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## The role of the pharmacist in health care and medical treatment in Saudi Arabia as perceived by the patient

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THE ROLE OF THE PHARMACIST IN HEALTH CARE AND MEDICAL  
TREATMENT IN SAUDI ARABIA AS PERCEIVED BY THE PATIENT

A Thesis

Presented to

the Faculty of the Graduate School

University of the Pacific

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

Mohammed H. Al Haidari

April 1982

# THE ROLE OF THE PHARMACIST IN HEALTH CARE AND MEDICAL TREATMENT IN SAUDI ARABIA AS PERCEIVED BY THE PATIENT

## ABSTRACT

Saudi Arabia, one of the developing countries, has a number of problems with the health care and medical treatment of the Saudi people. This study was undertaken to identify and to examine some of these problems and the role of the pharmacist in health education.

A questionnaire was developed and sent to 200 Saudi students in the United States; 111 completed questionnaires were returned. The questionnaire was also sent to Saudi Arabia where 51 persons were interviewed. Results of the questionnaire indicated that some of the problems identified were due to the attitudes of the person interviewed and others resulted from the quality of pharmaceutical services which were provided. Some patients in Saudi Arabia want a "cure" from the first contact with the physician; some do not want to use the medications for a long period of time, for example, those who are undergoing treatment for chronic diseases. Some go to more than one physician and may receive prescriptions for two or more drugs. Others may discontinue the drug and not return to the physician. Some may obtain their medications without a prescription and others may use the medication(s) prescribed for other persons. Generally, it was determined that the services provided by the pharmacist were not what the patient expected and wanted. Also poor communication between the patient and the pharmacist was identified. Language problems were the usual cause cited.

These problems may lead to treatment failure and/or an increase in the incidence of adverse drug reactions or drug-drug interactions.

Recommendations were developed in an attempt to alleviate some of these problems. These recommendations include the requirement that each hospital keep a medical record for each patient, and also that a medication record for each patient be kept in the pharmacy to avoid the duplication of medications (prescriptions). The law or regulations which restricts the availability of medicines without a prescription from any pharmacy inside the hospitals or from market pharmacies should be adhered to and enforced by the pharmacists.

Appointments for outpatients should be made to reduce the crowds of people at the doctor's office or at the pharmacy windows. This will encourage good communication and allow more time for the physician, pharmacist and the patient to discuss the disease and treatment. To overcome poor communications due to the language barrier, it is important that only those physicians and pharmacists who can speak the Arabic language work in the outpatient departments.

Encouragement of patient participation in his treatment can be provided by enhancing health education in the media such as in newspapers and on radio and television programs. The pharmacist should play a role in solving these problems by monitoring drug therapy.

The appendix contains a proposal which specifies the types of information which should be provided to Saudi patients regarding their prescribed medications. The diseases included in the appendix were selected as examples because they are rather common in Saudi Arabia.

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## CHAPTER I

### INTRODUCTION

Saudi Arabia has an area of approximately 2,000,000 km<sup>2</sup> and has a population of approximately 7,600,000. There are 89 hospitals which have 12,000 beds, 299 outpatient health centers which are run by physicians and 383 dispensaries which are run by auxiliaries. There are approximately 4700 physicians, 8% of whom are Saudi and 6400 nurses, 14% of whom are Saudi (1).

Saudi Arabia has specialized hospitals which have sophisticated equipment and well trained staff. The services in these hospitals are excellent. They are controlled by different departments of the government, such as the Ministry of Health, Defense, Interior, the National Guard, and the University (2). There are three types of services available especially in villages and rural areas. The first type which is called Type A, has two physicians and several nurses and unskilled personnel. The second is Type B which has one physician and one nurse, and the third is Type C (Health Point) which is staffed by a nurse or a pharmacist assistant and one servant. All hospitals have large outpatient departments (2).



A weekly television program, called "Medicine and Life" is run on five stations in Saudi Arabia (3). It requests the viewers to send letters asking about health problems which the program could explain or upon which they could give advice. Five thousand two hundred forty letters were received during the past five years and 786 randomly selected letters were analyzed. Six hundred four letters asked specifically about the writers' own illnesses. The major problems that the viewers mentioned in the letters are listed in Table 1. Another report (4) included a list of primary care problems, and involved the first 166 patients who attended the outpatient clinic in the Riyadh Military Hospital (between 9 October and 20 October, 1978). The 166 patients presented, had 240 medical problems (incidence 1.4 problems per patient) and Table 2 lists the problems in descending order of incidence.

Saudi Arabia, one of the developing countries, has problems concerning health care and treatment of diseases. These problems can be summarized as follows: Many patients want a cure from the first contact with the physician; some do not want to use the medications for a long period of time; the patient may change his doctor and may receive two prescriptions; and the patient may stop or discontinue his medications without returning to the doctor. The person may use medications obtained from friends or relatives, or may go directly to the pharmacy to get his medications without a prescription and without realizing the potential hazards

Table 1. The 15 Main Health Problems Mentioned by Correspondents to the Television Program (Medicine and Life) (3).

Problems	Male	Female	Total
Infective and parasitic diseases	22	13	35
Neoplasm	6	4	10
Endocrine, nutritional and Metabolic diseases	31	21	52
Disease of the blood and blood forming organs	15	9	24
Mental disorders	32	14	46
Disease of nervous system	28	19	47
Disease of circulatory system	6	10	16
Disease of digestive system	41	23	64
Disease of respiratory system	28	12	40
Disease of genito-urinary system	13	40	53
Complications of pregnancy	--	11	11
Disease of musculo-skeletal and connective tissue	15	12	27
Disease of skin	19	45	64
Congenital anomalies	7	5	12
Accident and poisoning	5	2	7

Table 2. Occurrence of 240 Medical Problems in 166 Patients seen at the Out Patient Department, Riyadh Military Hospital (4).

Problem	No. of Problems	Percentage
Gastrointestinal	51	21.3
Cardiovascular	49	20.4
Dermatological	33	13.8
Respiratory	29	12.1
Genito-urinary	19	7.9
Neuropsychiatric	18	7.5
Musculo-skeletal	14	5.8
Endocrine	10	4.2
Obstetric	8	3.3
Iatrogenic	5	2.1
General debility	4	1.7

of self medication. Communication between the physician and the patient is frequently inadequate, and communication between the pharmacist and the patient is usually poor.

In Saudi Arabia, the patient frequently goes from one clinic to another and from one physician to another. Patients can buy non-narcotic analgesics and tranquilizers without a prescription.

The Dean of the School of Pharmacy at the University of Riyadh has stated:

"...like many other developing countries, several factors contributed to the less than optimal use of drugs in Saudi Arabia. Some of these contributing factors were unawareness among the public about the danger involved in self medication, poor patient compliance, the availability of most of the non-narcotic drugs without a prescription, a lack of adequate drug information, poor physician-patient-pharmacist communication, and the promotional activities of drug companies." (5)

A study was conducted by Dr. Al Sebai (1) of three health centers in rural areas of Saudi Arabia. These centers did not differ from those in other parts of the country, especially the out-clinic patient departments of general public hospitals. This study showed that the physician spent approximately three minutes with the patient due to

the large number of people and lack of physicians. This time did not allow the physician the opportunity to diagnose or to treat the condition properly. This study also showed that diagnosis was based upon clinical impressions without any diagnostic facilities. Medications were sometimes dispensed indiscriminately. Sixteen patients were interviewed after they had been discharged from the outpatient department. Only four of the sixteen knew their diagnosis of their illness, and only five patients of the sixteen knew how to use the medication prescribed for them. This study showed that 30% of all prescriptions were for antibiotics and 18% of these antibiotics were chloramphenicol. Injections of chloramphenicol were given to the children. Twenty-four percent of the prescriptions were antipyretics and analgesics. The author concluded that antibiotics were used indiscriminately. For example, patients may receive one injection of an antibiotic and then enough oral doses for three days of treatment, which he or she may not use. From the above, it was clear that the patients in these centers failed to absorb the information which was given to them. The study concluded that these centers did not perform their function in an adequate manner due to several factors or reasons. The reasons given were (1) lack of physicians' understanding of their role, (2) shortage and inappropriate distribution of Saudi physicians, and (3) inadequate planning,

supervision, and follow-up of the function. This study concluded that the main problem was the lack of health education in the people served, which resulted in poor community participation.

