

— Improving access to appropriate antimicrobials.

— Improving use of antimicrobials.

— Strengthening health systems and their surveillance capabilities.

— Enforcing regulations and legislation.

— Encouraging the development of appropriate new drugs and vaccines.

2.16 Drug use indicators for primary health care facilities

In 1993, WHO and INRUD developed and published a standard methodology for selected drug use indicators in health facilities. (WHO, 1993; Quick, et al,1997) Since then, several intervention studies have been conducted using these indicators, and review of the published studies with adequate study design was presented at the 1st International Conference for Improving the Use of Medicines (ICIUM) in Thailand in 1997. These indicators can be used to identify problems in general prescribing and quality of care at the health facilities. Results from the use of these indicators can help identify the motives for irrational use and other problems in the use of medicines. The data collected can then be used to design appropriate interventions and to measure the impact of those interventions (ICIUM,1997).

Table (2.4): Derived standard values for the WHO prescribing indicators

(ICIUM,1997) 1. Average number of drugs per encounter	1.6 - 1.8
2.Percentage of encounters with an antibiotic prescribed	20.0 - 26.8 %
3.Percentage of encounters with an injection prescribed	13.4 - 24.1 %
4.Percentage of drugs prescribed by generic name	100 %
5.Percentage of drugs prescribed from the essential drug list or	100 %

formulary	

(ICIUM,1997)

2.17 Strategies for promoting judicious use of antibiotics

The clinically and economically inappropriate use of antibiotics is a major international problem which receives comparatively little attention. There is both overuse and under-use. The consequences include preventable mortality and morbidity from treatment failure and unnecessary adverse effects of drugs, increased selection pressure on antibiotic resistant micro-organisms and waste of scarce health care resources. While these problems affect all countries, they are most acute in developing countries that can least afford them (WPCCID,1996). Also it is estimated that half or more of all medicines are used inappropriately worldwide, both by providers and consumers (Holloway, 2005). A review by WHO in 2004 of 630 medicine use surveys done during 1990-2004 in developing and transitional countries shows that more than half of all patients are not treated in compliance with clinical guidelines (WHO, 2004). The overall WHO Medicine Strategy for 2004-2007. was 4 policy, access, quality & safety and rational use. A major step towards rational use of medicines was launched in 1977 with the publication of the first World Health Organization's Model List of Essential Medicines., designed to help countries formulate their own national lists. In 1989, the International Network for the Rational Use of Drugs (INRUD) was formed to conduct multidisciplinary intervention research to promote the rational use of medicines with a particular emphasis on resource poor countries. (WHO, 2002). The desired goal is clinically appropriate, cost-effective and equitable use of antibiotics in order to slow the development of antibiotic resistance and improve health outcome, to attain this, the recommended strategies are:

1. Informational and educational factors and policies

“To write prescriptions is easy, but to come to an understanding with people is hard” (Kafka, 1952). Most doctors are aware that antibiotic resistance is an emerging problem created largely by the overuse of antibiotics (Schwartz , Bell , and Hughes, 1997). This widespread awareness of doctors suggests that providing information or education alone will be insufficient to change their prescribing behavior. Overcoming barriers to more judicious prescribing will require development of materials to support change, implementation of effective techniques to catalyze that change, and development of supportive structures in healthcare organizations. Key elements include evidence based recommendations for diagnosis and treatment backed by professional societies; materials for patient education; and information to facilitate provider-patient communication (Edward, and Benjamin, 1998). Educational approach attempt to inform or persuade prescribers, dispensers, or patients to use antibiotics in the proper, rational and efficient way. There are many types of this approach such as continuing medical education (CME) activities (meetings, conferences, online access) (Christakis, et al 2001), in-service training, face-to-face education, small group discussions, seminars, workshops and printed education materials (Ross-Degnan, et al,1992; Smith, 1996; Kafle, et al 1992). Some studies have shown that a short, interactive, problem-oriented training course using appropriate training materials significantly improved drug prescribing practices (Laing , and Ruredzo, 1989; Widyatuti , Andajaningsih, and Dwiprahasto 1999). One important foundation for long-term improvement in drug use is improving the quality of pre-service training about therapeutics.(Montagne, 1995; Geest, 1987). Face to face education or persuasion is a common intervention strategy. It consists of interactive group discussions for prescribers and / or patients. The principle of this method is to talk directly to practicing prescribers and patients about appropriate antibiotics use. Approaches based on face-to-face contact are educational outreach, patient education and influencing opinion

leaders (Management Science for Health, 1997; Soumerai, McLaughlin, and Avorn ,1989; Ross-Degnan et al 1992; Ross-Degnan et al 1997). In educational outreach or "academic detailing", which is usually used to improve prescribing practices after completion of training, brief, targeted, face-to-face educational visits to clinicians, principles of communications theory and behavioral science are combined with conventional education technique (Soumerai, and Avorn 1990). This method provides information to physicians about medicines that are often used inappropriately and to promote their replacement with more therapeutic alternatives (Soumerai, and Avorn 1990). It is successful but may not be practical or cost-effective in many countries (Thomson et al, 2000). Another educational approach, small group discussion, attempts to explore the underlying causes of irrational use of medicines. Results are then used to develop specific interventions (Santoso et al ,1996). Also on site a small-group face-to-face educational intervention had greater effect in reducing the inappropriate use of medicines than a large-group formal seminar away from the work-site (Suryawati, 1993). Similarly Many studies have shown that education at an individual or small group level and peer education are effective strategies to change doctors' antibiotic prescribing behaviour (Ekedahl, et al 1995). The effectiveness of peer education is enhanced when the message is delivered or endorsed by local opinion leaders and is made relevant to the doctor's own practice. Previous successful programmes have used retired doctors, (Schaffner, et al 1983) and clinical pharmacists (Avorn , and Soumerai, 1983). Establishing credibility, defining clear objectives for behaviour change, and repetition and reinforcement are all important for peer education (Soumerai , and Avorn 1990). Also engaging local opinion leaders in the process of disseminating targeted educational messages to their peer group has been shown to be another successful strategy (Finkelstein et al, 2001). Patient or consumer education has an important role in improving irrational use of drugs since inappropriate prescribing patterns may derive from the

demands of patients. These demands are often exaggerated by prescribers to justify their prescribing habits. (Management Science for Health , 1997; WHO,1997). At health facilities in developing countries, the average patient contact time is often only one to three minutes (Ross-Degnan et al, 1993). This is too short for effective communication, and prescribers will not consult guidelines or other information if they are forced to see one patient a minute (Holloway, 2005). Printed materials including posters, scientific literature, pharmacy and therapeutics newsletters, journals and printed guidelines are examples of printed materials used as interventions. In general, using printed materials alone as the way to improve prescribing is based on two assumptions. The first is that the main reason for incorrect prescribing is a lack of information. The second is that if prescribers had the correct information, their prescribing would automatically improve (Management Science for Health, 1997). However this is not always the case. Studies in Western countries have shown that distributing printed education materials alone resulted in brief, very small or non-existent improvements in prescribing. Many times these material are not even read by prescribers (Soumerai, 1990). Also previous studies have shown that didactic sessions alone do not help. (Thomson, 2001). Providing feedback to clinicians regarding their own antibiotic prescribing practices has been a successful technique for achieving behavior change (Schoenbaum, 1993). Feedback can entail comparisons with peers or with a standard or indicator. As with practice guidelines, feedback may be most effective when the system is developed with local input, where clinicians accept the measures as important, fair, and relevant to their own practices. New communications technologies such as the internet enhance the potential to disseminate practice guidelines and provide feedback to clinicians. Computer assisted decision support has been used effectively to improve antibiotic prescribing in hospitals and could be extended to outpatient settings (Evans et al, 1998). The willingness of a busy practitioner

to use computer support during consultations with patients, however, has not been assessed. A limitation of all these intervention strategies is that some providers will participate and others will not. Convincing local opinion leaders to change practices will result in eventual diffusion of the changes throughout the community, leading to a change in the standard of care. For this reason, identifying and educating opinion leaders as a priority group would be effective, particularly if resources are limited. Educating future healthcare providers about the importance of judicious antibiotic use will have long term impact and is a useful adjunct to strategies focused on current providers (Gaur , and English, 2006). A multifaceted approach is needed to increase the public's understanding of antibiotic resistance and to change expectations about use of antibiotics. The key elements should include a public relations campaign, clinic based education, and community outreach activities. Conducting a public relations campaign with paid advertising is an effective but expensive strategy to change health related behavior. Educating the public about the difference between bacterial and viral infections, and the potential risk of taking antibiotics, is more complex than other health education messages because the risk to benefit ratio is less clear. A successful public relations effort will require expertise in marketing and communications. In recent years the popular media have been increasing their coverage of antibiotic resistance, and this can enhance the impact of other public education efforts (Edward , and Benjamin, 1998). Medical providers should also seek opportunities for community partnerships to disseminate similar messages widely. For example, educational information can be disseminated through community organizations, schools, childcare centers, and pharmacies. In the short term, patients are likely to benefit from a reduction in unnecessary visits and therapy. In the long term, it is likely that decreased rates of resistance will improve health and cost outcomes (Edward , and Benjamin, 1998).

2. Managerial and infrastructural factors and policies

Managerial strategies attempt to improve drug decision-making by a variety of techniques including use of specific processes, forms, packages and monetary incentives. The interventions using this approach include developing and implementing Essential Drug Lists or Drug Formularies, Standard Treatment Guidelines, implementing drug supply kit system, monitoring and feedback, establishing representative Pharmacy and Therapeutics Committees, establishing structured drug prescribing form, providing cost information, and set-up financing (Management Science for Health, 1997; Laing , Hogerzeil ,and Ross-Degnan,1997). A recent review has suggested that locally developed guidelines are more likely to be accepted and followed than those developed nationally without local input or recognition of local needs (Grimshaw and , Russell 1993) . Essential Drug Lists or Drug Formularies provide prescribers with a list of the drugs felt to be most effective and economic in treating important health problems (Ross-Degnan et al, 1997). Standardized diagnostic and treatment protocols are decision rules, which lead health workers to the most appropriate actions based on patient symptoms and clinical signs (Holloway, 2005). Certain factors are important in determining how effective such guidelines will be in changing behavior in different settings, for example, how the guidelines are produced, how the guidelines are disseminated and whether the guidelines are "user-friendly" (Quick , Laing , and Ross-Degnan , 1991). A study from Uganda showed that implementing Standard Treatment Guidelines followed by training and supervision was more effective in reducing the average number of drug prescribed and percentage of cases given antibiotics compared to distributing STG alone (Kafuko , Zirabamuzaale ,and Bagenda, 1999). Another study from Tanzania showed that developing and implementing STGs followed by monitoring reduced incorrect treatment (Wiedenmayer, et al, 1999). Drug supply kits

are an extreme example of the essential drug list concept where a limited number of drugs are supplied in fixed quantities at a regular interval to health facilities. Drug kits are usually used in peripheral areas, which are difficult to supply effectively. (Laing,1990; Ross-Degnan et al,1997) One study of an essential drugs kit program in Yemen showed that the number of drugs prescribed in the intervention district was 1.5 per patient compared to 2.4 in the comparison area, and that both antibiotic use (44% vs. 66%) and injection use (24% vs. 58%) were lower. However, kit systems are more suitable for emergency than regular supply situations (Hogerzeil, et al, 1989). Implementing self-monitoring prescribing practices in health facilities is another type of managerial intervention. In general, there are three steps for implementing self-monitoring. The first is identifying suspected problems in drug use. The second is developing self-monitoring tools and the third is implementing self-monitoring method. A key aspect of the self-monitoring intervention includes the active involvement of the local staff at all stages of the study and use of locally meaningful indicator (Ross-Degnan et al,1997; Laing , Hogerzeil, and Ross-Degnan 1997). Another managerial approach, the utilization audit, involves collecting and analyzing data on past or current prescribing by health facilities, clinical departments, or individual prescribers. Data on performance are usually fed back to prescribers. (Ross-Degnan et al,1997). Drug and Therapeutics Committee (DTCs) to ensure the safe and effective use of medicines in the facility or area under its jurisdiction in developing countries (DTCs) are less established and their success often limited due to a lack of experienced staff and a high staff turnover (Holloway, 2005). Also there has been little critical evaluation of the clinical or economic impacts of this approach in developing countries (Management Science for Health,1997). But in developed countries the beneficial role of hospital therapeutic committees in the promotion of rational prescribing habits, monitoring of drug usage and cost containment are well established (Weekes, and

Brooks 1996). These committees promotes the rational use of drugs through the development of relevant policies and procedures for drugs selection, procurement and use as well as through the education of patients and staff. Additionally they define an antimicrobial utilization review program, with audit and feedback on a regular basis to providers, and promotion of active surveillance of the nature and amount of antimicrobial use in the hospital. The use of delayed prescribing techniques, (Butler, 1998) a strategy of providing the patient with a prescription for an antibiotic but asking that the prescription not be filled unless symptoms do not get better within a few days has been successfully used in one study (Macfarlane et al, 2002).

Infrastructure troubles as lack of laboratory and other diagnostic facilities; high workloads that limit the time spent with patients especially in the public sector; the lack of access to health facilities and drug outlets, especially for rural population; the limited public resources for health departments to enforce regulations or provide independent information and education (WPCCID,1996). Finally, fiscal management strategies may also improve prescribing practices. Providing cost information can encourage physicians and paramedical staff to consider cost in their selections. This includes using cost bar graphs, drawing up facility drug budgets, and printing prices in drug manuals and on requisition forms (Management Science for Health,1997). Supervision with audit, monitoring and peer group review structured order forms, automatic stop orders have all been found to be effective in promoting improved prescribing. Also junior doctors will not prescribe contrary to their chiefs (Holloway, 2005).

3. Regulatory factors and policies

Regulatory factors restrict choices and limit decisions in the use of medicines. Important factors in the health system include: Registration of medicines to ensure that only safe

efficacious non expensive medicines of good quality are available in the market and that unsafe non-efficacious medicines are banned (Holloway, 2005). As long as there is enforcement of registration decisions, not allowing a drug to be registered is an effective strategy to control use. However, banning a product which is already in use carries the risk of encouraging unintended substitutions of drugs which are equally unsafe or ineffective. (Laing, Hogerzeil, and Ross-Degnan, 1997) For example, there is some evidence from Bangladesh that the banning of all antidiarrheals resulted in increased use of metronidazole and mebendazole as "antidiarrheal" substitutes (Chowdhury et al, 1999). Licensing of health professionals to ensure that all practitioners have the necessary competence with regard to diagnosis, prescribing and dispensing; licensing of medicine outlets to ensure that all supply outlets maintain the necessary stocking and dispensing standards; limiting prescription of medicines by level of prescriber, this includes limiting certain medicines to being available only with prescription; setting educational standards for health professionals and developing and enforcing codes of conduct; this requires the cooperation of the professional societies and universities; monitoring and enforcing regulation of medicines promotion to ensure that it is ethical and unbiased i.e. reliable, accurate, truthful, informative, balanced, up-to-date, capable of substantiation and in good taste. Regulatory strategies are extremely important but often poorly enforced. In many developing countries, many prescribers and dispensers are unqualified and unlicensed, many outlets are not licensed, prescription drugs, including antibiotics and injections, are freely available over-the-counter and there is a great deal of unethical and uncontrolled promotion of medicines (Holloway, 2005).

A number of countries have adopted regulations to encourage the use of generic, non-branded drugs. Generic products offer therapeutic efficacy equal to their branded equivalents at much lower cost. In addition, since prescribers and dispensers are often

unaware of the exact ingredients of a drug, regulations requiring generic prescribing or allowing generic substitution can cause unintended errors in therapy (Ross-Degnan et al, 1997). A study from the Philippines showed that the implementation of a drug generic law without education had a lower impact on prescribing practice than regulation paired with education and sanctions (Ross-Degnan, et al, 1997). Administrative incentives and sanctions to encourage appropriate behavior include awards for appropriate prescribing, (WPCCID,1996). Limiting authority to prescribe certain drugs to specialized units, supplying reserve antibiotics only after consultation and approval from an infectious disease expert, automatic stop orders for prophylactic antibiotics and limiting the range of antibiotics for which sensitivity tests are routinely reported (WPCCID,1996). There is a risk with this type of arbitrary limits that patients will not receive essential drugs that they need. Previous study in developed country showed that prescription limits can results in increased use of other, more expensive types of health care (Soumerai, et al,1997). Regulatory interventions may have unintended impacts that could adversely affect the program. Great care should be taken in planning, implementing and monitoring the intended impacts of any regulatory action (Management Science for Health, 1997).

4. Economic factors and policies

Economic factors offer incentives and disincentives in the use of medicines. Important factors in the health system include:

(1) Perverse financial incentives such as:

• Prescribers' salaries from drug sales so encouraging over-prescription of medicines and the use of more expensive medicines.

• Flat prescription or consultation fees covering all medicines in whatever quantities so encouraging poly-pharmacy.

• Insurance policies that reimburse non-essential medicines, incorrect doses and incorrect treatments.

(2) Appropriate financial incentives such as:

• Separation of prescribing and dispensing functions.

• Fees per medicine item preferably covering a full course.

• Insurance policies that reimburse essential medicines and correct treatments.

Economic policies influence very strongly the use of medicines use, yet they are often introduced without regard for their possible impact on use of medicines promotion of medicines (Holloway, 2005).

5. Multiple Interventions

In general combining interventions is likely to have a synergistic effect. A study from Indonesia showed that disseminating leaflets combined with face-to-face education reduced antibiotic use and increase ORS use in diarrhea at health centers (Gani , Tangkilisan , and Pudjilestari,1999).

2. 18 Determinants of antibiotic use in developing countries

Determinants of antibiotic use by community members

Drug use is strongly influenced by cultural preferences and beliefs. Prescribers, dispensers, and consumers share similar perceptions on health, illness, and antibiotics. Antibiotics are often perceived as "strong", almost magical medicines, capable of curing nearly any kind of disease. Many cultures believe that antibiotics also have the ability to prevent disease.

People are willing to pay high prices for antibiotics, and if they cannot afford a full course, will purchase them in smaller quantities. *Self-medication* is often seen as an important determinant of improper antibiotic use. However, a patient's decisions about whether and

how to use antibiotics are themselves influenced by more fundamental factors, e.g. lack of access to appropriate health care, poverty, or the stigma associated with having certain illnesses. Interventions should address these underlying determinants of self-medication, rather than focusing exclusively on the phenomenon itself. The decision to self-medicate or to seek care from other sources is determined by perceived symptoms, knowledge about treatment options, and their availability and accessibility. Advice may be sought from physicians, pharmacists, pharmacy clerks, paramedics, traditional healers, family, or friends at any time during an illness. Each group of advisers has its own specific characteristics, advantages, and disadvantages.

Determinants of antibiotic prescribing

It is commonly believed that physicians' practices are largely determined by what they know about illness and about correct prescribing, but there is little evidence to support this assumption. There are frequent discrepancies between biomedical knowledge and prescribing practices. Knowledge may be necessary for good practice, but improving knowledge may not improve prescribing. Peer norms and the local medical culture are other important influences on antibiotic prescribing. Prescribers in industrialized countries may fear legal action for not practicing evidence-based medicine, but their colleagues in non-industrialized countries may be more concerned about losing clients if they do not deliver a fast cure. Many doctors report that patient demand influences their prescribing decisions. Giving a prescription is perceived as the easiest way to end a consultation, but little is known about whether patients can be satisfied by less harmful drugs than antibiotics. Financial incentives are an important factor to prescribers, and fear of losing business or the higher profit margins of expensive drugs may result in inappropriate practices. Some physicians believe their reputations would suffer if they do not prescribe

desired antibiotics. This economic rationale is especially strong in private settings where patients pay for services (Radyowijati and Haak,2002).