The patient in Saudi Arabia needs more information about health matters and more effort and time must be spent in health education. In studies comparing the primary care system (first contact) and first level primary care, Dodd (6) presented several illustrative cases. The cases demonstrated some patients' reactions to and opinions of their problems.

Case I:

"A middle-aged Sergeant in the Army who had burning epigastric pain for fifteen years. The pain interferes with his life and makes him miserable; it has been investigated with several barium meals and much treated. He says that it is brought on by eating large, fatty meals or hot spicy food and that it is not too bad when he takes antacid. When it was suggested that he might avoid his pain by modifying his diet, he rejected it because he did not want always to be taking medicine. He just wanted a straight-forward, once and for all cure of his pain."

Case II:

"A Captain in the Air Force, both he and his wife have had asthma for four years. About three years

ago he was given, by a doctor in the town, Betamethasone tablets, which produced a very remarkable cure. He continued to buy them in the market even after they had lost their anti-asthmatic effect and made him obese, hypertensive, and cushingoid. He was sent to London where his asthma was controlled and he was weaned off his steroids. He came home feeling much better and in fact, believed that he was cured. He was very upset when the asthma recurred six months later. He came to the clinic to see if we could cure him."

Case III:

"A man aged about 60, who has had diabetes for about four years. At present there is no sign of complications. His principle symptoms are polyuria and occasional burning micturition. He has attended two private doctors in the town, each of whom has prescribed a different hypoglycemic agent. According to his symptoms each day he takes one or the other, both or none of his tablets."

These cases indicate that patients have a poor knowledge of their diseases. From the above cases one can understand the feelings and reactions of uneducated patients about their diseases and treatments.

1. The patient does not realize the danger of the

illness or disorder, unless it is very severe and leads to hospitalization.

2. The patient wants a cure from the first contact with the physician. He thinks that just one visit is sufficient.

3. The patient does not want to use the medications for long periods of time in chronic disease states.

4. ~~He or she does not recognize the benefits and~~ limitations of the medications.

5. The patient may discontinue his medications suddenly without returning to the physician.

6. He does not realize the dangers of medication. He may misuse or abuse these medications and experience dangerous adverse drug reactions.

7. The patient may go to more than one physician for the same illness and receive different prescriptions. He may use both of these prescriptions or just one or none of them.

Another study (7) was done in a Riyadh military hospital of 10 women between age 21-32 years. They were asked why they did not attend antenatal clinics. The reasons given for the failure of the women to participate included: fear of the doctor; they did not know what the clinic was for; or they were feeling well and did not need to visit the clinic. When they were asked about the importance of attending the antenatal clinic, all the responses were "we do not understand the importance of these clinics."



Five thousand two hundred and forty letters were received in the television program (3) and 786 randomly selected letters were analyzed. Sixty-one percent of the correspondents were male ranging in age from 15 to 25 years. Six hundred four letters asked specifically about the correspondents' own illness. One hundred forty-six letters out of 786 asked about general health problems. Two hundred forty letters which were received included questions about a specific treatment for the correspondents' complaints. Three hundred sixty letters mentioned the fact that the writer had already sought medical advice. One hundred thirty-two of the 786 mentioned that they had been seen by more than one physician. Thirty-two letters explained that they had visited a traditional healer who practiced Arabic medicine. This study concluded that consulting more than one physician at the same time is a common practice, and the majority who wrote these letters were young people interested in their own health. The author recommended further health education programs and the introduction of these programs into the schools (3).

The pharmacist can have an active role in improving the health care in Saudi Arabia. He can be a source of information regarding the appropriate use of medications, and the pharmacist could provide educational services for the out-patient such as:

1. The importance of taking medicine as directed.
2. Appropriate dosage schedule.
3. Determination of drug(s) already being taken by the patient which might interfere with any newly prescribed medications.
4. What drugs, food, or over-the-counter medications to avoid while on the newly prescribed therapy (8).

~~There are several functions which the pharmacists can perform such as:~~

1. Obtaining and maintaining a patient data base for use in making pharmaceutical decisions affecting patient care.
2. Advising the patient on OTC drug therapy.
3. Consulting with physicians about therapeutic goals and end points, appropriate drug therapy, and product selection.
4. Consulting with patients about the proper use of prescription medications.
5. Referring the patient to appropriate health care personnel on the basis of problem assessment.
6. Safely dispensing, distributing, and administering medications to patients.
7. Identifying manifestations of any drug toxicities and taking appropriate action.
8. Serving as a source of health and drug information for the patient. (9)

The pharmacist may play a role and influence the selection of over-the-counter (OTC) medications, and the advice concerning the appropriate use of OTC medication is the responsibility of the pharmacist. The pharmacist should give an accurate therapeutic consultation (10).

#### Statement of Purposes

The purpose of this study was to determine the types of and the level of information which should be provided to Saudi patients about their prescribed medications, and to identify problems concerning the patient's use of medications prescribed by outpatient departments. A questionnaire was designed to elicit the above information. This thesis analyzed the results obtained from the questionnaire, and from this information makes recommendations regarding the role of the pharmacist in health education in Saudi Arabia. To address the information deficiencies identified in the survey, an appendix was prepared which includes examples of some diseases which are common in Saudi Arabia. Included for each disease is a description of the disease and possible causes, drug treatment, instruction to the pharmacist and instruction to be given to the patient regarding the medications.

## CHAPTER II

### METHODOLOGY

A questionnaire (Figure 1) was developed, and sent to various cities in different parts of the United States.

The cities were Stockton, Chico, Redwood City, and Sacramento, California; Portland, Oregon; and Washington, D.C. These cities were selected because they have a relatively large population of Saudi students. The majority of these students are males living temporarily in the United States. When they finish their studies, it is anticipated that they will return home. A questionnaire was developed and sent to 200 Saudi students in the United States; 111 completed questionnaires were returned. Ninety-three students were male and 18 were female. The distribution of the students who completed the questionnaire was as follows: Redwood City, 16; Chico, 16; Sacramento, 16; Portland, Oregon, 25; Washington, D.C., 20; and Stockton, CA, 18. These students represented different parts of Saudi Arabia which included all of the five regional divisions, West, East, North, South, and the Middle.

The format of the questionnaire is presented in Figure 1. It was requested that these questions be answered as

to the respondents' behavior and experience in Saudi Arabia and not their experience in the United States. The questionnaire shown in Figure 1 was also sent for administration in Riyadh, Saudi Arabia in order to get responses for comparison with the answers given in the United States. Fifty-one persons (44 males, 7 females) completed the questionnaire. The majority of respondents were male because it is difficult to get responses from females in the unmixed society which exists in Saudi Arabia, especially in the middle region.

## Figure 1

Questionnaire

These questions relate to our society in Saudi Arabia. Please answer them honestly and relate them to our society.

Name: \_\_\_\_\_

Age: \_\_\_\_\_ Sex: \_\_\_\_\_ Occupation: \_\_\_\_\_

School: \_\_\_\_\_

City in Saudi Arabia that you came from: \_\_\_\_\_

1. When do you go to the physician (doctor), or to the hospital?
  - a) immediately after you feel sick
  - b) wait a while, and then go
  - c) only if you feel very sick
2. Do you always complete the course of medication (drug) which the doctor prescribed for you (gave you) according to the directions?
  - a) Yes
  - b) No
3. After you feel better, do you continue to take your treatment (drugs)?
  - a) always
  - b) frequently
  - c) sometimes
  - d) never
4. Do you go to the pharmacy (drug stores) directly to get your medication (treatment) without going to the physician?
  - a) sometimes
  - b) frequently
  - c) always
  - d) never
5. Do you use the medications of others (such as friends and relatives) if you think your sickness is similar?
  - a) always
  - b) sometimes
  - c) frequently
  - d) never
6. Do you visit more than one physician (doctor) for the same illness?
  - a) sometimes
  - b) always
  - c) never
7. If you have drugs (medications) from past illnesses (diseases) which the doctor gave you, do you use those medications (drugs) without going to the doctor?
  - a) Yes
  - b) No

Figure 1. Continued

8. How would you like the pharmacist to give you information about your treatment (medication, drugs)?

- a) written      b) orally (verbally)      c) both

9. Do you think the time which the pharmacist spends with you at windows of the pharmacy is enough to understand or to ask about your medications?

- a) enough      b) not enough

10. What kind of information would you like the pharmacist to give you concerning your treatment (your medications)?

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11. Are you satisfied with the services which the pharmacist gives you in Saudi Arabia?

- a) Yes      b) No

If you answered NO, please explain: \_\_\_\_\_

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## CHAPTER III

### RESULTS

The questionnaire was completed by one hundred eleven Saudi students living in the United States and 51 persons living in Saudi Arabia. The age and sex distribution of the respondents living in the United States are given in Table 3, and the age and sex distribution of 51 respondents living in Saudi Arabia are given in Table 4.

The answers of each group are summarized in Table 5 (United States respondents) and Table 6 (Saudi Arabia residents). The answers to question #10 in Figure 1 and part of answers to question 11 in Figure 1 were comments from the respondents.

A comparison (Table 7) was made between the answers of the questionnaire which was administered in Saudi Arabia and the one which was sent to the students from Saudi Arabia in the United States. This comparison includes the percentage of people from 51 Saudi Arabians who answered the questions. All of these people were asked the same questions (Figure 1) except question No. 7 which was inadvertently omitted to Saudi respondents living in Saudi Arabia.

The answers to question #10, Figure 1, "What kind of information would you like the pharmacist to give you



Table 3. The Age Distribution of Saudi Students in the United States Responding to the Questionnaire.\*

Gender	Age Range	Number
Males	18-24	43
	25-31	44
	32-38	5
	Over 38	<u>1</u>
Total		93
Female	18-24	15
	25-31	1
	32-38	1
	Over 38	<u>1</u>
Total		18

\*The majority of persons answering were males because the majority of Saudi students in the United States are male.

Table 4. The Age Distribution of the People in Saudi Arabia Responding to the Questionnaire.\*

Gender	Age Range	Number
Male	18-24	16
	25-31	7
	32-38	9
	Over 38	<u>12</u>
Total		44
Female	18-24	3
	25-31	1
	32-38	1
	Over 38	<u>2</u>
Total		7

\*The majority of persons answering were males because it is difficult to get responses from females in the unmixed society which exists in Saudi Arabia.

Table 5. The Results of the Questionnaire From 111 Saudi Students in the United States.

Questions	Males	Females	Total (%)
1. When do you go to the doctor or the hospital?			
a. immediately after feeling sick	26	4	30 (27%)
b. wait a while, and then go	27	5	32 (29%)
c. only if they feel very sick	40	9	49 (44%)
2. Do you always complete medicine as prescribed by the doctor?			
a. Yes	51	10	61 (55%)
b. No	42	8	50 (45%)
3. After you feel better do you continue to take medicine as prescribed?			
a. Always	7	0	7 (6%)
b. Frequently	17	5	22 (20%)
c. Sometimes	41	7	48 (43%)
d. Never	28	6	34 (31%)
4. Do you go to the pharmacy directly to get medicine without going to the doctor?			
a. Always	53	8	60 (54%)
b. Frequently	7	2	9 (8%)
c. Sometimes	6	0	6 (6%)
d. Never	28	8	36 (32%)
5. Do you use the medications of others (i.e. friends, relatives) if you think that your sickness is the same as theirs?			
a. Always	3	0	3 (3%)
b. Frequently	25	6	31 (28%)
c. Sometimes	2	1	3 (3%)
d. Never	63	11	74 (66%)

Table 5. Continued

Questions	Males	Females	Total (%)
6. Do you visit more than one physician for the same illness?			
a. Sometimes	53	12	65 (59%)
b. Always	6	0	6 (5%)
c. Never	34	6	40 (36%)
7. If you have a medicine for a past illness (prescribed by a doctor) would you use it again for the same illness without seeing the doctor?			
a. Yes	33	5	38 (34%)
b. No	60	13	73 (66%)
8. How would you like the pharmacist to give you information about your medicine?			
a. Written	27	1	28 (25%)
b. Verbally	5	4	9 (8%)
c. Both	61	13	74 (67%)
9. Do you think the time the pharmacist spends with you at the window is enough to ask or understand about your medicine?			
a. Enough	27	5	32 (29%)
b. Not Enough	66	13	79 (71%)
11. Are you satisfied with pharmacists services in Saudi Arabia?			
a. Yes	29	6	35 (32%)
b. No	64	14	76 (68%)

Table 6. The Results of the Questionnaire Administered in Saudi Arabia out of 51 Surveyed.

Questions	Males	Females	Total (%)
1. When do you go to the doctor or to the hospital?			
a. immediately after feeling sick	9	1	10 (20%)
b. wait awhile, and then go	19	2	21 (41%)
c. only if they feel very sick	16	4	20 (39%)
2. Do you always complete the course of medication which the doctor prescribed for you according to the directions?			
a. Yes	37	2	39 (76%)
b. No	7	5	12 (24%)
3. After you feel better do you continue to take your medication as prescribed?			
a. Yes	18	1	19 (37%)
b. No	28	6	34 (63%)
4. Do you go to the pharmacy directly to get medicine without going to the doctor?			
a. Yes	13	1	14 (28%)
b. No	31	6	37 (72%)
5. Do you use the medications of others (i.e., friends, relatives) if you think that your sickness is the same as theirs?			
a. Yes	12	4	16 (31%)
b. No	32	3	35 (69%)

Table 6. Continued

Questions	Males	Females	Total (%)
6. Do you visit more than one physician for the same illness?			
a. Yes	12	2	14 (28%)
b. No	32	5	37 (72%)
8. How would you like the pharmacist to give you information about your medication?			
a. written	20	5	25 (49%)
b. verbally	6	1	7 (14%)
c. both	18	1	19 (37%)
9. Do you think the time which the pharmacist spends with you at the windows of the pharmacy is enough to understand or to ask about your medications?			
a. Enough	13	1	14 (28%)
b. Not Enough	31	6	37 (72%)
11. Are you satisfied with the pharmacists services which the pharmacist gives you in Saudi Arabia?			
a. Yes	14	3	17 (34%)
b. No	30	4	34 (66%)

Question No. 7 was inadvertently omitted.

Question No. 10 elicited comments from the respondents.

Table 7. Comparison of the Answers to the Questionnaires Administered in the U.S.A. (111 persons) and Saudi Arabia (51 persons).