2.19 Methods of changing physicians' behavior

Six general methods of changing physicians' practices have been described: education, feedback, participation by physicians in efforts to bring about change, administrative rules, financial incentives, and financial penalties (Eisenberg ,1986). Although each method has shown some success on its own, interventions that rely on more than one method appear to be the most successful.

Education

Changes in practice can occur with continuing medical education, however, especially when the curriculum is designed to change specific types of behaviors (White et al,1985). Clinical practice guidelines, another form of education, have gained popularity as a means of influencing physicians' practices (Audet, and Greenfield, 1990). Such guidelines are primarily educational, in that they attempt to inform practitioners about optimal strategies for diagnosis and management. Most studies of the effect of practice guidelines have examined changes in physicians' practices, not changes in patient outcomes. Even by this measure, clinical practice guidelines have been remarkably unsuccessful in influencing physicians (Kosecoff et al,1987; Lomas et al,1989).

Why are most physicians not influenced by practice guidelines? Several explanations have been offered. First, some guidelines are not written for practicing physicians, but focus instead on the current state of scientific knowledge (Lomas, 1991). Physicians may have difficulty applying guidelines of this type to specific patients. Second, physicians may disagree with or distrust guidelines written by so called national experts. Interviews with

practicing physicians indicate that many rely primarily on their own experience or colleagues' recommendations in deciding whether to adopt new techniques or interventions (Greer,1988). Finally, physicians may choose to ignore guidelines because of non clinical factors, such as financial incentives or the fear of malpractice litigation. Thus, despite the current enthusiasm, guidelines by themselves appear to have a limited role in influencing physicians' practices. Although guidelines themselves may not change practice, providing such guidelines to "opinion leaders" (men and women named by their peers as trusted sources of clinical information) appears to offer great promise in altering physicians' practices. In one study, the rate of cesarean section was dramatically reduced when *opinion leaders* were *recruited, trained, and returned to their communities to educate their colleagues* (Lomas et al,1991). In another study, dramatic changes in the perioperative use of antibiotics were seen when department leaders were given literature-based practice guidelines and asked to disseminate them to their colleagues (Everitt et al,1990). The changes in practice that followed this intervention persisted for at least two years. Dissemination of guidelines through opinion leaders is probably more efficient than targeting individual physicians for education (a process referred to as ("*academic detailing*") (Soumerai, and Avorn.,1990).

Feedback

Feedback involves giving physicians information about how their practices or patient outcomes compare with those of other physicians or with an external standard (such as a practice guideline).

Participation by Physicians in the Effort to Change

Many efforts to change physicians' behavior are imposed by outsiders who may not share physicians' personal and professional concerns. Theories of change (Klein,1976) and

common sense suggest that physicians will oppose changes they perceive as threatening to their livelihood, self-esteem, sense of competence, or autonomy. Thus, interventions that decrease physicians' decision-making authority, reduce their income, challenge their professional judgments, or appear to compromise patient care *are more likely to fail*. According to these notions, involving physicians in the effort to effect change should make change less threatening. It seems especially important that physicians perceive the proposed changes as beneficial to patients (or at least not harmful). Meeting this goal is particularly challenging at a time when the nation is seeking to limit expenditures for health care (Klein,1976).

Administrative Interventions

When other efforts fail, changes in behaviour can be sought by means of administrative interventions. At one extreme, changes in behaviour can simply be encouraged either by creating barriers to undesired practices (for example, requiring the approval of a specialist for certain tests or medications) or by reducing barriers to desired practices (for example, by simplifying order forms). At the other extreme, changes in behaviour can be required by laws, regulations, or institutional policies. Interventions that force physicians to alter their practices are in widespread use. Programs in which pharmacists and physicians review prescriptions of antibiotics for inpatients have been successful in reducing expenditures on drugs (Coleman, et al,1991). However, such programs require new personnel (or assign additional responsibilities to existing personnel) and must be maintained indefinitely in order to achieve results. Simpler administrative interventions, such as altering order forms to reflect the preferred dosing intervals for antibiotics (Avorn et al,1988) or eliminating certain diagnostic tests from order forms, (Zaat, Van, and Bonte,1992) have been successful.

Financial Incentives and Penalties

No particular type of intervention is inherently effective, particularly when it is used in isolation. Whether an intervention succeeds depends on the circumstances in which it is used. In general, combinations of methods are superior to single methods of intervention.

Chapter 3

Conceptual Framework

Chapter 3: Conceptual Framework

3.1 Framework

Is a logical structure of meaning that guides the development of the study , to make research finding more clarified and meaningful. Also framework ties together a bunch of discrete components into something more useful and provide direction for the research (Artinian,1982)

3.2 Conceptual map

One strategy for expressing a framework is conceptual map that diagrams the interrelationships of the concepts and statements (Artinian,1982; Fawcett,1999; Moody, 1989; Newman,1979; Silva,1981) .

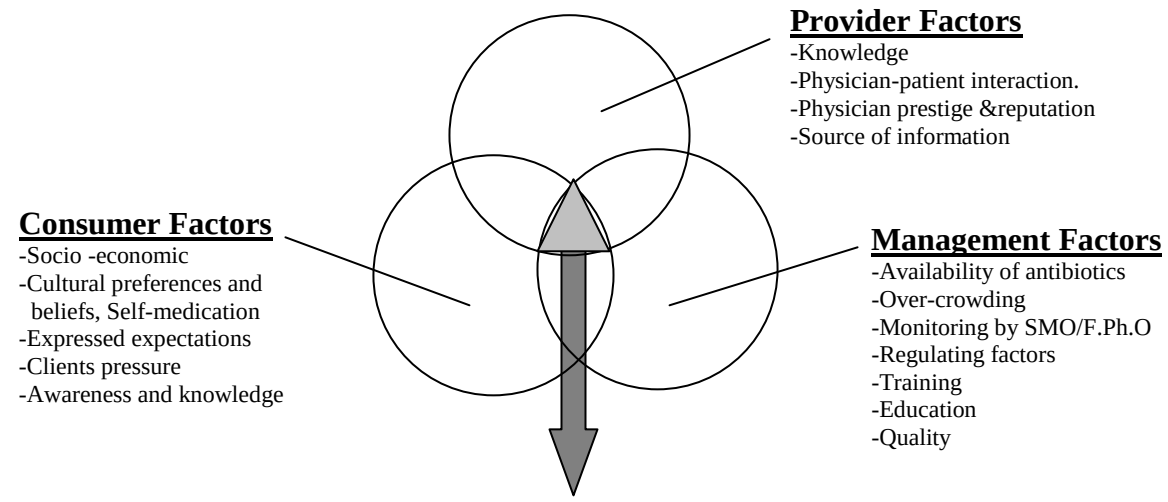
A conceptual map summarizes and integrates what is known about a phenomenon more succinctly and clearly than literary explanation and allows one to grasp the gestalt of a phenomenon, it should be supported by references from literature (Artinian,1982). In addition a conceptual map is developed to explain which concepts contribute to or partially cause an outcome as shown in the figure.

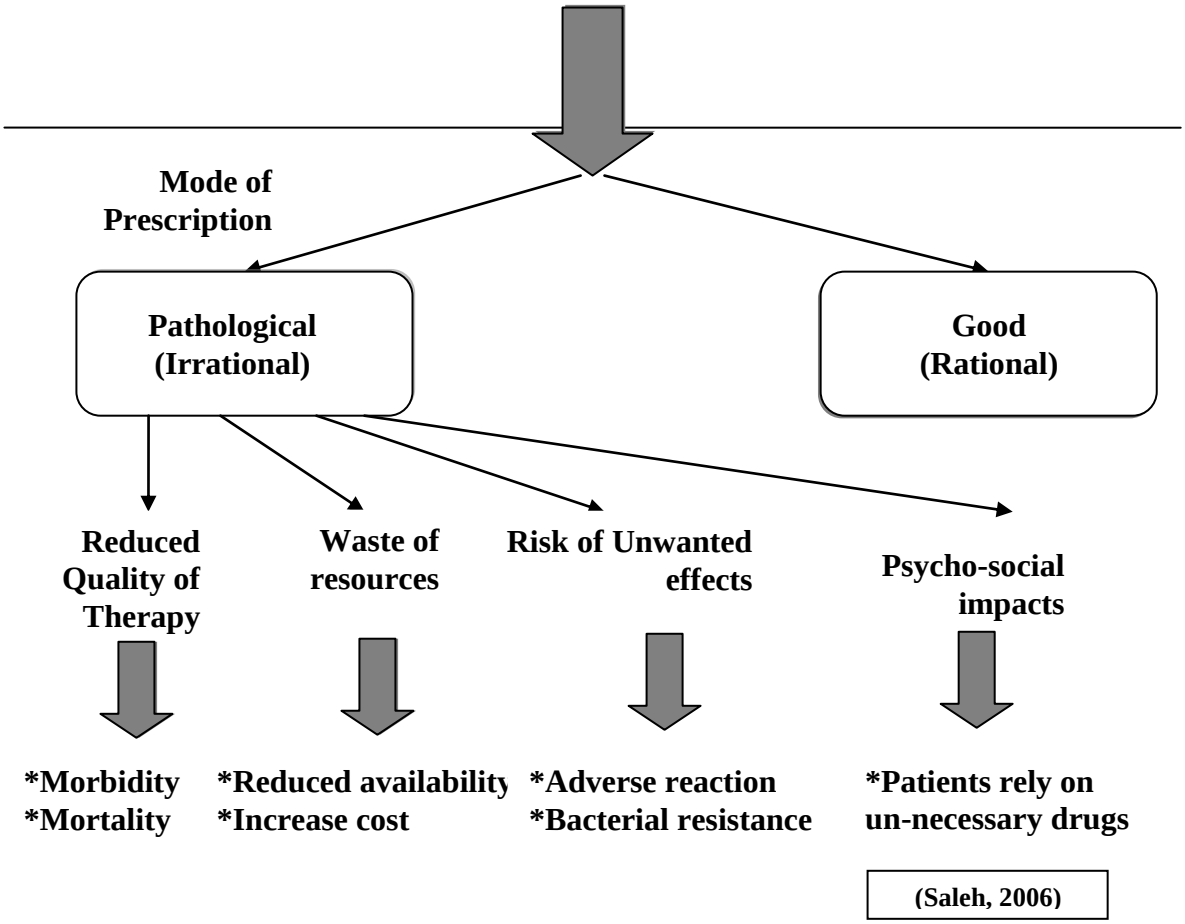
3.3 Factors that could affect the antibiotics prescribing decision

In our study there are many factors that could affect the antibiotics prescribing decision of the general practitioner and may contribute to either rational (good) prescribing pattern or irrational (pathological) prescribing pattern of antibiotics with the consequence of reduced quality of therapy , waste of resources ,risk of unwanted effects, and psycho-social impact.

These factors are divided into three groups as shown in the Framework :

Framework: Factors affecting the decision to prescribe antibiotics





(Saleh, 2006)

1-Provider Factors

Physicians influence antibiotic use in three ways: by writing prescriptions , by prescribing and directly dispensing drugs, or by giving verbal recommendations to buy antibiotics. Doctors' practices can legitimize popular choices of antibiotics, and their previous prescribing can be an important factor in determining self-medication. Despite their importance, there is evidence that some people prefer not to consult physicians for day-to-day health problems, because of the high cost and time investment, lack of trust, or the easier availability of pharmacies. Providers influence on antibiotics prescription affected by the following:-

Knowledge

It is commonly believed that physicians' practices are largely determined by what they know about illness and about correct prescribing, but there is little evidence to support this assumption. There are frequent discrepancies between biomedical knowledge and prescribing practices. Knowledge may be necessary for good practice, but improving knowledge may not improve prescribing. Peer norms and the local medical culture are other important influences on antibiotic prescribing (Radyowijati and Haak,2002). Clinicians also may prescribe antibiotics as a rapid means of treating patients' symptoms rather than taking the time to educate patients that antibiotics are not always necessary, especially if a viral infection is suspected. Moreover, clinicians may prescribe antibiotics as part of a defensive approach to avoid the potential sequel of not prescribing for patients with bacterial infection (Hamm , Hicks, and Bemben,1996).

Physician-patient interaction

Physician-patient interactions are often inadequate. They can be short e.g., a mean of 54 sec was recorded in a Bangladeshi study (Guyon etal,1994), and of poor quality e.g., in Mexico, poor patient-physician communication was partially responsible for the non-compliance of patients with antibiotic regimens (Reyes, et al,1997). Also drug situation analysis by Obeidallah et al 2000 at West Bank and Gaza Strip revealed the average consultation time (minutes) in Gaza Shiffa hospital was 2 minutes and in Rimal PHC clinic was 1.9 and overall average was 1.96 minutes. Prescribers in industrialized countries may fear legal action for not practicing evidence-based medicine, but their colleagues in non-industrialized countries may be more concerned about losing clients if they do not deliver a fast cure. Many doctors report that patient demand influences their prescribing decisions. Giving a prescription is perceived as the easiest way to end a consultation, but little is known about whether patients can be satisfied by less harmful drugs than antibiotics (Radyowijati and Haak, 2002).

Physicians' prestige and reputations

Some physicians believe their reputations would suffer if they do not prescribe desired antibiotics (Radyowijati and Haak, 2002).

Sources of information

These include authoritative and regularly up-dated independent sources of information such as drug formularies, antibiotic guidelines for the management of common conditions, drug bulletins and/or newsletters; ethical codes of conduct concerning pharmaceutical promotion and health workers' interaction with the pharmaceutical industry; data (from audits, surveys, research) about drug prescribing and consumption practices, attitudes,

beliefs, promotional techniques, adverse drug reactions, antibiotic-resistant organisms, etc.; information, education and communication campaigns (IEC) involving all stakeholders, targeting common problems, based on a clear understanding of prevailing drug prescribing and consumption habits, knowledge, attitudes, beliefs and cultural practices (WPCCID, 1996).

2- Consumer Factors

Socio-economic factors

Economic considerations are also important determinants of community antibiotic use. The decision to buy medicines, and the amount of it, is often influenced by factors such as a drug's price and a consumer's ability to pay. Poverty, and lack of access to appropriate health care, but these factors have not been well examined in research studies (Radyowijati and Haak, 2002).

Expressed expectations, clients pressure and physician- patient relationships

Many patients who consult clinicians expect an antibiotic to be prescribed; as a result, clinicians may feel pressured to write antibiotic drug prescriptions to satisfy patients and to maintain good physician-patient relationships. Receiving an antibiotic reinforces the patient's perception that antibiotics are warranted in similar situations. Thus, patients may continue to consult clinicians each time similar symptoms occur, expecting that antibiotics are again needed (Hamm , Hicks, and Bemben,1996). Also their demand for a "pill for every ill"; their expectation that every consultation ends with a prescription; and their perception that a "good" doctor writes "long" prescription; that more is better; their lack of knowledge, especially concerning the risk/benefit concept of medicine, and that patients or parents who expect antibiotics receive them more frequently (Ilett, Johnson, and Greenhill, 2000). These expectations are strongly associated with the patient's previous experiences of receiving antibiotic treatment for these illnesses (Coenen et al, 2004).

Cultural preferences and beliefs

Drug use is strongly influenced by cultural preferences and beliefs. Prescribers, dispensers, and consumers share similar perceptions on health, illness, and antibiotics. Antibiotics are often perceived as "strong", almost magical medicines, capable of curing nearly any kind of disease. Many cultures believe that antibiotics also have the ability to prevent disease. Common cultural beliefs about antibiotics include the notions that there is a pill for every symptom; antibiotics can heal many illnesses, including dyspepsia and headaches; and injections are more powerful than pills. The misuse of antibiotics frequently becomes integrated into the local culture (Haak and Hardon, 1988) (e.g., antibiotics are used to prevent diarrhea after eating suspected contaminated foods or (by prostitutes) to prevent sexually transmitted diseases (Lansang et al,1990) . People are willing to pay high prices for antibiotics, and if they cannot afford a full course, will purchase them in smaller quantities (Radyowijati and Haak, 2002).

Self-medication

Is often seen as an important determinant of improper antibiotic use. However, a patient's decisions about whether and how to use antibiotics are themselves influenced by more fundamental factors, e.g. lack of access to appropriate health care, poverty, or the stigma associated with having certain illnesses. Interventions should address these underlying determinants of self-medication, rather than focusing exclusively on the phenomenon itself (Radyowijati and Haak, 2002).

Awareness and knowledge

The decision to self-medicate or to seek care from other sources is determined by perceived symptoms, knowledge about treatment options, and their availability and accessibility. Advice may be sought from physicians, pharmacists, pharmacy clerks, paramedics, traditional healers, family, or friends at any time during an illness. Each group of advisers has its own specific characteristics, advantages, and disadvantages (Radyowijati and Haak, 2002).

3-Management Factors

Availability of antibiotics

Consistency of drug supply can also affect prescribing. Prescribers in health facilities may adjust prescribing practices to whatever drugs are in stock (Radyowijati and Haak , 2002).

Over-crowding

Clinicians with greater patient workloads prescribe antibiotics for ARIs more frequently (Pshetizky, Naimer, and Shvartzman, 2003).

Antibiotic monitoring systems

Supervision, auditing by SMO and Field Pharmacist Officer (F.Ph.O) considered as key elements in management.

Regulating factors

Formularies, or antibiotic treatment protocols often reduce antibiotic prescription rates (Cash,1996; Turnridge,1995). Adoption of a national essential drug list (EDL) can limit the antibiotics available to prescribers (WHO,1992; Mabadeje, Akintonwa, and Ashorobi

1991). Also clinician behavior can be influenced by restricting formularies (Melander et al,1999). However, implementation of these strategies does not guarantee optimal antibiotic use by clinicians in developing countries because the irregular drug supply, availability of drugs from unofficial sources, and financial constraints also affect antibiotic choices (Munishi, 1991).

Training

The qualifications and training of community health workers, as well as the quality of care they provide, vary from country to country. Unskilled personnel are less aware of the deleterious effects of inappropriate antibiotic use. For example, pharmacy technicians in Thailand prescribed rifampicin for urethritis and tetracycline for young children (Thamlikitkul,1988). A high proportion of patients in some developing countries are treated by untrained practitioners simultaneously with oral and injectable antibiotics administered with contaminated needles and syringes (Haak ,1988) for misdiagnosed noninfectious diseases (Fagbule and, Kalu 1995).

Education

Continuing medical education (CME) changes the attitude of clinicians. Studies of antibiotic misuse in Cuba and Pakistan (Gonzalez Ochoa et al, 1996) recommend continuing medical education for health workers as the single most important tool for combating antibiotic misuse. A study in Zambia has demonstrated the efficacy of education in reducing antibiotic prescription rates (Bexell et al, 1996). However, education has not been successfully implemented in many developing countries, where too often, governments and health workers cannot afford the time and money required for continuing medical education (Robles, and Polack 1997). Health workers in many

developing countries have almost no access to objective health information (Cash,1996). Pharmaceutical company representatives typically outnumber practitioners and often adversely influence their prescription habits (Ronsmans, Islam, and Bennish, 1996).

Quality of Antibiotics

The quality of many antibiotics and other drugs in developing countries is often below standards in the formulary. In Nigeria for example, substandard ampicillin, ampicillin/cloxacillin, tetracycline, and oxytetracycline capsules have been detected (Okeke, and Lamikanra,1995). In many cases, therapeutic failure is the only indication of substandard drugs. Analytic laboratories to detect substandard drugs are uncommon, and when they exist, health workers, distributors, and consumers are often unaware of them. Besides the risk for therapeutic failure, degradation products or adulterants in poor quality antibiotics can produce sub-inhibitory concentrations in vivo, which increase the selection of resistant strains. Drugs that do not comply with minimum standards are illegal in all countries.

3.4 Pathological prescribing pattern (Irrational)

Inappropriate or irrational prescribing may be regarded as *"pathological"* prescribing. It is estimated that half or more of all medicines are used inappropriately worldwide, both by providers and consumers. (Holloway, 2005). A review by WHO in 2004 of 630 medicine use surveys done during 1990-2004 in developing and transitional countries shows that more than half of all patients are not treated in compliance with clinical guidelines. Such *inappropriate use wastes resources and can cause poor patient outcomes, adverse drug reactions and increased antimicrobial resistance.*

Chapter 4

Methodology

Chapter 4: Methodology

The study is quantitative paradigm which is a formal, objective, systematic process were numerical data are used to obtain information about the world. This approach is used to describe variables, examine relationships among variables and determine cause and effect interaction between variables (Norbeck,1987). Also the quantitative researches hold the position that truth is absolute and that there is a single reality that one could define by careful measurement. To find truth, one must be completely objective, meaning that values, feelings and personal perception cannot enter in to the measurement of reality. Also quantitative researches believes that all human behavior is objective, purposeful and measurement (Burns and Grove,2005). This chapter describes how the study was conducted, it includes the study design, samples, setting, methods of measurement, process of data collection, pilot study, validity and reliability. To increase reliability of the study more than one instrument were used (instruments triangulation).

4.1 Study design

Analytic cross-sectional design which is a design used for the research that collect data on relevant variables one time only (data collected at the same time), it provides a snapshot of the variables included in the study. Two relevant instruments were chosen, WHO antibiotics indicators to review the prescribing practices of the GPs, and structured self administered questionnaire to evaluate their knowledge, attitude and practice. (instruments triangulation).The prescribing encounters will be reviewed retrospectively by drawing a random sample from the historical pharmacies records, and through the patient records retained at the health facility (cases >3 years and pediatric cases 0-3 years) using WHO

prescribing indicators . Half the sample should be drawn from each age group, which represent a mix of *general illness* encounters and ages (WHO,1993).

The essential elements in deciding between retrospective and prospective data for evaluation of antibiotics prescribing patterns are:

- Availability of adequate sources for retrospective data collection (pharmacy registration).
- Patient's records kept at the health facility.
- The specific data available in the patient files as date, diagnosis, name of antibiotics, dose and duration.

Since all are available, so we select the retrospective method, also retrospective data are easier to collect than prospective data, suffer fewer potential biases, and avoid *Hawthorne effect* of prospective study, due to the fact that the providers are aware that their behavior is being observed. To minimize bias due to seasonal variations or interruptions of the medical supply cycle we select the study period from July /2006 to December /2006.

4.2 Study population

The target population is the clients prescriptions (prescribing encounters) who attend the general clinic of UNRWA health centers in Gaza Strip from July to December /2006, and all the general practitioners who are prescribing medicine at UNRWA Health Centers in Gaza governorates.

4.3 Setting of the study

All the 15 UNRWA health centers in Gaza Strip were included in the study as in the table 4.1

Table (4.1) UNRWA network of primary health facilities and the response rate of the Questionnaire distributed to the GPs

Governorates	**Health Centers**	**Target population of GPs**	**Accessible population of GPs**	**Received questionnaire from GPs**	**Response rate**
North	Beit Hanoun	4	4	4	
	Jabalia	12	11	10	
Gaza	Rimal	12	9	7	
	El-Shati	5	4	4	
	Gaza Town	4	3	2	
	El-Zaitone	4	4	4	
Middle	Bureij	6	6	5	
	Nuseirat	12	12	12	
	Maghazi	4	4	3	
	Deir-Balah	4	4	4	
Kh-Younis	Kh-Younis	12	11	10	
	Maen	5	5	5	
Rafah	Rafah	12	8	8	
	Tal Elsultan	5	4	4	
	EL Naser	2	2	2	
	EL Shuka	(New opened)			
Total	16	103	91	84	92.3%

4.4 Sample size

Sample size were determined for the two target populations, the first was for the "prescribing encounters", which is estimated according to WHO recommendation, 1993. There should be at least 600 encounters included in cross-sectional survey and with a greater number if possible. So if 20 Health facilities are included we need a sample of 30 encounters per facility. If fewer facilities are included as in our study, a larger number of encounters should be selected per facility, so that a *minimum* of 600 encounters is reached (WHO,1993). In order to have a representative sample, and to draw conclusions about antibiotics prescribing behavior in UNRWA health facilities all the 15 UNRWA health facilities were included and 72 prescribing encounters per health facility will be chosen to have a sample size of 1080 encounters. The second sample size was for the general practitioners who are prescribing medicine at UNRWA Health Centers in Gaza governorates. As the target population is so small (103), so all the GPs were included in the study to ensure representative data.

4.5 Sampling procedures

To have a conclusions about antibiotics prescribing behavior it is important to follow the following procedures for drawing the samples of health facilities and 1080 prescribing encounters.

1- Health facilities sampling

The primary sampling unit is the *health facility*, this means that facilities are the first Units selected. Then we look for the client records which are sampled from the various facilities to measure the antibiotics prescribing indicators. Many factors related to antibiotics supply and utilization patterns vary at the facility level as geographical location (villages, camp,

and cities), so for that reasons it would be better to include as many different facilities as possible (WHO,1993). In our study all the 15 facilities were included .

2. Prescribing encounters sampling

As the sample size was 1080 and all the 15 UNRWA health centers were included in the study, so we have to draw 72 encounters per health facility, the following sections describe how to draw these encounters, from clients records.

Step 1:- confirm availability and accessibility of medical records: Possible sources of retrospective prescribing encounters data will be the pharmacy records which will provide us with the Ration Card Number for adult files and date of birth for child files.

Step 2:- Locate encounters to be included in the sampling frame. Locate the listing of all clients visits reported during the selected period, 6 months retrospectively from July/2006 to December/2006. These will constitute the *sampling frame* of "target population".

Step 3:- Select encounters at regular intervals over the study period (6 months).

We spread the 72 cases throughout that period 36 children (0-3years) and 36 adults (>3 years), this mean that we have to draw 6 cases every month for each group distributed two cases randomly every 10^{th} day (systemic random selection).

Regarding the sample of general practitioners *all* the GPs were selected who tend to exhibit consistent practices over times, so that a sample drawn at one point in time will provide basically the same results as a sample that covers a longer period (WHO,1993).

4.6 Instrument

To increase reliability of the study more than one instrument were used. The researcher developed two relevant instruments one is self administered structured questionnaire (Annex 4) mainly of close ended questions, to evaluate the knowledge, attitude , practices and personal data of the general practitioners of UNRWA health centers, in order to

achieve the objectives of the research. The scale was validated by 8 experts of different specialties, their comment and evaluation was taken in consideration.

The questionnaire is constructed of four parts:

- Part A: General Practitioner *Knowledge* was assessed by close ended questions related to the concept of antibiotics, generic names, and sources of information.
- Part B: General Practitioner *Attitude* evaluated using the driving forces that influencing GPs' intention (Favor/ Disfavor) to prescribe antibiotics.
- Part C: General Practitioner *Practices* related to examination of the cases, prescribing practices, availability and use of UNRWA Formulary and its effect on prescribing behavior.
- Part D: General Practitioner *personal data* the last part of the questionnaire due to its sensitivity and privacy , which is related to age, gender, years of experience, place of graduation, and training courses about antibiotics.

The second one is checklist about WHO antibiotics prescribing indicators (Annex 6) which is internationally approved, but in order to be more relevant, some modifications was done as the coding of data related to encounters age, antibiotics prescription, numbers of drugs, antibiotics injections, antibiotics from EDL, names of antibiotics and diagnosis mentioned. Data was collected from clients records, and the data collectors recoded the information directly on the checklist.

4.7 Pilot Study

Prior to the process of actual data collection a pilot study was conducted to:

- Refine data collection instrument and methodology.
- Predict where proposed instruments are inappropriate, too complicated, or need modifications.

- Examine reliability and validity of the research instruments, and to have experience with the subjects, setting methods of measurements. In the words “Do not take the risk. Pilot test first” (De.Van,1993).

A pilot study for self administered questionnaire where 8 general practitioners were selected conveniently from different clinics, results of analysis revealed a need for some modification as open ended change to close ended, coding process to facilitate data analysis, and change in the nature of one question about knowledge of generic name. Also the checklist of antibiotics indicators was examined for 33 prescription of antibiotics encounters, some modification in the coding of the indicators were done. The pilot subjects were not included in the study.

4.8 Ethical consideration

1. Permission from the UNRWA C.F.H.P. (Chief Field Health Program).(Annex 3).
2. Ethical clearance from Helsinki committee in Gaza was obtained.
3. Informed consent: as an attached letter to the questionnaire to protect the participants right by: (Annex 2)

   -Ensuring confidentiality by using coding to hide the identity of the participants.

   -All collected data will be kept confidential between the researcher and respondents.

   - Ensure benefit and there is no risk.

4.9 Eligibility criteria

The criteria of general practitioners and the prescribing encounters in the sample decided before hand.

4.9.1 General practitioner:

Inclusion criteria: all the general practitioners who exhibit consistent practices over times during the last year or more at UNRWA clinics.

Exclusion criteria: general practitioner who are on long leave, performing administrative services at the clinics, or on job creation program.

4.9.2 Prescribing encounter:

Inclusion criteria: The sample of general illness encounters reflected in the adults (>3 years) and pediatric cases (0-3 years) which will be drawn from separate sources, Family Files and Child Health Records respectively, half the sample took from each age group , spread evenly over the chosen period from July to December 2006.

Exclusion criteria: clients who receive care for dental, ante-natal care, and non-communicable disease excluded from the study.

4.10 Data collection

The data collected retrospectively from the selected samples of family files, and child health records by checklist of WHO antibiotics prescribing indicators and from all GPs by self administered questionnaire. The checklist used to create rates, averages, and other summary measures to describe the nature and extent of antibiotics prescriptions. The questionnaires used to collect data about knowledge, attitude, practices of general practitioners and also personal data, which were administered to group of general practitioners to : Save money and time, and to provide higher response rate . The sequence of data collections from the health centers, first the questionnaires were given to the group

of G.P, and then collect the clients files from the clerks of the health facility after having the sample from the pharmacy records via systematic random selection, after completing checklist WHO indicators, the questionnaires is collected.

4.11 Response rate

The response rate among GPs was 92.3%

4.12 Validity and reliability

Content validity :

Prescribing encounters checklist is adopted from WHO guidelines (How to investigate drugs use in health facilities WHO,1993) so its valid as its internationally approved. The self administered scale was validated by 8 experts of different specialties, their comment and evaluation was taken in consideration.

Reliability:

To improve reliability we adopt the following :

- Increase the numbers of measurements (two instruments).
- The items selected are relevant to the topic of the measurement.
- Standardize the measurements.
- Standardize the implementation.

4.13 Period of study

The research started in the year 2006 first with introduction, literature and conceptual framework in June 2006, after approval of the proposal by the School of Public Health Alquds University and ethical letter was sent to the Helsinki committee. Self administered constructed questionnaire and Prescribing encounters checklist were completed on

February 2007 after a pilot study. A permission from the Chief Field Health Program of UNRWA (C.F.H.P), start actual data collection on May 2007. and completed on October/2007.

4.14 Data entry and analysis

Statistical Package For Social Sciences (SPSS) used for entry and analysis of data, constructing of the frequency tables of the study variables formulate the following: The percentage of encounters with an antibiotics prescribed, the percentage of medicine prescribed by generic name, and the percentage of availability of clinical guidelines and EDL. "Chi-square tests" is used for analyzing the relationship between two categorical variables and "t-students test" for continuous variables to assess whether the means of two groups are statistically different from each other, its appropriate whenever you want to compare the means of two groups . "One Way ANOVA" (analysis of variance) statistical analysis used to compare several groups for particular measure, its one way to deal with the relationship between one particular measure(Dependent variable), its a continuous variable and one factor (Independent variable) its categorical variables of nominal or ordinal type , the factor here forms from three or more groups. The aim of One Way ANOVA to compare the mean of the dependent with each categories of independent. P Value <0.05 was considered statistically significant.

4.15 Limitations

Data from dispersed subjects (all UNRWA clinic) will increase the cost with each location, retrospective review of medical records during the last 6 months /2006 needs a lot of effort and time and some file may be lost. Also two instruments were used which is time consuming.

Chapter 5

Results and Discussion

Chapter 5: Results and Discussion

A sample of 1080 prescriptions were studied 72 from each clinic**,** 50% from family files and 50% from child health records using WHO prescribing indicators in addition to 84 structured questionnaire from the general practitioners who practiced more than one year at UNRWA health centers. WHO indicators enable to evaluate several aspects of the GPs prescribing pattern such as percentage of encounters with an antibiotics prescribed, percentage of antibiotics prescribed by generic name, percentage of commonest antibiotics prescribed, average number of drugs per encounter, percentage of encounters with an injectable antibiotics prescribed, in addition to diagnosis mentioned and demographic characteristics of the encounters. It is a cost-effective and provide a simple tool for quickly and reliably assessing the critical aspects of pharmaceutical use in primary health care and no need to expend more resources on these features (WHO,1993).

5.1 WHO antibiotics prescribing indicators

5.1.1 Descriptive finding

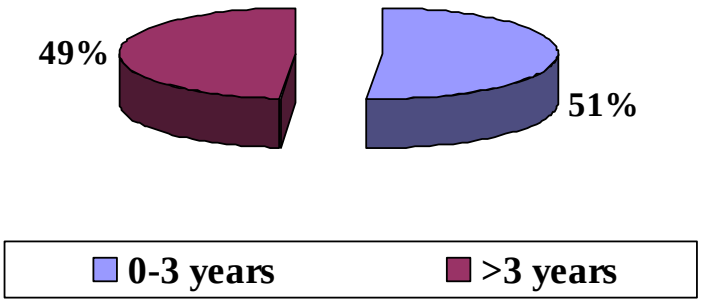
5.1.1.1 Demographic characteristics of study cases

Distribution of the study cases according to demographic characters age and gender revealed the following results.

Percentage distribution of the encounter's age

The result of the study showed that 51.4% are from 0-3 years and 48.6% are more than three years. This is in fact according to our intended plan of study to have 50% from each group for representative sample.

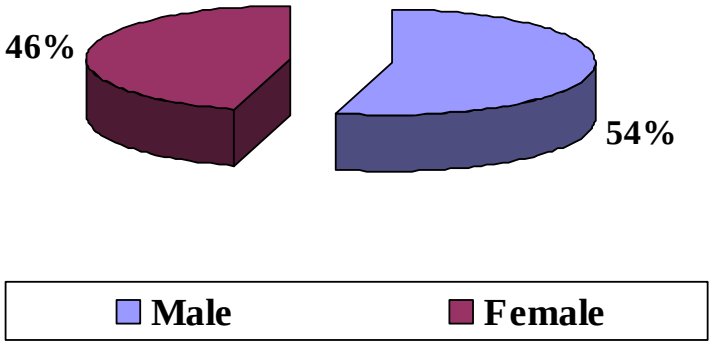
Figure 1: Percentage distribution of the study cases by age



Percentage distribution of encounter's gender:

The male cases were higher than the female cases 54.5% and 45.5% respectively

Figure 2: Percentage distribution of study cases by sex



With the sex ratio male : hfemale equal to 1.197 which is similar to the ratio of total population in Gaza Strip whic is equal to 1.04 (World Fact Book for Gaza Strip,2007)., it is similar to El Khoudary study, 2002 where the male children (55.2%) and female children (44.8%).

5.1.1.2 Frequency of diagnosis noted in the prescriptions

Table (5.1) The predominant diseases in descending rank were upper respiratory tract infections (URTI) (37.1%), diseases of GIT (9.1%), diseases of skin and subcutaneous tissues (6.7%), common colds (5.1%),conjunctivitis represented (3.4%), musculoskeletal diseases (3.1%), allergy (2.6%), lower respiratory tract infection (2.6%), anemia (2.4%), candidiasis (2.2%), acute influenza (1.8%),wheezy chest(1.5%), injuries (1.5%), others (1.4%), fever for investigation (1.3%), headache (0.8%),renal disease (0.7%), post vaccination fever (0.6%), burns (0.4%), STD (0.3%), growth retarded (0.3%), parasitic infestation (0.2%), congenital anomalies (0.2%), piles (0.1%), epilepsy (0.1%), and in (14.6%) no diagnosis were reported in the clients files, this inappropriate prescription needs more GP's attention, and 46.2% of them were prescribed antibiotics, the lowest percentage were piles and epilepsy reached 0.1% respectively. No antibiotics were prescribed for some of the diagnosis as headache, parasitic infestation, fever for investigation, STD, anemia, growth retarded, post vaccination fever, piles, and epilepsy which represent 6.1% of all the diagnosis. Also the study revealed that URTI and LRTI were prescribed antibiotics in 82.8% and 89.3% respectively. Similarly studies from various parts of the world report that over 80% of patients with viral respiratory tract infection receive antibiotics (WHO,2002). Elsewhere acute respiratory infections (20.14%) were the most common illness followed by traumatic injuries for attending the health facilities in Western Nepal (Shankar et al, 2005) .

Table (5.1): Distribution of all the study cases according to the diagnosis and antibiotics prescription

Variables "All the diagnosis"	Antibiotic prescription				Total	%
	Yes		No			
	#	%	#	%		
1-URTI	332	82.8%	69	17.2%	401	37.1%
2-No diagnosis	73	46.2%	85	53.8%	158	14.6%
3-Diseases of GIT	41	41.8%	57	58.2%	98	9.1%
4-Skin disease	41	56.9%	31	43.1%	72	6.7%
5-Common Cold	3	5.5%	52	94.5%	55	5.1%
6-Conjunctivitis	34	91.9%	3	8.1%	37	3.4%
7-Musculoskeletal disease	2	5.9%	32	94.1%	34	3.1%
8-Allergy	1	3.6%	27	96.4%	28	2.6%
9-LRTI	25	89.3%	3	10.7%	28	2.6%
10-Anemia	-	-	26	100.0%	26	2.4%
11-Candidiasis	3	12.5%	21	87.5%	24	2.2%
12-A Influenza	3	15.8%	16	84.2%	19	1.8%
13-Injuries	13	81.3%	3	18.8%	16	1.5%
14-Wheezy chest	9	56.3%	7	43.8%	16	1.5%
15-Others	4	26.7%	11	73.3%	15	1.4%
16-Fever for investigation	-	-	14	100.0%	14	1.3%
17-Headache	-	-	9	100.0%	9	0.8%
18-Renal diseases	8	100.0%	-	-	8	0.7%
19-Post vaccination fever	-	-	6	100.0%	6	0.6%
20-Burns	4	100.0%	-	-	4	0.4%
21-Growth retarded	-	-	3	100.0%	3	0.3%
22-STD	-	-	3	100.0%	3	0.3%
23-Congenital Anomalies	2	100.0%	-	-	2	0.2%
24-Parasitic Infestation	-	-	2	100.0%	2	0.2%
25-Epilepsy	-	-	1	100.0%	1	0.1%
26-Piles	-	-	1	100.0%	1	0.1%
Grand total	598	55.4%	482	44.6%	1080	100%

5.1.1.3 Antibiotic prescription according to diagnosis

Table (5.2) showed that more than half of the antibiotics prescribed was for RTIs 59.7% (URTI 55.5%,and LRTI 4.2%) the second commonest antibiotics prescription were for GIT disease 6.9% and skin diseases 6.9%. Similarly, data from the National Center for Health Statistics in the United States indicate that approximately three quarters of all antimicrobial drug use resulting from physician office visits is for RTIs (McCaig, and

Hughes,1995). Very few cases of viral infections were prescribed antibiotics (Common Cold and A Influenza each 0.5%), cases with no diagnosis was provided antibiotics in 12.2%. Most "outpatient" RTIs (ie, acute bronchitis, nasal pharyngitis /common cold, and nonspecific upper RTIs) are caused by respiratory viruses for which antibiotic use is not warranted. Although RTIs are caused primarily by viral pathogens and therefore show little or no response to antibiotic treatment (Kaiser, Lew, and Hirschel,1996).