Questions	Percentage of 51 respondents in Saudi Arabia (No.)	Percentage of 111 students in the United States (No.)
1. When do you go to the doctor or to the hospital?		
a. immediately after you feel sick	20% (10)	27% (30)
b. wait awhile, and then go	41% (21)	29% (32)
c. only if you feel very sick	39% (20)	44% (49)
2. Do you always complete your medications as prescribed?		
a. Yes	76% (39)	55% (61)
b. No	24% (12)	45% (50)
3. After you feel better do you continue to take your medication or treatment as prescribed?		
a. sometimes	--*	43% (48)
b. frequently	--*	20% (22)
c. always (yes)	37% (19)	6% (7)
d. never (no)	63% (32)	31% (34)
4. Do you go to the pharmacy directly to get your medication (drug) without going to the doctor or without a prescription?		
a. sometimes	--*	54% (60)
b. frequently	--*	8% (9)
c. always (yes)	28% (14)	5% (6)
d. never (no)	72% (37)	32% (36)

Table 7. Continued

Questions	Percentage of respondents in Saudi Arabia (No.)	Percentage of 111 students in the United States (No.)
5. Do you use the medications of others such as friends or relatives, if you think that your sickness is the same?		
a. sometimes	--*	28% (31)
b. frequently	--*	3% (3)
c. always (yes)	31% (16)	3% (3)
d. never (no)	69% (35)	61% (74)
6. Do you visit more than one physician for the same illness?		
a. sometimes	--*	59% (65)
b. always (yes)	28% (14)	5% (6)
c. never (no)	72% (37)	36% (40)
8. How would you like the pharmacist to give you information about your medication?		
a. written	49% (25)	25% (28)
b. verbally	14% (7)	9% (9)
c. both	37% (19)	67% (74)
9. Do you think the time which the pharmacist spends with you at the window of the pharmacy is enough to understand or to ask about your medications?		
a. Yes	28% (14)	29% (32)
b. No	72% (37)	71% (79)
11. Are you satisfied with the services which the pharmacist gives you in Saudi Arabia?		
a. Yes	34% (17)	32% (35)
b. No	66% (34)	68% (78)

\*These choices were inadvertently omitted from the questionnaires administered in Saudi Arabia.



concerning your treatment?" can be summarized as follows:

1. How to use the medication correctly.
2. What the patient should do if there are any adverse reactions.
3. What the patient should do if he forgets to take the medications.
4. The possible side effects of the medications.
5. How long the drug should be used, and information regarding necessity for refill.
6. The storage of the medications, and the expiration date.
7. If there are any foods which interfere with the treatment.
8. What the dangers of overdose are and what to do if overdose occurs.
9. Why the doctor gave them a specific drug for their illness.
10. Some information about their illness.
11. Explanations of all information concerning their treatment.

Question #11, Figure 1, asked, "Are you satisfied with the services which the pharmacists give you in Saudi Arabia?" Possible answers were "yes" or "no," and if the answer was "no," an explanation was requested regarding dissatisfaction with the service. The explanations are represented by the following:

1. Pharmacists do not care about the patients.
2. Pharmacists are foreigners and they can not speak Arabic.
3. Pharmacists do not give enough information to the patient.
4. Pharmacists do not always give written instructions concerning the use of the medications.
5. Limitation of time available with the pharmacist due to the crowds of people at the windows of the pharmacies.
6. Writing on the label is handwritten and is difficult or impossible to read.
7. The explanations which are given orally do not satisfy the patients because they are unable to hear due to the noise from the crowds of waiting people.

## CHAPTER IV

### DISCUSSION

Table 7 shows a comparison between responses from Saudi students living in the United States and responses from students residing in Saudi Arabia. In response to question No. 1, "When do you go to the physician (doctor) or the hospital?" the two groups showed a similarity in that a large percentage of both groups chose the answer "only if you feel very sick." This indicates they may not realize the dangerous nature of their illness. Question 2 (Table 7) asked, "Do you always complete the course of the medication which the doctor prescribed for you according to the directions?" The answers given by the two groups show that a large percentage from both groups may not follow the instructions which were given and it indicates that this percentage is greater among the students living in the United States than among the correspondent living in Saudi Arabia. This indicates that the role of the pharmacist is to inform the patient whether he needs to refill the prescription or not, and to emphasize that the patient must complete or continue to take the medications as prescribed.

The patient often stops taking the medications at the first sign of relief. This is confirmed by the answers

to question No. 3 (Table 7) which asked, "After you feel better do you continue to take your medication or treatment as prescribed?" which indicated that a high percentage of both groups never continued to take the medications after they felt better. The apparent discrepancy between the responses to these two questions may be explained as follows: Two responses were inadvertently omitted to Saudi respondents living in Saudi Arabia. It is possible that persons who answered "Never" would have selected one of the omitted choices. An alternative explanation is that interpretation of the two questions is different. The respondents may have believed that they should have taken the medications just until they felt better. The responses to question No. 5 (Table 7) which asked, "Do you use the medications of others such as friends or relatives if you think that your sickness is the same?" indicated that one third of each group may use the medications of friends or relatives if they think their sickness is the same. The reasons why they would do this are unclear since health care is provided without cost. However, this is a frequent occurrence which may lead to dangerous complications of illness, drug-drug interactions, or adverse drug reactions. The pharmacists can improve patient medication compliance by the use of the following procedures (11):

1. Multiple medication consultation
2. Patient follow-up reminders to reinforce patient's

- knowledge of proper self-administration techniques.
3. Advising physician regarding patient medication non-compliance.
  4. Medication consultation delivered in the proper environment.
  5. Additional information in printed or handwritten handouts presented to patient.

The factors which may lead to drug therapy problems in outpatient clinics due to the services which are provided to the patient include:

1. Availability of non-narcotics and tranquilizers without a prescription (5) which can lead to misuse or abuse of the drugs, or to drug-drug interactions. Question No. 4 (Table 7) asked "Do you go to the pharmacy directly to get medicine (drugs) without going to the doctor (without a prescription)?" The answers indicated that in both groups, there are some who go directly to the pharmacy to get medications without a prescription.
2. Absence of a patient's medical record in the hospital or in the pharmacy. Even if the record exists, the patient may go to another clinic or hospital and because of this, it is difficult to recognize the duplication of prescriptions. In answers to questions No. 6 (Table 7) which asked, "Do you visit more than one physician for the same illness?", the

responses from the students from Saudi Arabia living in the United States indicated that 65 of the 111 may see another doctor and may receive another prescription. They may use the two prescriptions together or they may not. Case III (6) in the Introduction described a 60 year old man who had visited two private doctors; each doctor gave him a different hypoglycemic agent and he used both. The answers to question No. 6 indicated that a significant part of the population change their doctor quickly concerning the same illness because they want an immediate cure from the first visit to the doctor, and do not understand either their disease or the treatment.

3. Poor communication between the physician, pharmacists, and the patient due to the language barrier and due to the limited time which the physician and pharmacist spend with the patient.

Patient compliance can be improved by educating the patient, and the most important factor is better communication between the patient and health care professionals. Bal (12) has written about the communication problem of non-English speaking persons in England. He made several suggestions for physicians to remember when they deal with non-English speaking patients: talk slowly, simply and clearly; repeat words; avoid medical terms; and use logical sequence,

illustrations, pictures, and models. He also recommended the use of an interpreter if possible. On the other hand, in Saudi Arabia the majority of the people speak the Arabic language only and it is difficult for them to communicate with the physician or pharmacists, or pharmacists assistants who cannot speak Arabic. Eliminating the language barrier may play a significant role in increasing patient compliance.