Table (5.2): Percentage of antibiotic prescription according to diagnosis

Variables	Frequency	Percentage of antibiotics prescribed
URTI	332	55.5
Eye diseases	34	5.7
Candidiasis	3	.5
LRTI	25	4.2
Wheezy chest	9	1.5
GIT diseases	41	6.9
Musculoskeletal	2	.3
C cold	3	.5
Skin diseases	41	6.9
Renal disease	8	1.3
Congenital anomalies	2	.3
A Influenza	3	.5
Injuries	13	2.2
Allergy	1	.2
Burns	4	.7
Others	4	.7
No diagnosis	73	12.2
Total	598	100.0

5.1.1.4 Frequency of antibiotics prescribed

In table (5.3) and according to the general practitioner's prescribing pattern antibiotics were prescribed in 55.4%, the consumption is broken down into eight major antibiotic classes:

Penicillin class (29.2%) were the commonest group of antibiotics prescribed to the clients , Cephalosporine class (6.1%), tetracyclines class (0.6%), macrolides class (6.1%), Sulphonamide and trimethoprim class (8.2%), Quinolone class (.4%) Anti-infective

dermatological drugs (1.3%) Anti-infective ophthalmological agents (3.5%), this study showed wide variation in preference for different antibiotics, and antibiotics other than the dermatological and ophthalmological medicines was 50.7% (Figure 3).

Similarly El Khoudary study in Gaza 2002 has shown that Penicillin class was the commonly prescribed antibiotic 72%, Sulphonamide and trimethoprim class 20%, macrolides class 5% and Cephalosporine class 3% . Elsewhere our findings are in accord with Iranian study in Babol, as the most prescribed antibiotics was penicillin specifically amoxicillin and amoxicillin /clavulanic acid, penicillin was prescribed in 33.2% of encounters for male GPs and 27.9% for female GPs (Moghadamnia, Mirbolooki ,and Aghili,2002). Similarly in Norway, the most commonly prescribed antibiotic in general practice for common airways diseases was penicillin V. (Straand, Rokstad,and Sandvik ,1998). The same also in sharjah United Arab Emarates, antibiotics commonly prescribed were penicillin (most frequently amoxicillin) (Hasan, Das, and Mourad 1997). As mentioned before Penicillin represented the most frequently prescribed antibiotics in all countries, ranging from 31% (Finland) to 63% (Denmark) of the total outpatient antibiotic use. For cephalosporin, the proportional use ranged from 0.2% (Denmark) to 20% (Greece), for macrolides from 6% (Sweden) to 30% (Greece) and for quinolones from 2% (Denmark) to 12% (Spain, Portugal and Italy) of the total outpatient antibiotic use (Ferech et al ,2006). The high rate of penicillin prescribed could be related to the low cost, fewer side effects, proven effectiveness, safety and the broad availability of the medication.

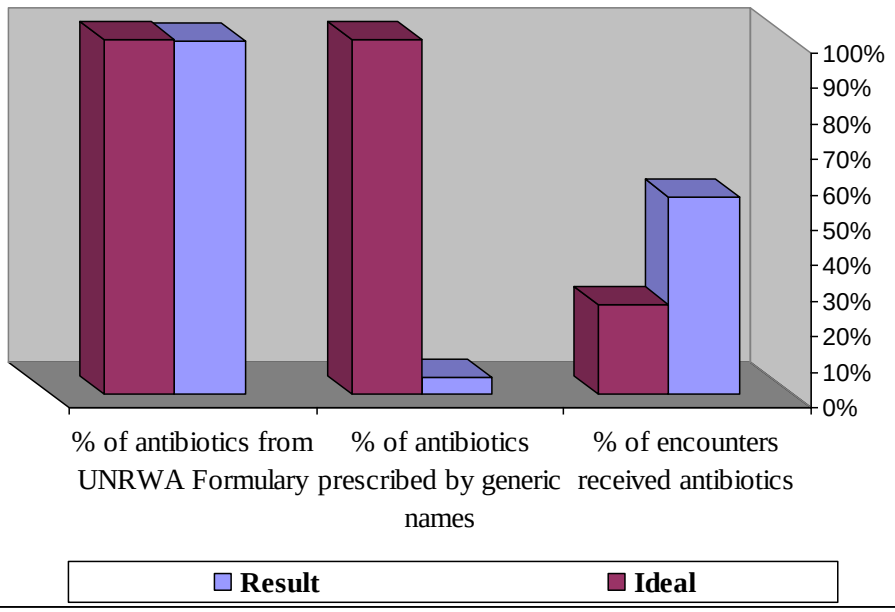
Table (5.3): Distribution of antibiotics prescribed

Variables	Frequency	Percentage
Percentage of antibiotics prescribed	598	55.4%
Antibiotics other than dermatological drugs and ophthalmological agents	546	50.5%
Distribution of antibiotics prescribed according to their names		
Penicillin class	314	29.1%
Cephalosporine class	66	6.1%
Tetracycline class	7	.6%
Macrolide class	66	6.1%
Sulphonamide and trimethoprim class	89	8.2%
Quinolone class	4	.4%
Anti-infective dermatological drugs	14	1.3%
Anti-infective ophthalmological agents	38	3.5%
Total	598	55.4%

5.1.1.5 WHO antibiotics prescribing indicators

In table (5.4) the percentage of encounter receiving antibiotics was 55.4%, also the percentage of encounter receiving antibiotics injection was 2.2%, in addition to the percentage of antibiotics prescribed by generic names was 4.5%, meanwhile the percentage of antibiotics prescribed from UNRWA Formulary was 99.7%. (Figure4)

Figure 4: WHO antibiotics prescribing indicators



This study is not the first in UNRWA health department to quantify the GP's prescribing behavior, the result revealed over-consumption of antibiotics as the rate was 55.4 %. Globally the antibiotics figures for unwarranted antibiotics prescription stands at roughly 50%, exceeding the ideal of WHO 20%-26.8%, (ICIUM, 1997).

In fact the inappropriate use of antibiotics has often been identified as problem in effective health care delivery and results in wastage of scarce resources and wide spread health hazards (WHO, 2006). The irrational antibiotic use is a very serious global public health problem, and much more action is needed otherwise we run the risk of returned to the pre-antibiotic era. Reducing the extent of antibiotics prescription at UNRWA health centers poses multiple challenges for the clinician and the key managers, necessitating urgent interventions at all levels. The results of this study have important implications if injudicious use of antibiotics continues in this way, the emergence and the prevalence of antimicrobial resistance as well as the costs of health care will ever increase.

Frequency of antibiotics prescribed

The over all antibiotics prescribing rate is 55.5%, for age group (0-3) 50.8% and for age group (>3years) 60.2% ranging at different governorate from 49% to 63% , a finding in line with previous UNRWA studies, in 1999 and 2004 which were 53% and 58.2% respectively, but higher than the recorded rate 45% in West Bank and Gaza by Obeidalla et al 2000, however study of El Khoudary ,2002 about the use of antibiotics in pediatrics' acute respiratory infection in PHC in Gaza showed that 77.8% of study cases were prescribed antibiotics. Over-use of antibiotics is a global problem, affecting the developing and developed countries, in Sudan 63% , England 60.7% (Majeed and Moser, 1999) and Islamic Republic of Iran 58% (Cheraghali, et al 2004), and in Babol city in Iran 2002 the overall prescription rate was 61.9%. (Moghadamnia, Mirbolooki, and Aghili, 2002). Also in Jordan antibiotics were prescribed in 60.9 percent of encounters (Otoom, et al ,2002), in Pakistan, antibiotics were prescribed in 52 percent of encounters. (Hafeez et al ,2004) and in western Nepal antibiotic was prescribed in 59.9 percent of encounters. (Shankar et al, 2005). However, in Indonesia (1990), Pakistan (1998) and West Bengal, India, (1999) rates in excess of 70% were observed.(WHO,2004b). Also in Norway 48% (Straand, Rokstad, and Sandvik,1998).

Generally the result is higher than the ideal level of WHO (20-26%), it is worth to mention that the overuse of antibiotics is still a problem in UNRWA Gaza Field such prescribing behavior may be related to both the physician's and patient's attitude towards patient management, and use as needed prescriptions that reduce antibiotics consumption should be encouraged, exploration of patient expectations and providing appropriate information to patient during the consultation may help to reduce the prescribing rate.

Percentage of encounter receiving injectable antibiotics

There are great variations in attitudes towards injections across different society, although the majority are unnecessary. In our study the percentage of encounter receiving injectable antibiotics is low, (2.2%). The WHO average of injectable *drugs* is 13.4%-24.1% (ICIUM,1997). Percentage of encounters with an injection prescribed should be as low as possible because of the risk of communicating diseases and the increased use of healthcare resources. Elsewhere the prescription of injected drugs is high as in Iran, the national average was 41%, with considerable variation ranging from 3%-80% (Cheraghali, et al ,2004). Previously in Babol city Iran injections were prescribed in 58 percent of encounters (Moghadamnia, Mirbolooki, and Aghili ,2002). Also in other areas as Western Nepal an injection was prescribed in 2.25 percent of encounters (Shankar et al, 2005). In addition the results of 35 country studies from 1988 to 2002 which have been evaluated using the WHO standard methodology revealed that on average over 23% of consultations resulted in an injection (WHO,2004b) and Countries with the highest percentage of injections (over 60%) included Indonesia (1988), Pakistan, Uzbekistan and Ghana (Pavin, et al ,2003). Apparently patients and or physicians consider that injections are more effective than oral drugs. In general the decision to administer an antibiotics by parenteral rout is influenced by three factors: Reduce gastrointestinal absorption in patients, lack of appropriate oral antibiotics, specific disease and related severity. The cost of injection therapy is almost always higher than oral dosage forms, and patients requiring parenteral therapy, except in emergency situations, should be referred to a hospital. overall, it is estimated that up to 90% of injections are unnecessary, because alternative, safer routes of administration are available (Pavin, et al ,2003). Excessive use of injections, particularly prevalent in low-income countries, leads to a widespread hazard to health in countries where injection safety cannot be guaranteed (WHO,2004a). Worldwide, it is estimated that unsafe injections

account for 8 million infections of hepatitis B a year, 2 million of hepatitis C, and 75 000 cases of HIV (Simonsen et al ,1999). In a survey in Zaire, two-year-olds had received an average of 24 injections (Mann , et al 1986). In Moldova, where 50% of hepatitis B cases are associated with unsafe injection practices, 39%–57% of the population received at least one injection per year *(Weekly Epidemiological Record,* 1999). In Tanzania (Nsimba , Massele ,and Makonomalonja,2004) and Uzbekistan (Pavin, et al ,2003) injections were prescribed in 38 and 57 percent of encounters respectively also in Jordan, the percentage of encounters where an injection was prescribed was low, at 1.2% overall (range 0%–8.3%) (Khoury and Mawajdeh,2004). In some cultural settings, antimicrobials given by injection are considered more efficacious than oral formulations. This tends to be associated with the over prescribing of broad-spectrum injectable agents when a narrow spectrum oral agent would be more appropriate. Gumodoka et al reported that one in four patients in their medical districts received antimicrobials by injection and that approximately 70% of these injections were unnecessary (Gumodoka et al,1996).

Percentage of antibiotics prescribed by generic name

The percentage of antibiotics prescribed by generic names was very low on average 4.5%, the ideal value by ICIUM, 1997 was 100% so there is great need to emphasize the importance of using the generic names in our prescriptions as the UNRWA Formulary is written by generic names. To change this situation we require information and education measures to encourage prescribing by generic name and ensure commitment by GPs. In western Nepal A total of 1395 drugs (63.5%) were prescribed by generic name (Shankar et al, 2005). The number is more than the (44 %) prescribed by generic name in a previous study (Kafle, Pradhan, and Shrestha, 1992). In Iran 98 percent of drugs were prescribed by generic name (Moghadamnia, Mirbolooki, and Aghili ,2002) which is much higher than the majority of developing countries. In an Ethiopian study more than 89 percent of drugs

in health centers and 71 percent in health stations were prescribed by generic name (Desta et al,1997). In sharejah 1997 all drugs where prescribed by proprietary names (Trade names) and no mention to generic names (Hasan, Das, and Mourad, 1997). In our study there is no statistical significance between governorates about prescription by generic names the highest value is in the middle (5.8%) and lowest is in Khan Younis (1.3%) and on average (4.5%). It is similar to Jordan as the overall percentage of drugs prescribed by generic name was (5.1%) but low when compared with that of Tanzania (82%), India (59%), and Nigeria (58%) (WHO,1993). Study of the world medicines situation in 35 countries from 1988 to 2002 revealed on average more than 60% of medications were prescribed by generic name for the 26 countries (WHO,2004). In Pakistan, India, Uzbekistan and Namibia less than 50% of medications were prescribed as generics (Simonsen, et al, 1999).

Percentage of antibiotics from UNRWA Model Formulary

In our study 99.7% of antibiotics were prescribed from UNRWA Model which clarify the high compliance of GPs with the essential drugs list available at UNRWA clinics, its similar to the WHO ideal value 100%. Active implementation of an Essential drug list has been recommended by UNRWA as an important measure to improve rationalization of medicine prescriptions. The percentage is higher than that reported elsewhere, in Jordan the percentages of prescriptions involving drugs from the essential drugs list averaged 93% (Otoom, et al 2002). In Nepal 75.6 percent of drugs were prescribed from the Essential drug list (Shankar et al, 2005). Study of the world medicines situation in 35 countries from 1988 to 2002 revealed on average, that over 60% of the drugs were prescribed from an essential medicines list, but in Namibia (2001), only 12% of medicines prescribed were from the essential medicines list (WHO,2004a). The majority of low- and middle-income

countries use essential medicines lists in selecting their medicines and are more likely to use these to limit procurement choices than are high-income countries.

Table (5.4): WHO antibiotics prescribing indicators used in the study

Indicators	Results	Ideal values*
Percentage of encounters receiving antibiotics	55.4%	<25%
Percentage of encounters receiving antibiotics injection	2.2%	13.4-24.5%**
Percentage of antibiotics prescribed by generic names	4.5%	100%
Percentage of antibiotics from UNRWA Formulary	99.7%	100%

(* WHO). (**For all injected drugs).

5.1.1.6 Average number of drugs per encounter

As shown in table (5.5) the average number of drugs prescribed per encounter was 2, the minimum value was 1, the maximum value was 5, and SD = 0.805. This is also similar to the result of Fatouh study in Gaza, 2005 rate of 1.92 and better than the result of Obeidalla et al average 2.55 in West Bank and Gaza in 2000 but more than the ideal value of WHO 1.6-1.8 (WHO,1993) , our result is also better than the regional Arabic country, as in Jordan the mean number of drugs was 2.3 (Otoom et al,2002) while in Sharjah, United Arab Emirates the average number of drugs prescribed per encounter was 2.7 (Hasan, Das, and Mourad 1997). Elsewhere in non Arabic country as in Western Nepal the average number of drugs per prescription was 1.5 (Shankar et al, 2005) which was higher than the previous study in 2003 were average of drugs prescribed 1.26 (Shankar et al, 2003). A

study in Pakistani public sector health facilities had reported a mean of 2.7 drugs per prescription (Hafeez et al, 2004). Also a study in Iran had reported a high average of 4.4 drugs per encounter (Moghadamnia, Mirbolooki, and Aghili ,2002). This finding reflects the fact that UNRWA in comparison with other developing countries, has reasonable prescribing practices towards polypharmacy. Increased number of drugs can lead to increased risk of drug interactions, errors of prescribing, toxicity and non-compliance.

Table (5.5): Drugs prescribing indicators used in the study

Indicators	**Results**	**Ideal**
Average number of drugs	2	1.6-1.8
Minimum	1	-
Maximum	5	-
S.D	0.805	-

5.1.2 Inferential statistics

5.1.2.1 Specific diagnosis that affect on antibiotics prescription

Table (5.6) shows that the percentage of RTIs who were prescribed antibiotics (83.2%), more than Wheezy chest (56.3%), and Flu like syndromes (8.1%). The difference between the groups reached a statistical significant level (X^2= 177.3, P= 0.000). Numerous studies have shown widespread unnecessary use of antimicrobials in patients with viral upper respiratory tract infections (Gaur et al,2005). In a study by Macfarlane et al the authors assessed patients' views and expectations when they consult their general practitioners in the UK with acute lower respiratory symptoms and the influence these have on management. They found that most patients think their symptoms are caused by infection, think an antibiotic will help, and want antibiotics. Three quarters of previously well adults in this study consulting with the symptoms of an acute lower respiratory tract illness received antibiotics even though their general practitioners assessed that antibiotics were definitely indicated in only a fifth of such cases, (Macfarlane et al, 1997). Also in the United States more than a fifth of all antibiotic prescriptions for children and adults are written for upper respiratory tract infections or bronchitis, conditions that are almost always viral (Nyquist, et al ,1998;Gonzales, Steiner, and Sande,1997).

Table (5.6): Chi-Square test for specific diagnosis that affect on antibiotics prescription.

Variables Specific diagnosis	**Antibiotics prescription**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
RTIs	357	83.2%	72	16.8%	177.31	0.000
Wheezy chest	9	56.3%	7	43.8%		
Flu like syndromes	6	8.1%	68	91.9%		

5.1.2.2 Encounter's demography (age and gender) that affect on drugs prescriptions

Table (5.7). t-Student test is used to explore the relation between the numbers of drugs prescribed and the age of the encounters, the test is used to assess whether the means of two groups are statistically different from each other. In relation to the number of drugs prescribed, and the age groups, no statistical significant differences between the two mean groups (P-Value 0.071). Regarding gender the means for both male and female are closely similar in the number of drugs prescribed , no statistical significant difference between groups was found (P = >0.333).

Table (5.7): t-Student test for encounter's demography that affect on drugs prescriptions.

Depen. variables: "Drugs prescription"	**Indepen.variables: Demography**	**N**	**Mean**	**S.D**	**t**	**P-value**
# of drugs prescribed	Up to 3 years	555	1.97	0.836	-1.249	0.071
	> 3 years	525	2.03	0.77		
	Male	589	2.03	0.818	1.326	0.333
	Female	491	1.97	0.788		

5.1.2.3 Clinic governorate that affect on number of drugs prescription

One way ANOVA for the relation between number of drugs prescribed and governorates, used to measure the statistical significance differences between different group means. The number of drugs prescription (the dependent variables) which is a continuous variables that will be examined for similarity of the means for every governorate.

In the table (5.8) there were mild differences between the means of governorates ,with the highest mean was for Gaza (Town) (2.07) and the lowest mean was for Khan-Younis (1.93), but there was no statistical significant differences between the different governorates in relation to the mean of drugs prescribed (P value=0.409).

***Table (5.8): One way ANOVA test for clinic governorate that affect on drugs prescription*.**

Dep. Var. "Drugs Prescription"	**Indep. Var. "Clinic Governorate "**	**Mean**	**Sum of Squares**		**DF**	**Mean square**	**F**	**P-Value**
# of drugs prescribed	Middle Khan-Younis Rafah North Gaza	1.99 1.93 1.97 2.01 2.07	Bet. Groups	2.582	4	0.645	0.996	0.409
			Within groups	696.41	1075	0.648		
			Total	698.99	1079			

5.1.2.4 Encounter's demography, and clinic governorate that affect on antibiotics prescription

Chi-square test for the relation between the independent variables as encounters age, gender, and clinic governorate. For the encounter age the percentage of antibiotics prescribed for the age (> 3 years) was 60.2% and for age (0-3 years) 50.8%, the difference between groups reached statistical significance (P Value= 0.002), regarding the genders didn't reach statistical significance (P=0.55), in relation to governorates the highest antibiotics prescription was for the Gaza governorate (62.5%) and the lowest was for the middle governorate (48.8%) which reach the statistical significance (P=0.007), mostly explained by different factors as socioeconomic level, clients expectations, and attitude of the GPs, further studies could be needed to investigate the reasons.

Table (5.9): Chi-Square test for encounter's demography (age, gender) and clinic governorate that affect on antibiotics prescription.

Variables	**Antibiotics prescription**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
Age groups:						
0-3 years	282	50.8%	273	49.2%	9.605	0.002
>3 years	316	60.2%	209	39.8%		
Gender:						
Male	331	56.2%	258	43.8%	0.358	0.550
Female	267	54.4%	224	45.6%		
Governorates:						
North	88	60.7%	57	39.3%	14.161	0.007
Gaza	180	62.5%	108	37.5%		
Middle	137	48.8%	144	51.2%		
Khan-Younis	74	50.3%	73	49.7%		
Rafah	119	54.3%	100	45.7%		

5.1.2.5 Encounter's age, gender, and clinic governorate that affect on antibiotics injections.

In the table (5.10) there was no statistical significance for antibiotics injection in relation to encounter age group (P=0.946) and the same for encounter gender (P=0.654).

In some cultural settings, antimicrobials given by injection are considered more efficacious than oral formulations. Gumodoka et al reported that one in four patients in their medical districts received antimicrobials by injection and that approximately 70% of these injections were unnecessary (Gumodoka et al,1996).

Table (5.10): Chi-Square test for encounter's demography (age, gender) that affect on antibiotics injections

Variables	**Antibiotics injection**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
Age groups: 0-3 years >3 years	 6 7	 2.1% 2.2%	 276 310	 97.9% 97.8%	0.005	0.946
Gender: Male Female	 8 5	 2.4% 1.9%	 324 262	 97.6% 98.1%	0.201	0.654

5.2 Questionnaire

5.2.1 Descriptive analysis

5.2.1.1 General practitioners personal data:

A sample of 84 general practitioners were included in the study from all UNRWA health centers with different education, skills, and experience with response rate about 92.3%. Table (5.11) clarifies the important personal data of the general practitioners which include gender, age, years of experience, place of graduation and if they had received training courses about antibiotics or not.

As shown in the table (5.11) the majority were male general practitioners represented about (79.7%), the remaining were female. In relation to age of GP varied from 26 to 60 years, the mean was 42.29, the median 45.5, and SD equal to 10.1867, more than half (53.6%) aged more than 45 years (>45 years), few (15.5%) from (36-45 years) and the remaining (31%) from (26-35). The majority 64.3% have experience more than 10 years, experience from 0-5 years were 22.6% and from 6-10 years were 13.1%. Regarding place of graduation of the general practitioners the majority were graduated from Arabic countries (69.3%), while the remaining (30.7%) from non Arabic countries.

Most of the respondent (51.3%) have received training courses about antibiotics and the remaining (48.7%) have not. Arabic study of the percentage of women in the labor force in 2003 showed that the highest was in Somalia 43% the lowest in United Arab Emirates 13% other countries as Jordan 24% and Egypt, Lebanon, and Sudan 30%, Oman 17% (Ifad and Firdos,2005).

The percentage of GPs aged (26 -35) is 31% which indicates a high hiring rate of young staff who had low experience about technical instructions including the UNRWA Formulary Model and STG. The high rate of recruitments were in response to the expansion of health services and to improve quality of care by decreasing clients/GPs load.

The percentage is similar to other local study at government sector were the physicians age group (25-34) was 33.8% (Fatouh, 2005).The mean age of the GPs was 42.29, similarly the mean age of the physicians were 43.6 and 40 years in (Hutchinson and Foley ,1999) and (Fatouh study,2005) respectively.

In relation to place of graduation 69.3% graduated from Arabic countries and only 51.3% have received training about antibiotics indicating the need for in-service training to ensure update knowledge of GPs and information about new medicines. In the study there were statistical significance between training courses received by GPs and antibiotics prescribed in sure bacterial diagnosis (P=0.003). Elsewhere in the Netherlands after nine months training intervention which consisted of group education meetings, with a consensus procedure on indication for and type of antibiotics and with training in communication skills; monitoring and feedback on prescribing behavior, group education for assistants of general practitioners, the prescription rates in the intervention group fell from 27% to 23%, whereas the control group's rose 27% to 37% (Welschen, et al, 2004). In a study reported by Steinke et al, non-training practices in Tayside, UK were in general found to prescribe significantly more antibiotics as well as a higher proportion of broad spectrum penicillin, a higher proportion of newer antibiotics and a greater number of different antibiotics per doctor compared to training practices (Steinke et al,2000).

The same concept advocated by the 1985 Nairobi conference , that initial efforts to improve drug use were based on a simple rational actor model which assumed that problems in drug use stemmed from knowledge deficits, among prescribers and consumers and that education and training were appropriate strategy to improve medicines use. Also study by Ross-Degnan et al ,1997 in improving pharmaceutical use in primary health care in developing countries have tested the impact of fourteen interventions of educational strategies such as training seminars and workshops, three (21.4%) of these intervention

achieved large improvement in primary care pharmaceutical use ,seven (50%) showed moderate effects and four (28.6%) had little impact. Two of three interventions were carried out training in large groups using multiple problem oriented sessions (De Vries et al ,1995) at communicating skills.(Lopez linares,1991). The third intervention in Pakistan teaching Hospital (Qazi, Rehman, and Khan,1996) achieved 31% reduction in out patients antibiotics use for ARI , using small group training in case management followed by refresher seminars and ongoing supervision. The most effective training approaches were problem focused , role playing and practical skills development.

Also Gonzalez et al, 1996 found that reduction in community antibiotics use were twice as large (18.9% vs. 8.9%) when multi-method training and supervision for local physicians on ARI management was combined with intensive community education. Study by Ross-Degnan et al ,1997 showed that well-designed training interventions, whether conducted in large or small groups, can successfully improve targeted prescribing outcomes by an average of 15% or more. The impact of training seems to be increased by: employing multiple training modalities (lectures, group problem-solving, role playing, opportunity to practice skills); repeated sessions; focus on one clinical problem at a time; training at the work site; and using opinion leaders or district-level staff as trainers. Also in the present study there were Statistical Significance between of experience years and antibiotics prescribed in sure bacterial diagnosis (P values 0.013).

Table (5.11): Distribution of study General Practitioners by personal data

Variables	Frequency	Percentage
Gender:		
Male	63	79.7%
Female	16	20.3%
Total	79	100%
Age group:		
26-35	26	31%
36-45	13	15.5%
>45	45	53.6%
Total	84	100%
Years of experience		
0-5	19	22.6%
6-10	11	13.1%
>10	54	64.3%
Total	84	100%
Place of graduations		
Arabic countries	52	69.3%
Non Arabic countries	23	30.7%
Total	75	100%
Governorate:		
North	14	16.7%
Gaza	17	20.2%
Middle	24	28.6%
Khan-Younis	15	17.9%
Rafah	14	16.7%
Total	84	100%
Receiving training courses: about antibiotics:		
Yes	40	51.3%
No	38	48.7%
Total	78	100%

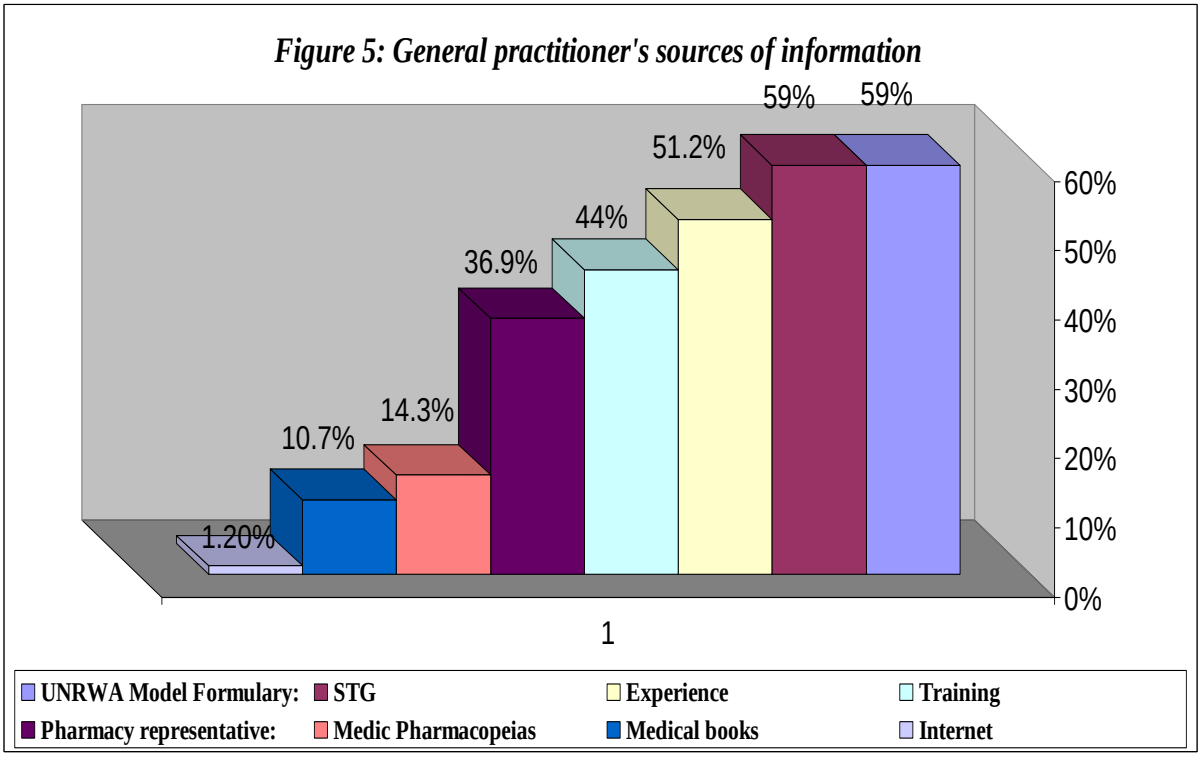
5.2.1.2 General Practitioners knowledge

Table (5.12) illustrated the variables related the respondents knowledge, regarding the definition of an antibiotics it was moderate as (67.9%) provide correct answer, while (32.1%) provide incorrect answer. The vast majority of GP (89.3%) were aware about the danger to the clients associated with taking antibiotics, and (98.8) of the respondent were agreed with the statement of "rational antibiotic use".

About half of the respondent (48.2%) mentioned the seven correct generic names of antibiotics, while (26.5%) mentioned six correct names out of seven, (22.9%) mentioned five or less, and (2.4%) incorrect. Regarding the importance to know the generic names (71.4%) of the respondent mentioned the values to know the generic names of antibiotics.

Sources of information

Knowledge which rely on guidelines as UNRWA Formulary and STG and researches aim to reduce inappropriate variations in practice and to promote the delivery of evidence-based health care, but there are other sources of knowledge as experience, training courses and pharmaceutical representative**.** (59%) of the respondent mentioned "UNRWA Model Formulary" as a sources of information**,** also (59%) mentioned the STG, experience (51.2%), training (44%), pharmaceutical representative (36.9%). Medical pharmacopeias (14.3%), medical books (10.7%), and internet (1.2%) (Figure 5).



In many developing countries health workers have almost no access to objective health information (Cash R, 1996). Pharmaceutical company representatives typically outnumber practitioners and often adversely influence their prescription habits (Ronsmans Islam , and Bennish 1996) as reflected by sales of nonessential drugs and drug combinations (Hartog ,1993).

Table (5.12): Distribution of the study General Practitioners by their knowledge

Variables	Frequency	Percentage
What is the definition of an antibiotic:		
Antibacterial, antifungal, antiviral ,and anti-parasitic	12	14.3%
Drug kill or prevent growth of bacteria and fungi	9	10.7%
Drug kill or prevent growth of bacteria	57	67.9%
Drug prevent growth of bacteria and parasite	1	1.2%
Non of the above	5	6%
Awareness of GP of any danger:		
Emerging of antibiotics resistance	1	1.2%
Allergy	5	6%
Kill friendly microbes	1	1.2%
Misuse	2	2.4%
all of the above	75	89.3%
Rational antibiotic use involves "The correct antibiotic, administered by the best route in the right amount, at optimum intervals for the appropriate period and after an accurate diagnosis"		
Yes	83	98.8%
No	1	1.2%
Mention the generic names		
All of them are correct	40	48.2%
Most of them are correct	22	26.5%
Some of them are correct	19	22.9%
Non are correct	2	2.4%
What is the importance of generic name of antibiotics: “Generic names facilitate good communication, avoid manipulation, monopolies &generate knowledge”		
Yes	60	71.4%
No	24	28.6%

5.2.1.3 General Practitioners attitude

The driving forces that influence (favor) the GP to prescribe antibiotics

As represented in the table (5.13), the majority (95.2%) mentioned that purulent discharge favor them to prescribe antibiotics, in addition to antibiotics resistance concern (48.2%) fever (65.1%)., patient satisfaction 8.3% and time pressure (72.6%).

Elsewhere in a study from five districts of Tamilnadu state, in India,: 285 general practitioners and specialists believed that antibiotics are over-prescribed, especially broad-spectrum antibiotic, and purulent discharge (65%), antibiotic-resistance concerns (48%), fever (40%), and patient satisfaction (29%) were proposed as the strong reasons to prescribe an antibiotic (Sivagnanam et al 2004). Factors like patient and time pressures, diagnostic and treatment uncertainties, poor patient compliance due to high cost and fear of antibiotic resistance are the key forces behind irrational prescription of antimicrobial combinations (Stohr, 2000).

The driving forces that decrease (disfavor) the GP to prescribe antibiotics

Patients request expectation (96.4%), potential return visit costs (94%), patients satisfaction (91,7%), treatment uncertainty (66.7%) and antibiotics resistance concern (51.8%). Similarly in Massachusetts Physician survey, 1998 in which the physicians indicated the factors which influenced them to increase antibiotic prescribing as purulent discharge 64%, diagnostic uncertainty 62%, Patient request 59%, and factors which decreased their overall prescription of antibiotics are concern over emerging antibiotic resistance, 66% , and medication cost, 33%. In Bharathiraja, et al ,2005, it was found that the presence of fever increased the likelihood of antibiotic being prescribed. This is largely due to the fact that the practicing physicians tend to consider fever as a sign of bacterial infection, which is not the case always . Also in over-crowding, clinicians with greater

patient workloads prescribe antibiotics for ARIs more frequently (Pshetizky, Naimer , and Shvartzman , 2003). Also a variety of factors contribute to the inappropriate use of antibiotics, such as patient expectations, time constraints imposed on the clinician, and the practice of defensive medicine (Audit Commission London, England: HMSO; 1994).

Physician time constraint is a factor that is frequently mentioned as a hypothesis for antibiotic overuse (Butler et al 1998). Also prescribing just to be safe increases when there is diagnostic uncertainty, lack of prescriber knowledge regarding optimal diagnostic approaches, lack of opportunity for patient follow-up, and/or fear of possible litigation (Paredes, et al 1996). When a parent or child has received an antibiotic prescription for an illness in the past, that experience engenders expectations that the same therapy is required should such symptoms recur (Mainous et al, 1997). Parental expectation is often cited as a reason for antibiotic prescriptions (Vinson, and Lutz ,1993). Patients' expectations and views and doctors' concern that the patient may otherwise re-consult had a powerful effect on doctors' decision to prescribe. Patients who did not receive an antibiotic that they wanted were more likely to be dissatisfied and re-consulted twice as frequently (Macfarlane, et al ,1997).

Attitude of clinicians could be changed by Continuous medical education (CME). Studies of antibiotic misuse in Cuba and Pakistan (McEachern, et al, 1991) recommend continuing medical education for health workers as the single most important tool for combating antibiotic misuse. A study in Zambia has demonstrated the efficacy of education in reducing antibiotic prescription rates (Berwick, Godfrey, and Roessner,1990). In industrialized countries, patients often pressure physicians to prescribe antibiotics (Paredes, et al, 1996).

Table (5.13): Distribution of study General Practitioners by their attitude

Variable: GP intention to prescribe antibiotics	Frequency	Percentage
Fever:		
Favor	54	65.1%
Disfavor	29	34.9%
Purulent discharge:		
Favor	80	95.2%
Disfavor	4	4.8%
Patient request expectation:		
Favor	3	3.6%
Disfavor	81	96.4%
Potential return visits costs		
Favor	5	6%
Disfavor	78	94%
Patient satisfaction		
Favor	7	8.3%
Disfavor	77	91.7%
Time pressure		
Favor	61	72.6%
Disfavor	23	27.4%
Treatment uncertainty		
Favor	24	28.6%
Disfavor	56	66.7%
Antibiotics resistance concern		
Favor	40	48.2%
Disfavor	43	51.8%

5.2.1.4 General practitioners practices

Table (5.14) illustrated the general practitioners practices (83.1%) prescribed antibiotics in sure bacterial diagnosis. Also (64.3%) have received UNRWA Model Formulary, (9.5%) mentioned that its in front of him (on the table), facing problems in using it (28.6%), and lead to improvement in prescribing pattern in (74.5%).

Clinical practice guidelines aim to reduce inappropriate variations in practice and to promote the delivery of evidence-based health care. In our study GPs response about using UNRWA Formulary in their prescription of antibiotics was as follow : currently using (71%), used in the past (9%), and not used (20%) the same mentioned improvement in 74.5% in prescribing pattern after using UNRWA Formulary. Also there were no statistical

significance relation ship between the use of UNRWA Formulary and antibiotics prescribed in sure bacterial diagnosis, (P=0.754). Although physicians interest in clinical guidelines has never been greater, uncertainty persists about whether they are effective, and doubts whether it can perform the behavior there was a good evidence that clinical guidelines and lists of essential medicines, when properly developed, introduced, and supported, improve prescribing quality and lead to better health outcomes (Grimshaw, and Russell ,1993).

Also it is important to mention that the dissemination of printed clinical guidelines or unbiased drug information alone is not sufficient to cause measurable improvements in behaviour, and consistently failed.

However, active dissemination of guidelines through staff training, peer group re-invention of guidelines, or audit and feedback has resulted in improved compliance with the guidelines (Ross-Degnan, et al,1997). Similarly in 1998 Massachusetts Physician survey, formularies were said to exert little influence on prescribing behavior only in 28%.

Table (5.14): Distribution of study General Practitioners by their practices

Variable	**Frequency**	**Percentage**
Antibiotics prescribed in:		
Suspected bacterial		
Yes	59	71.1%
No	24	28.9%
Viral		
Yes	1	1.2%
No	82	98.8%
Sure bacterial diagnosis		
Yes	69	83.1%
No	14	16.9%
Fear of serious condition		
Yes	22	73.5%
No	61	26.5%
Have you received UNRWA Formulary:		
Yes	54	64.3%
No	30	35.7%
Availability of UNRWA Formulary:		
In front of the GP	8	14.8%
In the drawer	17	31.4%
In the keyboard	6	11.1%
At home	23	42.5%
Did you use UNRWA Formulary in your prescription of antibiotics:		
Currently in using	39	71%
Used in the past	5	9%
Not used	11	20%
Problem in using UN Formulary:		
Yes	23	48.9%
No	24	51.1%
Improvement in prescribing pattern after using UNRWA Formulary		
Yes	35	74.5%
No	12	25.5%

5.2.1.5 Reported problems in using UNRWA Model Formulary

Table (5.15) illustrated problems related to UNRWA Formulary in which lack of time due to overcrowding was the most prominent factor (58.3%), followed by not all the antibiotics present in the Formulary (50%). Also insufficient knowledge (29%), difficult to be handled in front of the clients (25%), lack of motivation (25%), the rarest was the lack of continuous training in using it (12.5%).