Thus, the clinical pharmacist can play an active role in determining outpatient problems associated with their therapy. A study was done by Christensen, et al. (13) to determine the nature and the extent of outpatient drug therapy problems encountered by the pharmacists. It also described the types of drugs which were most frequently involved in these problems and the nature of changes in drug therapy problems due to pharmacist's intervention. These problems can be summarized as follows: (1) drug overuse, which included a wide number of drugs but no specific predominant one; (2) drug overuse, with antihypertensives, diuretics, and potassium supplements being the most frequently mentioned; (3) drug interaction which was classified into two categories, life threatening interaction such as phenylbutazone-warfarin, and moderate or non-life threatening interactions such as antacids and tetracyclines. The author concluded that there were two to four potential drug therapy problems per hundred prescriptions dispensed. They demonstrated the importance

of pharmacists in decreasing the incidence of these problems.

The amount of time the patient spends with the physician or the pharmacist is very limited because of the crowds of people waiting to be served. In reply to question No. 9 (Table 7) a high percentage of both groups indicated that the pharmacist does not spend enough time at the window explaining uses of the medications. This factor is caused by the large number of people waiting for their medications and the very little time the pharmacist assistant or the pharmacist has to spend with each patient. The large number of prescriptions that are filled may lead to mistakes in the filling and little time with the patient to give instructions. The answers to question No. 8 (Table 7) which asked "How would you like the pharmacist to give you information about your medication?" indicate that a high percentage of the U.S. respondents would prefer both written and verbal instructions while the respondents living in Saudi Arabia would prefer written instructions. In reply to question No. 10 (Figure 1) which asked, "What kind of information would you like the pharmacist to give you concerning your treatment?", the answers included the desire to know general information about the medications such as usage, side effects, adverse reactions, foods to avoid, storage, expiration date and specific information about the medications dispensed. These responses were similar to that which Herxheimer (14) suggested that the patient may ask.

In the reply to question No. 9 (Table 7) which asked



"Are you satisfied with the services which the pharmacist gives you in Saudi Arabia?" possible answers were "yes" or "no," and if "no," an explanation was requested. Approximately two thirds of each group were not satisfied with the services which are provided and the explanations were carelessness of the pharmacists, and poor communication with the pharmacist due to a) the language difference, b) limitation of time spent with each patient, c) crowds of people waiting and the high level of noise and inability to hear what the pharmacist is saying. The written instructions on the label are handwritten, difficult to read, and lack adequate information given by the pharmacist.

## CHAPTER V

### CONCLUSION

The factors or reasons which usually lead to the increasing incidence of adverse drug reactions, drug-drug interactions, and toxic reactions of medications in Saudi Arabia have been discussed. The out-patient in Saudi Arabia does not have a medical record in the outpatient department or in the pharmacy. It is important that hospitals and pharmacies keep records for the patient in an organized manner to avoid the duplication of prescriptions. The patient must be encouraged to cooperate with this system.

Since non-narcotic and tranquilizer drugs may be obtained without a prescription, it is important to follow the law or the regulations if there are any, and restrict availability of these medicines from any hospital pharmacy or from the market pharmacies without prescriptions.

There is poor communication between the physician and the patient and between the pharmacist and the patient due to the language barrier and the limited time which the physician and the pharmacist spend with the patient. The physicians and pharmacists who can speak the Arabic language should work in outpatient departments, and those who cannot speak Arabic should work inside the hospitals. Currently the patient is assigned

the name of a physician and then waits at the physician's office door with many other patients until called; this causes the physician to be in a hurry and spend less time with each patient. An appointment based on a triage system is recommended. Well experienced physicians working in the admission office could screen and classify the patients depending on the type and severity of illness. An appointment should be given to those patients who can wait. Patients needing immediate care would be seen by the appropriate physician. This will reduce the pressure on the pharmacy and will give the patient and the pharmacist or pharmacist assistant time to provide appropriate information and will give the patient time to ask questions about his illness and medications.

There is a lack of compliance by the patient regarding instruction for his treatment. Better patient compliance can be obtained by use of appropriate publicity in television, radio, newspapers, journals and by the introduction of health education as a requirement in the secondary schools.

The pharmacist should play an active role in helping solve these problems by monitoring drug therapy and thus preventing adverse drug reactions and interactions. Pharmacists can advise patients about possible dietary (food-drug) interactions, or other medical problems which may interfere with their treatment. The pharmacist should verbally explain to the patient the directions, possible side effects, and the

proper storage of medications. The pharmacist should provide typed instructions on how to use the drug, the expiration date, the name of the doctor, and the name of the person for whom the prescription is being filled. This should be typed on the label instead of handwritten and abbreviated.

Finally, the pharmacist must consider himself an educator and consultant regarding medications and health related problems. He should expand his role in these areas. The pharmacist must continue to study, and read journals to maintain and improve his information skills. The pharmacist should attend continuing education programs or conferences, have regular conferences with his colleagues, which will help him to be up to date.

The pharmacist has a unique position to reinforce medication instructions and make a valuable contribution to the drug therapy of each patient, since he is the last person which the patient sees. It is important for the patient to be given instructions and information by the pharmacist regarding the illness and/or treatment. This information should be given verbally to those people who cannot read, and in printed form explained in simple language for those who can read. He can provide printed pamphlets on specific diseases or drugs. He could prepare health educational materials for newspapers, television, radio to educate the public about medications and their appropriate use.

A proposal regarding the nature and level of information which pharmacists should provide to Saudi patients on their prescribed medications is presented in the appendix. This appendix does not represent all of the diseases which are common in Saudi Arabia, but contains examples of some classes of diseases which are mentioned in the introduction. The information given for each disease can be used as a source for additional labeling to provide more specific administration details, and to encourage the patient to participate in his treatment. It can also be used as a source of information for patient education or for handouts which can be given to the patient.

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APPENDIX



APPENDIX

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## INTRODUCTION

In a general public hospital or outpatient department, the factors usually leading to the treatment-failure, increased incidence of adverse drug reactions and harmful drug interactions, and toxicity of medication are the following: First, the patient rarely has a record in the hospital or pharmacy; even if a medical record exists in a particular hospital, the patient may go to another facility, making the recognition of overlap or the duplication of prescriptions extremely difficult. Second, the availability of non-narcotics and tranquilizers without a prescription contributes to the misuse or abuse of a drug, or to adverse drug reactions. Third, the communication between physician or pharmacist and the patient is usually very poor due to the difference in language and background and the insufficient amount of time devoted to each patient.

A questionnaire was developed and sent to Saudi students in the United States and a sample in Saudi Arabia asking them what they would like to know, in general, about diseases and their treatment. Their responses influenced the type of information given for each of the selected diseases in this appendix. The ensuing body of information is neither meant to be a comprehensive catalog of all diseases found in Saudi Arabia, nor a replacement for the physician, but rather

a proposal and aid to increase the awareness of the people and to help the pharmacist or pharmacist assistant understand what the patient needs to know. The aim of this paper is to look briefly at each of eleven diseases and conditions, focusing on the identification and methods of control of these diseases, instructions for the patient, the role of the pharmacist both to help in public health education of these and other medical problems, as well as to help decrease the incidence and improve the treatment of the selected diseases.

The first two chapters deal with two parasitic diseases common in Saudi Arabi, Giardiasis is common in Saudi Arabia because of several factors: First, the climate of Saudi Arabia is hot and very suitable for parasites. Second, there are some customs, especially hand-shaking, because of infrequent hand washing, which aid in the transmission of this disease. Third, most of the population eats by hand and often people, especially children, do not wash their hands before eating, leading to the increase in the incidence of Giardiasis especially with children. Finally, Saudi Arabia is an underdeveloped country. The majority of the population is not educated and poor sanitation exists almost everywhere.