Table (5.15): Distribution of study General Practitioners by reported problems in using UNRWA Model Formulary

Variable	Frequency	Percentage
Insufficient knowledge Yes No	 7 17	 29% 71%
Lack of training Yes No	 3 21	 12.5% 87.5%
Lack of time due to overcrowding Yes No	 14 10	 58.3% 41.7%
Difficult to be handled Yes No	 4 20	 16.6% 83.4%
Not all the antibiotics present in the Formulary Yes No	 12 12	 50% 50%
Difficult to be used in front of the clients(barrier) Yes No	 6 18	 25% 75%
Lack of motivation to change previous practices Yes No	 6 18	 25% 75%

5.2.1.6 Practices related to Standard Treatment Guidelines (STG)

Table(5.16) shows the respondent practices related to STG which is (72.3%) received the materials, (85.2%) using it (30.1%) facing obstacles in using it ,the majority (92.5%) reported improvement in using it, some of the respondents reported obstacles in using it, as doubts whether it can perform the behavior (31.2%), (37.5%) mentioned lack of familiarity with STG ,lack of agreement to the concept of guidelines about (31.2%) and patient related barriers (43.7%).

Table (5.16): Distribution of the study General Practitioners about practices related to Standard Treatment Guidelines (STG)

Variable	**Frequency**	**Percentage**
Receiving STG	60	72.3%
Using STG	52	85.2%
Obstacles in using STG	16	30.1%
Did you see improvement in using STG	50	92.5%
Reported obstacles in using STG		
Doubts whether it can perform the behavior	5	31.2%
Lack of familiarity with STG	6	37.5%
Lack of agreement to the concept of guidelines	5	31.2%
Patient related barriers	7	43.7%

5.2.1.7 Use of antibiotics as prophylaxis

Regarding uses of antibiotics as prophylaxis in the table (5.17) the respondents reported correct answers in (64.3%) which is the SBE & Rheumatic fever.

Table (5.17): Distribution of study General Practitioners about the use of antibiotics as prophylaxis

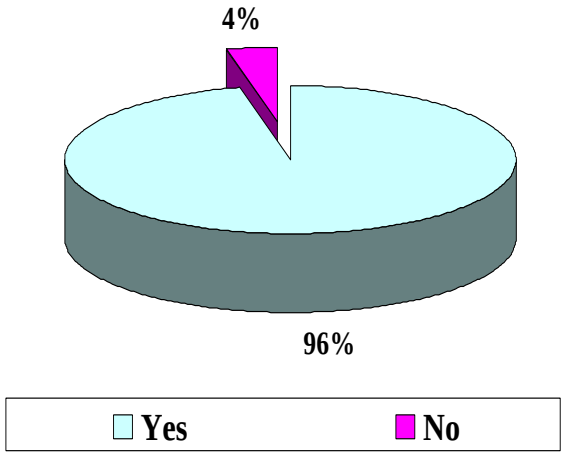
Variables	Frequency	Percentage
Uncertain condition		
Yes	10	11.9%
No	74	88.1%
Fear induced		
Yes	3	3.6%
No	81	96.4%
SBE&Rh-fever		
Yes	54	64.3%
No	30	35.7%
All of the above		
Yes	20	23.8%
No	64	76.2%
Non of the above		
Yes	9	10.7%
No	75	89.3%

5.2.1.8 General Practitioners believe about antibiotics over-prescription

In Figure (6) 96.4% of the respondents reported yes to the general question: Do you believe that antibiotics are over prescribed? Yes : 81 (96.4%), No : 3 (3.6%).

The same finding in Massachusetts Physician survey, 1998:in which 93% of respondents answered yes to the general question: Do you think physicians over-prescribe antibiotics?

Figure 6: General Practitioners' believe about antibiotics over-prescription



5.2.1.9 The most important factors that lead to over-prescriptions of antibiotics

Table (5.18) illustrate the analysis of the open ended question about important factors leading to over-prescriptions of antibiotics the most important were over-crowding (65%). Similarly clinicians with greater patient workloads prescribe antibiotics for ARIs more frequently (Pshetizky , Naimer , and Shvartzman, 2003). Other factors clients pressure (55.7%), antibiotics prescription without diagnosis (36.3%), outside prescription (31.2%), lack of knowledge of some GP (31.3%).The less important was that no evaluation and monitoring of antibiotics (2.5%), the role of job creation's GP (6%) and free of charge (6.17%) (Figure7).

Table (5.18): Distribution of the study General Practitioners by the most important factors that lead to over-prescriptions of antibiotics

Factor	**Frequency**	**Percentage**
1-Overcrowding:		
Yes	52	65%
No	28	35%
2-Clients pressure:		
Yes	44	55.7%
No	35	54.3%
3-Antibiotics prescription without diagnosis:		
Yes	29	36.25%
No	51	63.75%
4-Lack of knowledge of some GP:		
Yes	25	31.25%
No	55	68.75%
5-Outside prescriptions:		
Yes	25	31.2%
No	55	68.8%
6-Poor practices and commercial factor of private sector:		
Yes	17	21.12%
No	63	78.75%
7-To get red of some clients and avoidance of problems:		
Yes	12	15.18%
No	67	84.8%
8-Easy way adopted by the GP to satisfy the clients:		
Yes	11	13.75%
No	69	86.25%
9-Lack of laboratory investigations:		
Yes	9	11.25%
No	71	88.75%
10-No trust of the clients due to prescription without examin:		
Yes	9	11.2%
No	72	88.8%
11-Client-general practitioner relation:		
Yes	8	10%
No	72	90%
12-Economic constrains:		
Yes	8	9.8%
No	73	90.2%
13-No training courses about antibiotics:		
Yes	7	8.7%
No	73	91.25%
14-Belief that some clients will not cure without antibiotic:		
Yes	7	8.6%
No	74	91.4%
15-Low awareness of the clients about hazard of antibiotics:		
Yes	6	7.4%
No	75	92.6%

16-Free of charge: Yes No	 5 76	 6.17% 93.8%
17-Job creation Medical officer: Yes No	 5 78	 6% 94%
18-No evaluations & monitoring of antibiotics: Yes No	 2 79	 2.5% 97.5%

5.2.1.10 General Practitioners' opinion to promote more prudent use of antibiotics:

Table (5.19) illustrated the general practitioners opinion after analysis of the open ended question on how to promote more prudent usage of antibiotics, the results were about half the respondent mentioned that health education of the clients (48.7%), and workshop (47.4%). Other mentioned "to increase community awareness" by using media (28.6%), improving knowledge of GP (29.4%) and implementation of appointment system (25.6%) (Figure 8).

Table (5.19): Distribution of the study General Practitioners by opinion to promote more prudent use of antibiotics

Variable	**Frequency**	**Percentage**
1-Health Education of the clients Yes No	 38 40	 48.7% 51.3%
2-Workshop(training seminar) Yes No	 37 41	 47.4% 52.6%
3-Decreasing overcrowding Yes No	 26 52	 33.3% 66.7%
4-Improving knowledge of general practitioner Yes No	 23 55	 29.4% 70.6%
5-Increase community awareness by TV, Radio , and school health education programs Yes No	 22 55	 28.6% 71.4%

6-Appointment system Yes No	 20 58	 25.6% 74.4%
7-More follow up and supervision Yes No	 19 59	 24.4% 75.6%
8-Proper diagnosis, C&S Yes No	 17 61	 21.8% 78.2%
9-Strict regulation and dispensing of antibiotics Yes No	 13 65	 16.6% 83.45
10-Increase number of general practitioner Yes No	 12 66	 15.4% 84.6%
11-Provision of updated material UNRWA Formulary Yes No	 10 68	 12.8% 87.2%
12-Enough protection and support for the staff: Yes No	 7 73	 8.7% 91.3%
13-Continuous daily pharmacy prescription studies Yes No	 4 76	 5% 95%
14-Improving quality by adopting MHIS Yes No	 3 75	 3.8% 96.2%
15-More cooperation between staff Yes No	 3 75	 3.8% 96.2%
16-Cooperation between all sectors of health :UNRWA ,government, private sectors about importance of rational use of antibiotics Yes No	 3 77	 3.7% 96.3%

5.2.2 Inferential analysis

5.2.2.1 Relation between GPs personal data and antibiotics prescribed in fear of serious conditions

In table (5.20) *Chi-Square test* used to examine GPs personal data that affect on antibiotics prescribed in fear of serious conditions, the result were as follow:

Antibiotics prescribed in fear of serious conditions and age groups of GPs.

The age groups showed statistical significant differences regarding antibiotics prescribed in fear of serious condition (P=0.037). The age 26-35 showed the highest percentage (38.5%), mostly due to low experience and insufficient training.

Antibiotics prescribed in fear of serious conditions and gender.

The percentage for male GPs who prescribed antibiotics in fear of serious conditions was (25.8%) which is slightly higher than female GPs (25%), but the difference between groups did not reach statistical significant level (X^2=0.004, P= 0.947).

Antibiotics prescribed in fear of serious conditions and graduation countries.

The percentage of graduation from Arabic countries were antibiotics prescribed in fear of serious condition was (23.5%) which is lesser than those from non-Arabic countries (30.4%), but the difference between groups did not reach statistical significant level (X^2=0.396, P= 0. 529), the different GPs' educational backgrounds especially from schools in more affluent regions of the world (from more than twenty different countries) did not greatly influence their prescribing behavior.

Antibiotics prescribed in fear of serious conditions and training courses received about antibiotics.

The percentage for those who received training courses were antibiotics prescribed in fear of serious condition was (23.1%) which is lesser than those who did not received training

courses (28.9%). The difference between groups didn't reach statistical significant level (X^2= 0.345, P= 0.557).

Antibiotics prescribed in fear of serious conditions and years of experience.

The percentage for years of experience more than 10 years were antibiotics prescribed in fear of serious condition was (22.6%) which is lesser than 0-10 years (33.3%). The difference between groups didn't reach statistical significant level (X^2= 1.124, P= 0.289).

Table (5.20): Chi-Square test for Personal data that affect on Antibiotics prescribed in fear of serious conditions.

Variables Personal data	**Antibiotics prescribed in fear of serious conditions**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
Age group of GP: 26-35 years >=36	 10 12	 38.5% 21%	 16 45	 61.5% 79%	6.61	0.037
Gender: Male Female	 16 4	 25.8% 25%	 46 12	 74.2% 75%	0.004	0.947
Graduation countries Arabic Non-Arabic	 12 7	 23.5% 30.4%	 39 16	 76.5% 69.6%	0.396	0.529
Have you received training courses about A.B Yes No	 9 11	 23.1% 28.9%	 30 27	 79.9% 71.1%	0.345	0.557
Years of experience 0-10 >10	 10 12	 33.3% 22.6%	 20 41	 66.7% 77.4%	1.124	0.289

5.2.2.2 Relation between (personal data and Governorates) and antibiotics prescribed in suspected bacterial diagnosis

Antibiotics prescribed in suspected bacterial diagnosis and age groups of GPs.

The age groups showed no statistical significant differences regarding antibiotics prescribed in suspected bacterial diagnosis (P=0.687). The age (>36) showed the lowest percentage (68.6%), while age (26-35) was 73.1%.

Antibiotics prescribed in suspected bacterial diagnosis and gender.

The percentage for female GPs who prescribed antibiotics in suspected bacterial diagnosis was (75%) which is slightly higher than male GPs (69.4%), but the difference between groups did not reached statistical significant level (X^2=0.195, P= 0.659).

Antibiotics prescribed in suspected bacterial diagnosis and graduation countries.

The percentage of graduation from Arabic countries were antibiotics prescribed in suspected bacterial diagnosis was (70.6%) which was higher than those from non Arabic countries (65.2%), but the difference between groups did not reached statistical significant level (X^2=0.213, P= 0.644).

Antibiotics prescribed in suspected bacterial diagnosis and training courses received about antibiotics.

The percentage for those who received training courses were antibiotics prescribed in suspected bacterial diagnosis was (66.7%) which is lesser than those who did not received training courses (73.7%). The difference between groups didn't reach statistical significant level (X^2= 0.452, P= 0.501).

Antibiotics prescribed in suspected bacterial diagnosis and years of experience.

The percentage for years of experience more than 10 years were antibiotics prescribed in suspected bacterial diagnosis was (67.9%) which is lesser than 0-10 years (76.7%). The difference between groups didn't reach statistical significant level (X^2= 0.712, P= 0.399).

Antibiotics prescribed in suspected bacterial diagnosis and clinic governorate.

The governorates revealed statistical significant differences regarding antibiotics prescribed in suspected bacterial diagnosis (P=0.004), the Middle governorate showed the highest percentage (83.3%), Gaza (82.4%), Rafah (78.6%) Khan-Younis (71.4%) and the lowest North (28.6%)

Table (5.21): Chi-Square test for Personal data and Governorates that affect on antibiotics prescribed in suspected bacterial diagnosis.

Variables Personal data	**Antibiotics prescribed in suspected bacterial diagnosis.**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
Age group of GP: 26-35 years >=36	 19 35	 73.1% 68.6%	 7 16	 26.9% 31.4%	0.163	0.687
Gender: Male Female	 43 12	 69.4% 75%	 19 4	 30.6% 25%	0.195	0.659
Graduation countries Arabic Non-Arabic	 36 15	 70.6% 65.2%	 15 8	 29.4% 34.8%	0.213	0.644
Have you received training courses about A.B Yes No	 26 28	 66.7% 73.7%	 13 10	 33.3% 26.3%	0.452	0.501
Years of experience 0-10 >10	 23 36	 76.7% 67.9%	 7 17	 23.3% 32.1%	0.712	0.399
Governorates: North Gaza Middle Khan-Younis Rafah	 4 14 20 10 11	 28.6% 82.2% 83.3% 71.4% 78.6%	 10 3 4 4 3	 71.4% 17.6% 16.7% 28.6% 21.4%	15.495	0.004

5.2.2.3 Relation between (personal data and Governorates) and antibiotics prescribed as prophylaxis in SBE and Rh. Fever

Antibiotics prescribed as prophylaxis in SBE and Rh. Fever and age groups of GPs.

The age groups showed no statistical significant differences regarding antibiotics prescribed as prophylaxis in S.B.E and Rh. Fever (P=1.00). The age (>36) showed the same percentage (65.4%), as the age (26-35).

Antibiotics prescribed as prophylaxis in SBE and Rh. Fever and gender.

The percentage for female GPs who prescribed antibiotics as prophylaxis in SBE and Rh. Fever was (75%) which is slightly higher than male GPs (61.9%), but the difference between groups did not reach statistical significant level (P= 0.328).

Antibiotics prescribed as prophylaxis in SBE and Rh. Fever and graduation countries.

The percentage of GPs graduation from Arabic countries were antibiotics prescribed as prophylaxis in SBE and Rh. Fever was (71.2%) which was higher than those from non Arabic countries (60.9%), but the difference between groups did not reach statistical significant level (P= 0.379).

Antibiotics prescribed as prophylaxis in SBE and Rh. Fever and training courses received about antibiotics.

The percentage for those who received training courses were antibiotics prescribed as prophylaxis in SBE and Rh. Fever was (75%) which is higher than those who did not received training courses (55.3%). The difference between groups didn't reach statistical significant level (P= 0.067).

Antibiotics prescribed as prophylaxis in SBE and Rh. Fever and years of experience

The percentage for years of experience more than 10 years were Antibiotics used as prophylaxis in SBE and Rh. Fever was (64.8%) which is slightly higher than 0-10 years

(63.3%). The difference between groups didn't reach statistical significant level (P= 0.892).

Antibiotics prescribed as prophylaxis in SBE and Rh. Fever and clinic governorate

No statistical significant differences regarding Antibiotics prescribed as prophylaxis in SBE and Rh. Fever in relation to the governorates, (P=0.779).

5.22. Chi-Square test Relation between (personal data and Governorates) and antibiotics prescribed as prophylaxis in SBE and Rh. Fever.

Variables Personal data	**Used as prophylaxis in SBE and Rh. Fever**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
Age group of GP: 26-35 years >=36	 17 34	 65.4% 65.4%	 9 18	 34.6% 34.6%	0.00	1.00
Gender: Male Female	 39 12	 61.9% 75%	 24 4	 38.1% 25%	0. 956	0.328
Graduation countries Arabic Non-Arabic	 37 14	 71.2% 60.9%	 15 9	 28.8% 39.1%	0.775	0.379
Have you received training courses about A.B Yes No	 30 21	 75 % 55.3%	 10 17	 25% 44.7%	3.354	0.067
Years of experience 0-10 >10	 19 35	 63.3% 64.8%	 11 19	 36.7% 35.2%	0.010	0.092
Governorates: North Gaza Middle Khan-Younis Rafah	 9 10 17 8 10	 64.3% 58.8% 70.8% 53.3% 71.4%	 5 7 7 7 4	 35.7% 41.2% 29.2% 46.7% 28.6%	1.764	0.779

5.2.2.4 Use of UNRWA Formulary

Relation between use of UNRWA Formulary and antibiotics prescribing patterns:

In table (5.23) Chi-Square test used to examine the use of UNRWA Formulary that affect on antibiotics prescribing patterns, there were no statistical significant differences between the different groups (P value > 0.05).

Table (5.23): Chi-Square test for Use of UNRWA Formulary that affect on antibiotics prescribing patterns.

Variables antibiotics prescribing patterns	Currently using UNRWA Formulary				X^2	P-Value
	Used		Not Used			
	#	%	#	%		
Antibiotics prescribed in suspected bacterial diagnosis.					0.309	0.544
Yes	26	68.4%	12	31.6%		
No	13	76.5%	4	23.5%		
Antibiotics prescribed in fear of serious condition					0.125	0.724
Yes	9	75%	3	25%		
No	30	69.8%	12	30.2%		
Antibiotics used as prophylaxis in S.B.E and Rh. Fever					0.720	0.396
Yes	22	66.7%	11	33.3%		
No	17	77.3%	5	22.7%		

5.2.2.5 Relation between personal data and antibiotics prescribed in sure bacterial diagnosis

Antibiotics prescribed in sure bacterial diagnosis and years of experience

Table (5.24) showed that the percentage for years of experience more than 10 years were antibiotics prescribed in sure bacterial diagnosis was (90.6%) which is higher than 0-5 years (78.9%), and 6-10 years (54.5%). The difference between groups reached statistical significant level (X^2= 8.757, P= 0.013). Study by Bharathiraja, et al, 2005 showed that

physicians with more than 20 years of experience are less likely to prescribe antibiotics, (Bharathiraja, et al ,2005).

Antibiotics prescribed in sure bacterial diagnosis and training courses received about antibiotics

The percentage for those who received training courses were antibiotics prescribed in sure bacterial diagnosis was (97.4%) which is higher than those who did not received training courses (73.7%). The difference between groups reached statistical significant level (X^2= 8.867, P= 0.003). In a study reported by Steinke et al, non-training practices in Tayside, UK were in general found to prescribe significantly more antibiotics as well as a higher proportion of broad spectrum penicillin, a higher proportion of newer antibiotics and a greater number of different antibiotics per doctor compared to training practices (Steinke et al,2000).

Antibiotics prescribed in sure bacterial diagnosis and graduation countries

The percentage of graduation from Arabic countries were antibiotics prescribed in sure bacterial diagnosis was (86.3%) which is higher than those from non Arabic countries (82.6%), but the difference between groups did not reached statistical significant level (X^2=0.168, P= 0. 682), the different GPs' educational backgrounds especially from schools in more affluent regions of the world (from more than twenty different countries) did not greatly influence their prescribing behavior.

Antibiotics prescribed in sure bacterial diagnosis and gender

The percentage for female GPs who prescribed antibiotics in sure bacterial diagnosis was (87.5%) which is higher than male GPs (83.9%), but the difference between groups did not reached statistical significant level, (X^2=0.129, P= 0.720).

Antibiotics prescribed in sure bacterial diagnosis and age groups of GPs

The percentage for age group more than 45 years who were antibiotics prescribed in sure bacterial diagnosis was (90.9%) followed by (76.9%) for age group 36-45 years, the lowest was for age group 26-35 (73.1%). The difference between groups did not reached statistical significant level (X^2=4.130, P= 0.127).

Table (5.24): Chi-Square test for Personal data that affect on Antibiotics prescribed in sure bacterial diagnosis.

Variables Personal data	**Antibiotics prescribed in sure bacterial diagnosis**				**X^2**	**P-Value**
	Yes		**No**			
	#	%	#	%		
Years of experience						
0-5	15	78.9%	4	21.1%	8.757	0.013
6-10	6	54.5%	5	45.5%		
>10	48	90.6%	5	9.4%		
Have you received training courses about A.B					8.867	0.003
Yes	38	97.4%	1	2.6%		
No	28	73.7%	10	26.3%		
Graduation countries						
Arabic					0.168	0.682
Non-Arabic	44	86.3%	7	13.7%		
	19	82.6%	4	17.4%		
Gender:						
Male	52	83.9%	10	16.1%	0.129	0.720
Female	14	87.5%	2	12.5%		
Age group of GP:						
26-35 years	19	73.1%	7	26.9%	4.130	0.127
36-45 years	10	76.9%	3	23.1%		
>45 years	40	90.9%	4	9.1%		

5.2.2.6 Knowledge

In table (5.25): illustrate the sources of information (UNRWA Formulary, STG experience, training courses, and pharmaceutical representative) that affect on antibiotics prescribed in sure bacterial diagnosis.

Antibiotics prescribed in sure bacterial diagnosis and source of information (UNRWA Formulary)

The percentage for source of information (UNRWA Formulary) were antibiotics prescribed in sure bacterial diagnosis was (89.8%) which is higher than source of information not (UNRWA Formulary) (73.5%) The difference between groups did not reached statistical significant level (X^2=3.788, P= 0.052).

Antibiotics prescribed in sure bacterial diagnosis and source of information (STG)

The percentage for source of information (STG) were antibiotics prescribed in sure bacterial diagnosis was (85.7%) which is higher than source of information not (STG) (79.4%). The difference between groups did not reached statistical significant level (X^2=0.569, P= 0.451). Clinical practice guidelines, another form of education, have gained popularity as a means of influencing physicians' practices (Audet and Greenfield, 1990). Such guidelines are primarily educational, in that they attempt to inform practitioners about optimal strategies for diagnosis and management. Even by this measure, clinical practice guidelines have been remarkably unsuccessful in influencing physicians. (Lomas, et al, 1989). A study from Uganda showed that implementing Standard Treatment Guidelines followed by training and supervision was more effective in reducing the average number of drug prescribed and percentage of cases given antibiotics compared to distributing STG alone (Kafuko , Zirabamuzaale ,and Bagenda 1999). Another study from Tanzania showed that developing and implementing STGs followed by monitoring reduced incorrect treatment (Wiedenmayer et al 1999).

Antibiotics prescribed in sure bacterial diagnosis and source of information (Experience).

The percentage for source of information (experience) were antibiotics prescribed in sure bacterial diagnosis was (95.3%) which is higher than source of information not (experience) (70.0%). The difference between groups reached statistical significant level (X^2=9.496, P= 0.002).

Antibiotics prescribed in sure bacterial diagnosis and source of information (Training courses)

The percentage for source of information (training courses) were antibiotics prescribed in sure bacterial diagnosis was (94.6%) which is higher than source of information not (training courses) (73.9%). The difference between groups reached statistical significant level (X^2=6.255, P= 0.012), In many countries overall or region specific (for e.g. in rural areas) lack of trained health care providers combined with poverty, low literacy rate and out of pocket expenses for medical care have allowed untrained prescribers of antibiotics to flourish (Gaur and English ,2006).

Antibiotics prescribed in sure bacterial diagnosis and source of information (Pharmaceutical representative)

The percentage for source of information (Pharmaceutical representative) were antibiotics prescribed in sure bacterial diagnosis was (93.5%) which is higher than source of information not (Pharmaceutical representative) (76.9%). The difference between groups did not reach statistical significant level (X^2=3.828, P= 0.050).

In our study analysis of the relation between knowledge and practices of General practitioner , there was no statistical relation ship between UNRWA formulary as a source of information and antibiotics prescribed in sure bacterial diagnosis ,(P = 0.052) also the same there was no statistical relation ship between STG information source and antibiotics prescribed in sure bacterial diagnosis ,(P = 0.451). But there was statistical significance relation ship between experience as a source of information and antibiotics

prescribed in sure bacterial diagnosis, (P = 0.002), the same there was statistical significance between training and antibiotics prescribed in sure bacterial diagnosis, (P= 0.012) . But there was no statistical relation between pharmaceutical representative and antibiotics prescribed in sure bacterial diagnosis, (P = 0.05) which clarify appropriate prescribing behavior. Contrary elsewhere pharmaceutical representatives are often the major source, and sometimes the only source, of medicines information for prescribers and continuing medical education is also often heavily dependent on the pharmaceutical industry. A review by WHO in 2005 of 2700 articles on drug promotion showed that: prescribers who see sales representatives often prescribe more medicines and more new medicines than their colleagues who see sales representatives less often; and that direct to consumer advertising is associated with increased patient requests and prescriptions (Holloway,2005). Similarly Bharathiraja, et al study in 2005 showed the fact that the prescription was largely based on the beliefs, knowledge and experience of the physician rather than on the workload in the practice setting. The same result of Ross-Degnan, et al,1997 study were dissemination of printed clinical guidelines or unbiased drug information alone is not sufficient to cause measurable improvements in behavior. However, active dissemination of guidelines through staff training, peer group re-invention of guidelines, or audit and feedback has resulted in improved compliance with the guidelines. Also Physicians who updated their knowledge through academic methods like seminars, journals etc, were less likely to prescribe antibiotics when compared to those depending on the information provided by the pharmaceuticals. This is primarily due to the bias caused by the pharmaceuticals promoting their products (Bharathiraja, et al ,2005). Several explanations have been offered *Why are most physicians not influenced by practice guidelines?*. First, some guidelines are not written for practicing physicians, but focus instead on the current state of scientific knowledge (Lomas , 1991). Physicians may

have difficulty applying guidelines of this type to specific patients. Second, physicians may disagree with or distrust guidelines written by so called national experts. Interviews with practicing physicians indicate that many rely primarily on their own experience or colleagues' recommendations in deciding whether to adopt new techniques or interventions (Greer,1988). Finally, physicians may choose to ignore guidelines because of non clinical factors, such as financial incentives or the fear of malpractice litigation. Thus, despite the current enthusiasm, guidelines by themselves appear to have a limited role in influencing physicians' practices.

Table (5.25): Chi-Square test for sources of information (UNRWA Formulary, STG, experience, training courses, and pharmaceutical representative) that affect on Antibiotics prescribed in sure bacterial diagnosis.

Variables Sources of information	**Antibiotics prescribed in sure bacterial diagnosis**				**X^2**	**P-Value**
	Yes		No			
	#	%	#	%		
UNRWA Formulary						
Yes	44	89.8%	5	10.2%	3.78	0.052
No	25	73.5%	9	26.5%		
STG						
Yes	42	85.7%	7	14.3%	0.569	0.451
No	27	79.4%	7	20.6%		
Experience						
Yes	41	95.3%	2	4.7%	9.496	0.002
No	28	70.0%	12	30%		
Training courses						
Yes	35	94.6%	2	5.4%	6.255	0.012
No	34	73.9%	12	26.1%		
Pharmaceutical representative					3.828	0.050
Yes	29	93.5%	2	6.5%		
No	40	76.9%	12	23.1%		

Chapter 6

Conclusion and Recommendation

Chapter 6: Conclusion and Recommendation

Conclusion:

The aim of the study is to evaluate the antibiotics prescribing patterns and review the potential factors of inappropriate use.

The study revealed over-use of antibiotics, as the percentage per encounter was 55.4%, and for antibiotics other than dermatological and opthalmological was 50.8%. The over-consumption of antibiotics has great implications on the scarce health care resources, as the medication constitute the 2nd budget after salary, and antibiotics represented 14% of total expenditure (UNRWA,2006). Also it leads to reduction in quality of health care and increase antimicrobial resistance.

Great focus was given to cover the two dimensions of antibiotics prescriptions which were the consumers and health providers. The encounters antibiotics prescription was assessed by WHO prescribing indicators and the health providers prescribing behavior was evaluated by structured questionnaire related to knowledge, attitude and practice.

The WHO antibiotics indicators clarify the following areas:

High percentage of encounters with antibiotics prescribed, low percentage of antibiotics prescribed by generic names, 14.6% of prescription with no diagnosis, mainly (74%) in the Family Files. No mention for age in (49.5%) of the family files, the commonest diagnosis reported was URTI (37.1%) and (82.8%) of URTI were prescribed antibiotics, studies from various parts of the world report that over 80% of patients with viral respiratory tract infection receive antibiotics (WHO,2002), so years of prescribing antibiotics for viral respiratory infection have created a cycle of supply and demand, and misconceptions for the clients that every respiratory ill needs antibiotics pill. Breaking this cycle require public information, GPs education, and clients communication rather than prescribing to end the consultation. Most of antibiotics prescribed from UNRWA Formulary (99.7%) it is less

than 100% due to occasional availability of some donation medicines. There were statistical significance relationship between the antibiotic prescription and the following demographical factors: For governorate, the highest antibiotics prescription percentage was at Gaza governorate, and for age groups: The highest antibiotics prescription percentage was for adults, and the highest antibiotics injection mean was for 0-3 years.

Questionnair:

In relation to practice and personal data, 31% of GPs age from 26 to 35 years due to new recruitment, indicating their need for more training as there were statistical significance between age group 26-35 and antibiotics prescription in fear of serious conditions. Regarding training and experience, there were statistical significance relationship between GPs who received training and antibiotics prescribed in sure bacterial diagnosis and the same for GPs who had more than 10 years experience confirming the importance of both training and experience. It is important to mention that there was no statistical significance relationship between the place of graduation of GPs and antibiotics prescribed in sure bacterial diagnosis, indicating that the prescribers have graduated from different countries with similar prescribing behaviour.

Related to GPs knowledge, the present study emphasized the relation between the source of information as experience and training courses and antibiotics prescription in sure bacterial diagnosis, and no relation with UNRWA Formulary, STG and pharmaceutical representative.

It is important to mention that dissemination of clinical guidelines as UNRWA Formulary, STG alone is not sufficient to cause measurable achievement in prescribing behavior, but active dissemination of clinical guidelines, through staff training, support and follow up will greatly improve the prescribing behavior and better health quality. Also physicians interest in clinical guidelines has never been great, only 9.5% of UNRWA Formularies

available in front of GPs and 27.4% were at home, 71% currently using it and 48.9% facing problems in using it. Lack of knowledge represented by: 67.9% of GPs stated the correct definition of antibiotics, 48.2% mention the correct generic names of some of antibiotics, 71.4% mention the importance to know the generic names, 64.3% antibiotics used in sub-acute bacterial endocarditis and rheumatic fever as prophylaxis, 71.1% antibiotics prescribed in suspected bacterial diagnosis, and 11.9% antibiotics prescribed in uncertain condition as prophylaxis. So the best intervention is education approach and increase awareness about antibiotics use among the practicing GPs to dispel inappropriate information and initiate necessary steps to deliver the latest advances of knowledge. GPs attitude toward antibiotics prescription is generally good, but GPs favor to prescribe antibiotics in case of fever was 65.1%, time pressure 72.6%, treatment uncertainty 28.6% and antibiotics resistance concern disfavor 51.8% so the practicing GPs need to know that fever is not always a sign of bacterial infection and appropriate use of antibiotics is vital to reduce the development of further antibiotics resistance and not to prescribe antibiotics in uncertain condition.

There were statistical significance relationship between the antibiotic prescription and the following variables:

-GPs having >10 years experience and antibiotics prescribed in sure bacterial diagnosis (P=0.013).

-GPs age 26-35 years and antibiotics prescribed in fear of serious conditions (P=0.037).

-GPs at middle governorate and antibiotics prescribed in suspected bacterial diagnosis (P=0.004).

-GPs having received training courses and antibiotics prescribed in sure bacterial diagnosis (P=0.003).

-Sources of information (experience) and antibiotics prescribed in sure bacterial diagnosis (P=0.002).

-Sources of information (training courses) and antibiotics prescribed in sure bacterial diagnosis (P=0.012).

GPs opinion about over prescription of antibiotics

96.4% of respondents agree that antibiotics are over prescribed (Figure 6). The most important factors for over-prescriptions were: (Figure 7) Over-crowding 65%, clients pressure 55.7%, antibiotics prescribed without diagnosis 36.25%, lack of knowledge 31.25%, outside prescriptions 31.25%, poor practice of private 21%, to get red of clients 15.18%, and to satisfy clients 13.75%.

The most important ideas for promotion of more prudent use of antibiotics: (Figure 8) Health educations of consumers 48.7%, training 47.4%, decrease over-crowding 33.3%, improve knowledge 29.4%, increase community awareness by media and school health program 28.6%, appointment system 25.6%, follow up and supervision 24.4%, and proper diagnosis, C&S 21.8%.

Recommendation:

1- Active dissemination of independent un-biased information as therapeutic protocols and additional copies of UNRWA formulary and STG through staff training support and follow up to improve prescribing behavior and quality of care.

2- There is a need to provide training on implementation of self- monitoring tools (WHO antibiotics indicators) to all the SMO and auditing the prescriptions as well as giving feedback to the health centers.

3- Improving knowledge and change attitudes of prescribers by continuous in-service medical education, seminars and workshops, especially for newly recruited staff to dispel inappropriate information and initiate necessary steps to deliver the latest advances of knowledge, as lack of knowledge was important underlying factors.

4- Decrease over-crowding by recruitment of sufficient staff to decrease heavy patient load and time pressure.

5- Efficient enforcing regulations: as limiting authority to prescribe certain antibiotics to SMO and specialist , automatic stop orders for prophylactic antibiotics, fever is not always a sign of bacterial infection and so not an indication for providing antibiotics, in uncertain condition, in suspected bacterial diagnosis and fear of serious condition as appropriate use of antibiotics is vital to reduce the development of further antibiotics resistance, also instruct the GPs to report the diagnosis of the prescription as 14.6% of the encounters without diagnosis mainly (74%) in the family files, and encouraging the use of generic names of antibiotics.

6- Establishment of "UNRWA Therapeutic Committee" to ensure the safe, efficient and effective use of antibiotics.
7- Administrative incentives and sanctions to encourage appropriate behavior include awards for appropriate prescribing by incentives, promotion, and rewards.
8- Cooperation between all sectors of health: UNRWA, government, private sectors and NGOs about importance of rational use of antibiotics.
9- Caution during prescribing antibiotics for "outpatient" ARI's as it consumed more than half of antibiotics (59.7%) although mostly (>80%) due to viral infections.

Recommendation for further studies:

- The study needs to be repeated over time at the national level to maintain good quality health care.
- Further more it is essential to extend the study to private, and NGOs.
- It is important to deal with other aspect of WHO drugs indicators as patient care indicators and facility indicators.

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Annexes

Annex 1

بسم الله الرحمن الرحيم

السيد/ د/ بعد التحية

أنا الطالب / عيسى محمد عيسى صالح.

أرجو من سيادتكم تحكيم ووضع ملاحظاتكم أو مقابلتكم بخصوص (Questionnaire) الخاص بالبحث :

"Antibiotics prescribing patterns by UNRWA general practitioners primary health care Gaza 2006 ''.

حيث أنه متطلب لجامعة القدس كلية الصحة العامة وذلك للحصول علي رسالة الماجستير وهي تهدف إلى:

To evaluate the current prescribing patterns by the physicians and to identify the potential factors of irrational use of antibiotics in UNRWA health center/ Gaza Strip.

ملاحظة:

مرفق لكم بطيه الأداة، الأهداف، أسئلة الدراسة.

شاكرين لكم تعاونكم.

Annex 2 **بسم الله الرحمن الرحيم**

(نموذج موافقة لإجراء بحث صحي)

Informed consent

حضرة المشارك / المشاركة **المحترم / المحترمة**

بعد التحية

موضوع الدراسة :

تقييم أنماط وصف المضادات الحيوية من قبل الأطباء في عيادات الوكالة - قطاع غزة وكذلك معرفة العوامل المحتملة للاستخدام الغير رشيد لها , و قد تساعد الدراسة في تحسين استخدام المضادات الحيوية في عيادات الوكالة.

إنني أقوم بعمل بحث علمي وهو جزء من دراستي في برنامج ماجستير الصحة العامة في جامعة القدس - فلسطين.

سيتم جمع البيانات المطلوبة من سيادتكم من خلال الاستبيان الذي يحتوي على خيارات للإجابة على كل سؤال ، الرجاء اختيار الإجابة الأقرب للممارسة الواقعية ولن تستغرق أكثر من 10 - 15 دقيقة.

المشاركة في هذا البحث طوعية ولك الحق في الانسحاب في أي وقت تشاء وفي حالة الموافقة سيتم احترام السرية حيث لا حاجة إلى كتابة أسماء على الاستبيان لان الاهتمام بحثي وليس شخصي .

شكراً لتعاونكم

Annex 3

السيد/ مدير برامج الصحة / الدكتور أيوب العالم الموقر

تحية طيبة وبعد

الموضوع :

طلب الموافقة على القيام بدراسة تقييم أنماط وصف المضادات الحيوية من قبل الأطباء في عيادات الوكالة - قطاع غزة وكذلك معرفة العوامل المحتملة للاستخدام الغير رشيد لها.

أحيط سيادتكم علما بأنني أرغب بعد موافقتكم عمل البحث المذكور أعلاه حيث أنه متطلب أساسي من متطلبات التخرج في برنامج الماجستير لكلية الصحة العامة - جامعة القدس وأود أن أعلم سيادتكم بأن الدراسة ستكون في عيادة الوكالة وستشمل الفئات التالية:

1. الأطباء المعالجين في عيادات الوكالة.
2. ملفات المرضى من الفئتين :

- أقل من ثلاث سنوات : ملفات الأطفال .
- أكثر من ثلاث سنوات : ملفات العائلة .

هذا يتطلب المقابلة الشخصية مع الأطباء المعالجين وذلك لتعبئة الاستبيانات الخاصة بالبحث وكذلك أخذ عينات عشوائية من ملفات المرضى .

وعليه نرجو من سيادتكم التكرم بالموافقة وتوجيه التوصيات اللازمة .

وشكراً

Annex 4

1- Questionnaire: Serial No:_____

Part A:General Practitioner *Knowledge*

1-Please what do antibiotic mean for you?

1- It is an antimicrobial that have antibacterial , anti- fungal , anti-viral, and anti-parasitic. ☐

2- It is a drug that kill or prevent growth of bacteria and fungi. ☐

3- It is a drug that kill or prevent growth of the bacteria only. ☐

4- It is a drug that prevent growth of the bacteria and parasites. ☐

5- Non of the above. ☐

2-Are you aware of any danger to the clients associated with taking antibiotics?

1- Emerging antibiotic resistance. ☐

2- Allergic reactions. ☐

3- Antibiotics may kill “friendly” “good” microbes. ☐

4- Misuse. ☐

5- All of the above. ☐

6- Don't know. ☐

3-Rational antibiotic use involves:

The correct antibiotic, administered by the best route in the right amount, at optimum intervals, for the appropriate period and after an accurate diagnosis.

0- No ☐ 1- Yes ☐

4- Sources of information about antibiotics:

1- UNRWA Model Formulary "off Essential Medicine" ☐

2- Standard Treatment Guidlines (STG) ☐

3- Experience ☐

4- Training courses ☐

5- Pharmaceutical representative ☐

6- Others specify_____ ☐

5-Who should provide information for the clients about antibiotics?