The second chapter deals with amebiasis. Amebic dysentery is probably the most important tropical infection present in the Middle East, found in a large percentage of the population. There are several factors which contribute to this high percentage. First, the climate is hot and suitable

for parasites. Second, this infection is endemic in this area. Finally, the large population of flies contributes to the transmission of this infection. Generally, the most important promoting factor is the inadequacy of health education to enable the people to prevent this disease.

The third chapter discusses trachoma, a major problem in Saudi Arabia. It is worldwide in distribution but it is endemic in the Middle East. The high prevalence is due to the poor hygiene of people, the crowded living conditions, and the dusty windy weather.

Sexually transmitted diseases are the topic of chapter four. They are worldwide, as well, and not usually reported in Saudi Arabia because the patient does not often go to a physician. The refusal to report these diseases is a major problem. The reason that sexually transmitted diseases are included in this section is to help young people and others take care of these infections themselves and to help increase their awareness of their hidden problems.

The fifth chapter focuses on peptic ulcer, the incidence of which is increasing rapidly due to changes in the way of life and the daily living habits of the people. There is increasing evidence of smoking and an increase in stress. There are many commonly used drugs which may induce ulcers such as aspirin and phenylbutazone.

Chapter six is concerned with iron deficiency anemia, common, particularly in children, due to malnutrition or an unbalanced diet. The incidence is also common in women

because of frequent pregnancies and iron deficient diets.

The seventh chapter deals with rheumatoid arthritis. This disease was selected because of the difficulties of its management, the increase in the incidence of drug-drug interactions and the frequency of self-treatment.

Chapter eight, concerning adult onset diabetes mellitus, discusses this disease, and the symptoms and methods of monitoring the condition.

Hypertension in chapter nine is another important factor, along with diabetes, in causing heart problems and cerebral vascular accident, in Saudi Arabia.

Chapter ten discusses epilepsy, about which there are some misconceptions heightening the chances for several problems, such as uncontrolled seizures due to failure of the treatment, drug interactions which interfere with the treatment or adverse reactions from the treatment.

The Appendix concludes with glaucoma, which is common in elderly people. It is considered the first cause of blindness and hence frustration for many people.

The role of the pharmacist for outclinic patients includes consultation concerning the nature and symptoms of the disease, and the nature of the medications used in the treatment of the disease. In an attempt to achieve a balance of information for each disease, each chapter includes the following information:

1. A description of the disease and possible cause;
2. Drug treatment, usual drugs and dosage;

3. Instructions to the pharmacist for each disease and on his role in their treatment; and
4. Instructions to be given to the patient regarding the medication, and for infectious diseases, the means of preventing re-infection.

## Chapter 1

### GIARDIASIS, INFECTION(S)

Giardiasis is an infection by the parasite called *Giardia lamblia*. This parasite is from the family Hexamitidae. Motile giardia averages about 7 x 14 Mm and has two nuclei and four pairs of flagella and has a specific characteristic which is a suction disc on its ventral surface. The two stages of this parasite are (1) the trophozoite which cannot live outside the body, and (2) the pathogenic cyst form which exist as pairs (1). The hosts are mainly man, pigs, and monkeys (2). The mode of transmission is contaminated water, food and from one person to another. In Saudi Arabia flies play a major role in the transmission of this disease. The usual incubation period is 15 days and the average duration of symptoms is 44 days (1). This parasite lives in the duodenum and upper part of the jejunum. The disease can be symptomatic. The symptoms of long duration are diarrhea and accompanying weight loss from dehydration, and abdominal pain. The stool is watery and odiferous and sometimes the stool is accompanied by mucous. The disease interferes with intestinal functions resulting in malabsorption of fat, vitamin A, glucose, xylose, folic acid, and vitamin B<sub>12</sub> (which can cause other kinds of disease such as anemia) (13, 4, 5).

This infection is most common in children, is the first cause of steatorrhea and it mimics celiac disease (intestinal malabsorption characterized by diarrhea, malnutrition, bleeding tendency, and hypocalcemia) (4). The diagnosis can be confused with some kinds of allergies, such as milk proteins.

Occurrence of this disease is worldwide, but it is more common in areas with warm climate and poor sanitation. The susceptibility of the individual varies from one person to another and depends on many factors such as age (the occurrence more common in the elderly and children than in young adults). Gastroectomy, decreased gastric secretion, chronic pancreatitis, and malnutrition enhance the susceptibility of individuals (4).

The methods of control to prevent this infection are numerous. In general, the first thing is the health education of the people in order to increase the awareness about this disease. Second, the disposal of feces must be in a suitable place, far away from the public water supply and sewage systems should be improved. Third, there should be protection by chlorination of the public water supply from contamination. Fourth, victims and carriers (who work as food handlers in restaurants and food markets especially), must be educated regarding this infection. However, there is no isolation, quarantine or vaccination for this disease (6), and finally, the containment of flies, both by insecticide and sanitary measures, should constitute a major effort.



Treatment: The treatment of giardiasis infection depends on accurate diagnosis. The diagnosis of this infection is very difficult and it is based on the microscopic scanning for the cyst in the sample of feces, duodenum fluid, and jejunum fluid. Also, by the biopsy of intestine and looking for trophozoite in the second stage (6). Quinacrine hydrochloride (Atabrine) is usually the drug of first choice. The usual adult dose is 100 mg, three times daily for seven days. The dose for a child is 7 mg/kg of the body weight. An alternative drug, metronidazole (Flagyl), is given 2 gm daily for 3 days for an adult, 1 g daily for children above 7 years, 600 mg daily for children 3 to 7 years, and 400 mg daily for an infant. Some points should be discussed regarding these two drugs for the treatment of giardiasis. First, quinacrine hydrochloride is a very toxic drug, the effects of which include dizziness, headaches, mild gastrointestinal disturbance, chronic dermatitis, yellow discoloration of the skin after prolonged duration of use. Second, the toxicity of quinacrine is very dangerous and the treatment is as follows: If the patient needs respiration assistance, give oxygen, and intravenous fluid, and a vasopressor for hypotension. In acute toxicity, emesis or aspiration is recommended. The antidote is ammonium chloride which is administered at 12 gm daily by mouth for the purpose of enhancing urinary excretion (8). Finally, metronidazole (Flagyl) has toxic effects, but less severe than quinacrine. The side effects are gastrointestinal disturbance, anorexia, nausea,

vomiting, coated tongue, and darkening of the urine (8).

Metronidazole (Flagyl) is used with caution in pregnant women because there are reports it may cause cancer and thus is not recommended during the first trimester of pregnancy. Also, metronidazole should not be given with alcohol because it interferes with the metabolism of alcohol and produces a disulfiram-like reaction. Finally, metronidazole should not be used in patients with blood dyscrasias.

#### Some Characteristics of These Drugs

Characteristics	Metronidazole	Quinacrine HCl
Description	white, creamy crystalline	yellow, odorless
Taste	not bitter	bitter
Distribution	all over the body	concentrates in liver, pancreas, spleen
Excretion	via urine	via urine
Half life	6.2 hours	5 days
Excreted in breast milk	yes	yes
Storage	protect from light	airtight; protect from light

In conclusion, the best way to prevent this disease is education of the people to control, prevent transmission, and to help eradicate this disease.

How to Prevent Infection from Giardiasis:

1. Work toward the containment of flies inside the house.
2. Cover food and water to protect them from flies.
3. Wash with water all fruits and vegetables before eating them.
4. Do not drink standing rain water.
5. Use chlorinated water if possible, or boil the water.
6. Wash hands before and after eating.
7. If one person in your family is infected, go with him to the hospital and begin treatment.