1- General Practitioner ☐

2- Pharmacists ☐

3- Nurses ☐

4- 1 & 2 ☐

5- All of the above ☐

6-Please mention the generic *names* of the following antibiotics :

a. Azimex:_____ b Ogmine:. _____

c. Ciprocare:_____ d. Ultracept:_____

e. Keflex:_____ f. LAP:_____

g. Ospen:_____

7-What is the importance to know the generic names of antibiotics?

(0=No,1=yes)

1- Facilitate good communication between health providers &citizens as we use the same terminology for certain antibiotics ☐

2- Avoidance of manipulation ☐

3- Prevent monopolies of the antibiotics by avoiding use the trade name. ☐

4- Knowledge generation. ☐

5- All of the above ☐

6- Non of the above ☐

Part B:-General Practitioner *Attitude*

Factors influencing G.P intention (Favor / Disfavor) **to prescribe antibiotics in UNRWA Health facilities (Pressure to)**

	Factors	Favor(1)	Disfavor(0)
8-	Fever		
9-	Purulent discharge		
10-	Patient request expectation		
11-	Potential return visits cost		
12-	Patient satisfaction		
13-	Time pressure		
14-	Treatment uncertainty		
15-	Antibiotics resistance concern		

Part C: General Practitioner *Practices*

16- Do you examine every case before prescribing antibiotics?

1- Every case ☐ 2- Sometimes ☐

3- Rarely ☐ 4- Not at all (over-crowding) ☐

17- Antibiotics are prescribed in : (0=No,1=Yes)

1-Suspected bacterial diagnosis ☐ 2-Viral infection ☐

3-Sure bacterial diagnosis ☐ 4-Fear of serious Condition ☐

18-Have you received UNRWA Model Formulary?

1- Yes ☐ 0- No ☐ If No go to Q : 26

19- Availability of UNRWA Model Formulary "off essential medicine"?

(The data collector must observe the site of them) (0=Skip Q)

1- In front of the G.P. at the desk ☐

2- In the drawer ☐

3- In the key board ☐

4- Other places please specify_____ ☐

20- Did you use UNRWA Formulary in your prescription of antibiotics?

1- Currently using it ☐ 2-Used in the past ☐ 3-Not used ☐

If not used go to Q: 26 (0=Skip Q)

21-If currently using it or used in the past have you noticed any problem in using UNRWA formulary?

1-Yes ☐ 0-No ☐ (2=Skip Q) If No go to Q: 23

22- What problems do you face in using the UNRWA Formulary? (0=No,1=Yes,2=Skip Q)

1- Insufficient knowledge about antibiotics. ☐

2- Lack of continuous training on using it. ☐

3- Lack of time due to overcrowding. ☐

4- Difficult to be handled. ☐

5- Not all the antibiotics present in the EDL ☐

6- It is difficult to be used in front of the clients (barrier) ☐

7- Lack of motivation to change previous practices ☐

23- Did you see any improvement in prescribing pattern of antibiotics after using UNRWA Formulary? 1-Yes ☐ 0-No ☐ (2=Skip)

24 -Did you prescribe antibiotics outside UNRWA Formulary EDL?

1-Frequently ☐ 2-Sometimes ☐ 3-Never ☐ 4-Skip ☐

If never proceed to Q: 26

25 – If frequently or sometimes please mention the most common antibiotics were prescribed during the last year and for what reasons.

Antibiotics **(0=No,1=Yes,2=Skip)**	***Reasons***

26- Have you received Standard Treatment Guidlines (STG) about the use of antibiotics in the management of infectious diseases

1-Yes ☐ 0-No ☐ If no proceed to Q: 31

27-Have you used them during antibiotics prescriptions?

1-Yes ☐ 0-No ☐ (2=Skip)

If no proceed to Q: 31

28-Have you seen any obstacles in using STG?

1-Yes ☐ 0-No ☐ (2=Skip) If no go to Q : 30

29-What are the obstacles in using Standard Treatment Guidlines? (0=No,1=Yes,2=Skip)

1- Doubts whether it can perform the behavior ☐

2- Lack of familiarity with STG ☐

3- Lack of agreement to the concept of guidelines in general ☐

4- Patient-related barriers (difficult to be used in front of the clients) ☐

30-Did you notice improvement in antibiotics prescriptions by using STG?

1- Yes ☐ 0- No ☐ (2=Skip)

31- Did you use antibiotics as a prophylaxis: (1=Yes,0=No)

1- In uncertain conditions ☐

2- Fear induced ☐

3- In sub-acute bacterial endocarditis & Rh-fever ☐

4- All of the above ☐

5- Non of the above ☐

32- Do you believe that antibiotics are over prescribed?

1- Yes ☐ 0- No ☐

If no go to Q: 35 (0=No,1=Yes,2=Skip)

33-What are the most important factors that lead to over prescription of antibiotics in UNRWA\H.C

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

34 - Regarding your opinion expressed what would help to promote more Prudent(rational) usage of antibiotics : (0=No,1=Yes,2=Skip)

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

35-Any comment not covered in the questionnaire: (0=No,1=Yes).

_____
_____
_____
_____
_____
_____
_____

Part E: *Personal data*

36- Age: .....

37 -Gender: 1-Male ☐ 2-Female ☐

38-Years of experience: _____

39-Place of graduation: _____

40-Qualification: _____

41-Have you received training courses about antibiotics?

1- Yes ☐ 0-No ☐

If no don't proceed to Q: 42,43, 44,45.

42-How many times: (0=Skip)

1- One time ☐ 2-Two times ☐

3- Three times ☐ 4-Four times ☐

43-last time: (0=Skip)

1-One year ago ☐ 2- Two years ago ☐ 3-Three years ago ☐

4-Four years ago ☐ 5- Five years ago ☐

44- Is it sufficient : 1- Yes ☐ 0- No ☐ (2=Skip)

45-If no what do you suggest: (0=Skip,1=yes)_____
_____
_____
_____
_____
_____

Annex 5

Diagnosis Codes			
Code	**Diagnosis**	**Code**	**Diagnosis**
1	Ear, Nose and Throught (ENT)	16	Male genital
2	Eye disorders	17	Sexual Transmitted Diseases
3	Headache	18	Blood diseases
4	Migraine	19	Neoplasms
5	URTI	20	Congenital Anomalies
6	Candidiasis	21	A Influenza
7	Lower respiratory tract infection	22	Typhoid
8	Wheezy chest	23	Injuries
9	Diseases Of The Digestive System	24	Growth Retarded
10	Parasitic Diseases	25	Allergy
11	Musculoskeletal diseases	26	Post vaccination fever
12	Fever for investigation	27	Piles
13	C-Cold	28	
14	Diseases Of The Skin And Subcutaneous Tissue	29	
15	Renal diseases	30	

Classes of antibiotics (WHO)(Generic names)					
Penicillin: Code (1)					
Benzathine benzylpenicillin	Procaine benzylpenicillin	Phenoxymethylpenicillin (penicillin V)	Benzylpenicillin (penicillin G)	Amoxicillin	Co-amoxiclav
Cephalosporins: Code (2)					
Cephalexin					
Tetracycline: Code (3)					
Tetracycline capsules		Doxycycline capsules			
Aminoglycosides: Code (4)					
Gentamycine 80 mg					
Macrolides: Code (5)					
Erythromycine Syrup 125mg,Tab 250mg		Azithromycine Syrup 200mg ,Cap 250 mg			
Sulphonamide&Trimethoprim: Code (6)					
Co-Trimoxazole Syrup ,Tablet					
Quinolones : Code (7)					
Ciprofloxacine Tablet 250 mg		Norfloxacine Tablet 400 mg			
Anti-Infective dermatological drugs : Code (8)					
Neomycin Sulphate and Bacitracin Ointment		Silver Sulphdadiazine1% cream			
Anti-Infective Ophthalmological agents : Code (9)					
Chloramphenicol eye ointment	Tetracycline eye ointment	Sulphacetamide eye drops	Gentamcine eye drops		
Code (0)for drugs other than antibiotics					

Annex 6 **WHO Antibiotics prescribing indicator form**

Location:_____ Date:_____ * 0 = No 1 = Yes 2= Not applicable

serial	Date	Age	Gend M=1 F=2	# drugs	Antib (0/1)*	Generic (0/1/2)*	Antib.Inj (0/1/2)*	Antibiotic on EDL (0/1/2)*	Name Antibiotic	Diagnosis
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										
15										
16										
17										
18										
19										
20										
Total										
Average										
Percetage					% Of total cases	% Of total Antibiot.	% Of total Antibiot.	% Of total Antibiot.		

Annex: 7
Questionnaire (Arabic Version)

الجزء الأول: معلومات الطبيب العام

1. من فضلك ماذا يعني المضاد الحيوي :

أ. إنه مضاد للميكروبات لذلك فله فعالية ضد البكتيريا، الفطريات،الفيروسات، وكذلك الطفيليات. ☐

ب. إنه الدواء الذي يقتل أو يمنع نمو البكتيريا و الفطريات. ☐

ت. إنه الدواء الذي يقتل أو يمنع نمو البكتيريا فقط. ☐

ث. إنه الدواء الذي يمنع نمو البكتيريا والطفيليات. ☐

ج. ليس مما سبق. ☐

2. هل أنت واعي للمخاطر المصاحبة لاستخدام المضاد الحيوي على المريض؟

أ. انبعاث بكتيريا غير مستجيبة للمضادات الحيوية. ☐

ب. حساسية. ☐

ت. المضاد ممكن أن يقتل الميكروبات الصديقة والجيدة. ☐

ث. سؤ استخدام. ☐

ج. كل ما سبق. ☐

ح. لا أعرف. ☐

3. الاستخدام العقلاني للمضاد الحيوي يشمل:

اختيار المضاد الحيوي الأمثل، وإعطاؤه عن الطريق المناسبة بالكمية الصحيحة خلال فترة مناسبة بعد التشخيص الدقيق.

أ. نعم ☐ ب. لا ☐

4. مصادر المعلومات بخصوص المضاد الحيوي:

أ. دليل الوكالة الدوائي. ☐

ب. دليل المعالجة القياسي. ☐

ت. الخبرة. ☐

ث. الدورات التدريبية. ☐

ج. ممثلين شركات الأدوية ☐

ح. أخرى، حدد. ☐

5. من الذي يعطي معلومات للمريض عن المضاد الحيوي؟

أ. الطبيب. ☐

ب. مساعد صيدلي. ☐

ت. الممرض. ☐

ث. أ+ ب. ☐

ج. كل ما سبق. ☐

6. من فضلك أذكر الاسم العلمي لكل من المضادات التالية:

أ. أزمكس_____ ب. أقمنتين_____ ت . سيبروكسين_____

ث. التراسبت_____ ج. كفلكس_____ ح. بنسلين طويل المدى _____

خ. أسبن_____ .

7. ما هي أهمية معرفة الأسماء العلمية للمضادات الحيوية:

أ. يساعد في عملية التواصل الجيد بين مزود الخدمة والمواطنين من خلال استخدام نفس المصطلحات للمضادات الحيوية. ☐

ب. يمنع عملية التلاعب. ☐

ت. يمنع عملية الاحتكار للمضادات الحيوية عن طريق منع استخدام الاسم التجاري. ☐

ث. توليد المعرفة. ☐

ج. كل ما سبق. ☐

ح. ليس مما سبق. ☐

الجزء الثاني: التوجه للطبيب

العوامل التي تؤثر في توجه الطبيب (تحبذ أو لا تحبذ) لوصف المضادات الحيوية في عيادات الوكالة:

مسلسل	العامل	يحبذ	لا يحبذ
8.	ارتفاع درجة الحرارة		
9.	إفرازات صديدية		
10.	رغبات وتوقعات المريض		
11.	توقع تكلفة زيارة ثانية		
12.	إرضاء المريض		
13.	ضغط الوقت		
14.	شكوك حول العلاج الموصوف		
15.	اهتمام بظهور بكتيريا غير مستجيبة للمضادات		

الجزء الثالث : ممارسات الطبيب العام

16. هل تفحص كل حالة قبل وصف المضاد

أ. كل حالة ☐ ب. أحيانا ☐ ج. نادرا ☐ د. أبدا ☐

17. المضاد الحيوي يوصف في :

أ. اشتباه تشخيص بكتيري. ☐

ب. التهاب فيروسي. ☐

ت. التهاب بكتيري مؤكد. ☐

ث. الخوف من حالة خطيرة ☐

18. هل استلمت دليل الوكالة الدوائي:

أ. نعم ☐ ب. لا ☐ إذا لا اذهب للسؤال 26

19. مكان وجود الدليل الدوائي.

أ. على المكتب. ☐

ب. في الدرج. ☐

ت. في الدولاب (الخزانة). ☐

ث. مناطق أخرى حدد _____. ☐

20. هل استخدمت الدليل الدوائي أثناء الوصفات للمضادات الحيوية:

أ. حاليا أستخدمها ☐ ب. استخدمتها في الماضي ☐ ج. لا تستخدم ☐

إذا لا تستخدم اذهب للسؤال 26

21. إذا تستخدم حاليا أو استخدمت في الماضي هل لاحظت أي مشاكل

أ. نعم ☐ ب. لا ☐ إذا لا اذهب للسؤال 23

22. ما هي المشاكل التي تواجهك عند استخدام الدليل الدوائي:

أ. معلومات غير كافية عن المضاد الحيوي. ☐

ب. نقص في التدريب المستمر ☐

ت. قلة الوقت بسبب الازدحام . ☐

ث. صعب التعامل معه. ☐

ج. ليس كل المضادات مجودة في الدليل. ☐

ح. صعب استخدامه أمام المريض. ☐

خ. نقص في الحوافز لتغيير الممارسات القديمة. ☐

23. هل وجدت أي تحسن في عملية وصف المضاد الحيوي بعد استخدام دليل الوكالة الدوائي:

أ. نعم ☐ ب. لا ☐

24. هل توصف مضادات حيوية خارج الدليل:

أ. عدة مرات ☐ ب. أحيانا ☐ ج. أبدا ☐

إذا أبدا اذهب للسؤال 26

25. إذا كان عدة مرات أو أحيانا من فضلك أذكر أهم المضادات التي وصفت خلال العام الماضي ولماذا

المضاد	السبب

26. هل استلمت دليل المعالج القياسي حول استخدام المضادات في معالجة الأمراض المعدية:

أ. نعم ☐ ب. لا ☐

إذا لا اذهب للسؤال 31

27. هل استخدمت الدليل المعالج القياسي في وصفات المضادات الحيوية :

أ. نعم ☐ ب. لا ☐

إذا لا اذهب للسؤال 31

28. هل لاحظت أي معوقات من استخدام الدليل المعالج القياسي:

أ. نعم ☐ ب. لا ☐

إذا لا اذهب للسؤال 30

29. ما هي المعوقات التي لاحظتها من استخدام الدليل المعالج القياسي:

0 = لا 1 = نعم 2 = اقفز

أ. شكوك في إمكانية تعديل السلوك. ☐

ب. غير مألوف. ☐

ت. عدم وجود إجماع على مفهوم استخدام الدليل . ☐

ث. صعوبة استخدامه أمام المرضى. ☐

30. هل لاحظت تحسن في وصفات المضادات الحيوية مع استخدام الدليل المعالج القياسي:

أ. نعم. ☐ ب. لا ☐

31. هل تستخدم المضادات للوقاية من الأمراض:

أ. في الحالات الغير مؤكده. ☐

ب. دافع الخوف. ☐

ت. التهاب بطانة القلب البكتيري الغير حاد والحمى الروماتزمية. ☐

ث. كل ما سبق. ☐

ج. ليس ما سبق. ☐

32. هل تعتقد أن المضادات الحيوية توصف أكثر من اللازم.

أ. نعم ☐ ب. لا ☐

33. ما هي أهم العوامل التي تؤدي إلى الاستخدام المفرط في المضادات الحيوية في عيادات الوكالة.

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

34. بخصوص رأيك ما هي الأفكار التي يمكن أن تحسن استخدام المضادات الحيوية (الاستخدام الرشيد)

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

35. أي ملاحظات مهمة لم تغطى في الاستبيان.

_____

_____

_____

الجزء الرابع: معلومات شخصية

36. العمر :_____

37. الجنس: 1-ذكر ☐ **2- أنثى** ☐

38. سنوات الخبرة:_____

39. مكان التخرج:_____

40. مؤهلاتك الجامعية:_____

41. هل أخذت دورات تدريبية بخصوص المضادات الحيوية

1. نعم ☐ **2 . لا** ☐

إذا لا اقفز عن الأسئلة 42,43,44,45

42. كم مرة:

1. مرة واحدة. ☐
2. مرتان. ☐
3. ثلاث مرات. ☐
4. أربع مرات. ☐

43. آخر مرة :

1. قبل سنة ☐
2. قبل سنتان. ☐
3. قبل ثلاث سنوات. ☐
4. قبل أربع سنوات. ☐
5. قبل خمسة سنوات. ☐

44. هل التدريب كافي :

أ. نعم ب. لا

45. إذا لا ماذا تقترح.

_____

_____

_____

_____

Annex 8

WHO Drug Use Indicators for primary health care facilities

Core Drug Use Indicators

Prescribing indicators

1- Average number of medicines prescribed per patient encounter

2- Percentage of medicines prescribed by generic name

3- Percentage of encounters with an antibiotic prescribed

4- Percentage of encounters with an injection prescribed

5- Percentage of medicines prescribed from an EML or formulary.

Patient care indicators

1- Average consultation time

2- Average dispensing time

3- Percentage of medicines actually dispensed

4- Percentage of medicines adequately labelled

5- Percentage of patients with knowledge of correct dose.

Health Facility indicators

1- Availability of essential medicines list or formulary to practitioners

2- Availability of clinical guidelines

3- Percentage of key medicines available.

Complementary drug use indicators

1- Average medicine cost per encounter

2- Percentage of prescriptions in accordance with clinical guidelines.

3- Percentage of patients treated without drugs

4- Percentage of drug costs spent on antibiotics

5- Percentage of drug costs spent on injections

7- Percentage of patients satisfied with care they received

8- Percentage of health facilities with access to impartial drug information

Reference : (Management Science for Health, 1997) , (WHO,1993)


0 3 6 km
0 3 6 mi
34°20'
34°30'
31°30'
31°30'
Mediterranean Sea
Gaza
Dayr al Balaḥ
1950 Armistice Line
Khān Yūnis
palestine
31°20'
31°20'
Rafaḥ
EGYPT
Gaza International Airport
Abū 'Awdah (Joz Abu 'Awdah)
Israeli-occupied with current status subject to the Israeli-Palestinian Interim Agreement - permanent status to be determined through further negotiation.
34°20'
34°30'

Annex 10

Principles of academic detailing "Educational Outreach"

- Conducting interviews to investigate baseline knowledge and motivations for current prescribing patterns
- Focusing programs on specific categories of physicians as well as on their opinion leaders
- Defining clear educational and behavioral objectives
- Establishing credibility through a respected organizational identity, referencing authoritative and unbiased sources of information, and presenting both sides of controversial issues
- Stimulating active physician participation in educational interactions
- Using concise graphic educational materials
- Highlighting and repeating the essential messages
- Providing positive reinforcement of improved practices in follow up visits

Annex 11

Materials available to support an intervention program on antibiotic use

Principles of judicious antibiotic use for pediatric infections.

Academic sheets providing one page summaries of the principles of antibiotic use.

Posters for educating patients.

Pamphlets for educating patients.

Question and answer sheets for viral respiratory diagnoses.

A “prescription pad” including recommendations for symptomatic treatment for patients with viral respiratory infections.

A letter to childcare providers stating that the child can return to day care without an antibiotic.

These materials are available from the Centre for Disease Control and Prevention.(CDC)

(Edward A Belongia, and Benjamin Schwartz, 1998)