There is some information which the pharmacist should tell the patient about the disease and the treatment:

#### Instructions to the Pharmacist

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1. Be sure to give the patient the right directions on how to use the drug.
  2. Give the patient some information about the drug.
  3. Tell the patient "Do not drink alcohol."
  4. Tell the patient "There is some change in urine color."
  5. Tell the patient to complete the course and return to the hospital again.
  6. Give the patient the directions on how to store the medication including keeping the medication away from children.
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#### Instructions to the Patient

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1. Your medication (Flagyl) can undergo drug interaction with alcohol, so there is some problem regarding the intake of alcohol with this drug.
  2. Be sure to mention your medication to the other physicians or a lab manager who might want to take or to measure thyroid function, as the Flagyl will interfere with this.
  3. There will be changes in the color of your urine.
  4. Be sure there is no doubling of dosage and mention the name of your medication to any other physician you visit.
  5. Return to the hospital after completing the course of treatment; you may need another course of treatment.
  6. If you are a mother do not be confused between the diarrhea resulting from the allergies from milk and this disease. Go to the hospital if a child has diarrhea.
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## Chapter 2

### AMEBIASIS

Amebic dysentery is probably the most important tropical infection present in all of the Middle East. This infection is common in a large percentage of the population. There are several factors which contribute to this high percentage. First, the climate of Saudi Arabia is suitable for this parasite to live. Also, the large population of flies contributes to transmitting this infection. Second, this infection is considered an epidemic in this area. Saudi Arabia now is one of the developing countries where medical care is poor and the hygiene is sometimes very poor. Finally, the most important factor is that the health education is insufficient to educate the people to prevent this disease. This chapter will briefly discuss this infection and its treatment, in hopes that it will help people pay some attention to this infection, to help the reader at least to consider this infection as a major problem, and perhaps eventually eliminate it.

The prevalence of amebiasis ranges from 5% in most countries to 80% in countries with poor hygiene, especially tropical and subtropical countries (9, 10). The parasite causing the infection is called Entamoeba histolytica. This parasite is mobile and has two stages cyst and trophozoite. The trophozoite ranges from 10-60  $\mu\text{m}$ , and usually is 25  $\mu\text{m}$

in length. Also, the trophozoite has a nucleus which appears as a halo or a ring under the microscope. The cytoplasm consists of granules, food vacuoles, and red blood cells which the parasite has ingested. The pathogenic stage is the cysts which are able to survive outside a human body, in contrast to the trophozoite which can only survive a short period of time outside the human body (11). Not being acid resistant, the trophozoite is not contagious. The cysts are acid resistant and can stay in the soil, water or other fomites a long period of time (10). The mode of transmission for this disease depends on the mechanical transmission of the cysts. In Saudi Arabia, flies are considered the major mode of transmission. Food contamination by cysts or water contamination, plays a role in the transmission of pathogenic cysts (11). Roaches can also carry the cysts on their legs from feces to food or water and contribute to spreading the disease. Also, the cysts can spread from one person to another by unclean hands. This mode of spreading, especially with food handlers and food stores, is a major concern.

When a person ingests the cysts from one of the above sources it causes infection, but if the person ingests the trophozoite it is destroyed by gastric acid. The major problem is the asymptomatic infections in the carriers as this person is the active source of the infection (10). The pathogenesis of infection begins when the person ingests the cysts which are then converted to immature ameba going

into the large intestine. The immature ameba begins to invade the mucosa by secretion of alytic substance, and causes ulceration, from which the symptoms appear (10).

*Entamoeba histolytica* is not always pathogenic but sometimes can become pathogenic and cause serious disease under specific conditions: changing diet, increased cholesterol, change in hormones, patient under heat stress, and increased humidity. All of these stimulate or contribute toward changing the non-pathogens to pathogens. The symptoms of the disease are different from one disease state to another. The acute form is different from the chronic. Acute infection occurs after a large dose is ingested and is characterized by diarrhea with blood and pus present, the infection responded to treatment and is not serious if treated effectively. By contrast, the chronic illness is characterized by mild diarrhea with episodes of constipation.

A complication of the infection is anemia, it resulting from the loss of blood over a sustained period of time. This anemia is iron deficiency anemia and can be corrected by eating foods rich in iron, or an iron supplement (9). Another dangerous complication is abscesses of the liver. A recent study (14) showed some evidence that the abscesses of the liver were due to *Entamoeba histolytica* infection. Another possible complication is amebic pericarditis, which is rare (14, 15).

The usual host is man. Transmission occurs through the shedding of cysts in the feces with subsequent

contamination of food and water. The usual incubation period is two to four weeks, but the incubation period may vary from only a few days to as long as several months. There is no immunization against this parasite, but it is not contagious and thus the patient need not be quarantined.

Amebiasis can be diagnosed in several ways. First, the diagnosis could depend on the microscopic examination of different samples of feces, looking for cysts or trophozoites. With acute infection, trophozoites are found in the feces. Also, stool specimens must be examined immediately because trophozoites are destroyed by heat after a short period of time. Second, an indirect hemagglutination test on serum specimens could be administered (21). Third, one could use an antibody test. This test depends on the indirect--immunofluorescence test (IFT) for the serologic diagnosis of amebiasis. It is uncomplicated to administer; a few parasites need be present for diagnosis. It is good for identifying both acute and chronic infections (16). The fourth method of diagnosis is a liver scan for hepatic amebic abscesses.

Another method of diagnosis is proctoscopy and obtaining a sample and identifying ulceration. The parasite may be isolated by being cultured in a suitable medium. Any one of the above methods is not enough alone to give an accurate diagnosis of the illness, as there are different species of amebic infection and other easily confused similar infections, such as shigellosis, appendicitis, diverticulitis, and giardiasis.



The methods of control and prevention of the infection depend on personal hygiene. Some general principles to limit the spread of the infection are listed below.

1. The living environment inside the cities and villages must be made more sanitary.
2. Human feces must be disposed of in a sanitary way and covered.
3. The government is responsible for the protection of the public water supply, for using chlorine, iodine or sand filter to remove or destroy the infectious cysts.
4. Education is the best way to control the infection by increasing the awareness of the people in regard to hygiene and sanitation.
5. Eradication or diminution of the disease would be a major step to prevent transmission.
6. The Department of Public Health must investigate the restaurant workers and food handlers, and enforce standards of cleanliness.

On the personal level there are many methods to prevent the disease.

1. Hand washing after using the toilet, with hot water and soap.
2. Cover your food and your water to protect from the flies.
3. Use a suitable chemical to control the flies while using covering or screening on the windows and doors.

4. Remove the garbage every day.
5. Do not eat vegetables or fruit unless they are washed with chlorinated water.
6. Do not eat in restaurants where you are not sure about standards of cleanliness.
7. Wash your hands before eating any kind of food.
8. Always use boiled or chlorinated water (17, 21).

Treatment: The treatment of this infection varies with case and place of infection. Many drugs may be used. The following tables list these drugs, their characteristics and uses.

#### Drugs which are Used to Treat Amebiasis

Case	Drug of Choice	Alternative
Asymptomatic	Diiodohydroxyquin 65 mg tid x 20 days OR Diloxanide Furoate 500 mg tid x 10 days	Metronidazole 75 mg tid x 10 days
Mild infection	Paromycin 25 mg/kg in 3 doses for 10 days + Diiodohydroxyquin	Metronidazole
Serious infection	Metronidazole + Diiodohydroxyquin or Paromycin + Diiodohydroxyquin	Emetine HCl + Paromycin
Hepatic Abscesses	Metronidazole 750 mg tid x 10 days	Emetine HCl + chloroquine phosphate

Drugs used in the treatment of Amebiasis

Drug	Site of Action	Side effects	Drug interactions	Notes
Diodohydroxyquin	Acts in the bowel lumen	headache, pruritus, enlarged thyroid, optic neuritis	Effect on blood test because of the presence of iodine	high possibility of causing neuritis
Diloxanide Furate	bowel lumen	vomiting, pruritus, urticaria, flatulence		protect from light
Paromycin	bowel lumen	diarrhea, may cause damage to cranial nerve, deafness, kidney damage	malabsorption syndrome with sucrose	like neomycin, avoid with renal damage

Drug	Mechanism	Side effects	Drug Interaction	Comments
Metronidazole (Flagyl)	Amebicidals	gastrointestinal disturbances, anorexia, nausea, vomiting, darkening of the urine	Alcohol	Avoid with alcohol
Emetine HCl	inhibits RNA synthesis in tissue of organism amebicide	degenerative diseases of the heart, kidney, irritation causes vomiting, nausea, diarrhea, neuritic, hypotension, myocarditis	antihypertensive drug; there are synergistic effects	ECG monitor is recommended
Chloroquine Phosphate	inhibits protein synthesis,	headache, pruritus, gastrointestinal disturbance, psychic, drowsiness, convulsions, visual disturbance		quick absorption, toxic symptoms within 30 minutes

## Instructions for the Pharmacists (18, 19, 20)

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1. Most of the drug interactions, side effects, and adverse reactions of these medications should be known.
  2. Store these medications in a place protected from light.
  3. Tell the patient about any change in urine color, such as caused by Flagyl and chloroquine.
  4. Be familiar with the proper dose and the toxic dose and how to treat toxicity.
  5. Remember all of these notes:
    - a. Flagyl, as well as other drugs, is contraindicated in pregnancy.
    - b. Flagyl and chloroquine change urine color.
    - c. Paromycin interacts or interferes with absorption--the malabsorption syndrome.
    - d. Diiodohydroxyquin interferes with blood tests.
    - e. Emetine may cause hypotension and cardiac arrhythmias. It should be monitored in a hospital (ECG).
    - f. Avoid emetine during pregnancy.
    - g. Use emetine with caution in elderly.
    - h. Emetine is contraindicated in cardiac problems, or renal problems.
    - i. Diiodohydroxyquin is contraindicated with an impaired kidney or liver.
    - j. Corticosteroids therapy should be avoided if the patient has amebiasis because corticosteroids may enhance the severity of the disease.
    - k. Chloroquine phosphate should also be avoided during pregnancy, hepatic disease, or in the case of alcoholism.
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Instructions for the Patient (10, 19, 20)

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- A. Be sure that you do not double the dose or take another drug which may interact with your medication.
  - B. Tell your Doctor about any symptoms that you feel from your medication.
  - C. After you complete the course of the treatment return to the hospital for a follow up examination.
  - D. It is recommended that if you have an infection, go with your entire family to be investigated.
  - E. Do not take cortisone or an antiinflammatory drug as you may aggravate your problem.
  - F. Remember that the cleaner your are the safer will be from infection recurring.
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## Chapter 3

### TRACHOMA

Trachoma is a major problem in Saudi Arabia and other Middle East countries. It is a chronic disease caused by Chlamidia trachomatis, and is considered the leading cause of blindness in the world. It is an infectious disease, highly contagious, which infects the membrane lining of the eyelids, covering the front of the eye. The early or initial symptoms of this disease include redness in one or both eyes. The eye becomes swollen and the patient may feel a foreign body under the eyelids. Additionally, the patient is sensitive to light (photophobia) (22).

The incidence of this disease is high among children of 8 to 10 years. The disease may progress to a conjunctival scar and this may shrink causing the eyelid to turn inward so that it blinks constantly. It also may lead to corneal ulceration which can cause blindness (23). Acute inflammation, combined with upper respiratory infections such as sinusitis and otitis, is common. The chronic infection may produce kerato conjunctivitis which, involving the cornea, turns to scar formation and reduces capacity for sight (24, 25).

The causative agent is a Chlamydia, an obligate intracellular parasite. It has some characteristics of both virus and bacteria. It is similar to a virus in its

intracellular nature but differs by having DNA and RNA. It is similar to bacteria but lacks the mechanisms to produce energy and therefore, depends on the host cells. It can survive in the host cells and multiply by binary fission. These Chlamydia are incapable of synthesizing ATP and the host cells supply them with it. The genus is Chlamydia, but this is further categorized as Chlamydia trachomatis, Chlamydia psittaci. The chlamydia trachomatis is involved in trachoma and other diseases such as bilateral interstitial pneumonia, nongonococcal urethritis, salpingitis, cervicitis, and conjunctivitis (22).

It occurs worldwide, but is endemic in the Middle East. The high prevalence is due to first, the poor hygiene of the society; second, the crowded living conditions; third, the dusty windy weather also helps to increase the prevalence (22, 23, 24). The reservoir and the source of this infection is children under age 10, and usually under age five (23). The methods of transmission are numerous, but the most important factors are:

1. close contact eye to eye
2. birth canal infection, especially in the newborn
3. flies may carry Chlamydia from the discharge of an infected eye.
4. certain articles which come in contact with an infected person.

Trachoma is considered the disease of the family, especially in a crowded family with many children. Reinfection



is common especially in children in an area where trachoma is endemic (23). The infection is characterized by intra-familial transmission in Saudi Arabia (28). The infection may be latent. The infection does not express itself until a period of time when a person visits an endemic area, and anyone who has not had childhood trachoma may develop acute trachoma later.

The diagnosis is based on:

1. eye exam
2. looking under the microscope for cytoplasmic inclusion bodies
3. Chlamydia isolation
4. human serology (complement fixation) (22)

To prevent the infection on the individual person level, there are some guides to follows:

1. apply ointment (antibiotic) on each eye of newborn baby.
2. exclude the infected child from school.
3. improve the standard of cleanliness to avoid infection.
4. do not use the articles which belong to others who are infected.
5. use your own personal towels or articles which belong to you.
6. do not have contact with an infected patient.

There are several methods to control this infection on the societal level.

1. the most important factor is the education of the people to improve their personal hygiene.
2. educate the people to use individual towels, and toilet articles, and do not use other people's articles.
3. control flies by screening the doors and windows, and using suitable chemical sprays.
4. remove the garbage and eliminate the flies' breeding place.
5. begin investigation and screening of all preschool children, and treat the infected child.

Treatment: Tetracycline orally is the drug of choice for treatment of Chlamydia infection. It is bacteriostatic which inhibits the protein synthesis of Chlamydia. There are three types of tetracycline: short acting, intermediate, and long acting. They are available in different dosage forms: capsules, tablets, injections, and also ointment 1% - 3% as tetracycline hydrochloride. The usual dose is typically: 1% - 3% ointment, tablets of 250 mg or 500 mg three times daily for an adult (26).

Instructions to the Pharmacist

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1. Tetracycline will interfere with bone growth. Avoid dispensing tetracycline to pregnant women or young children.
  2. Tetracycline is used with caution especially in renal failure patient.
  3. Avoid dispensing Tetracycline to children up to 12 years of age because it will cause permanent discoloration of child's teeth.
  4. It should not be given with any hepatotoxic agents.
  5. Tetracycline may cause a deficiency in folate and cause anemia.
  6. Protect tetracycline from light to avoid photodegradation.
  7. Remove any tetracycline with darkening or change in color from your counter.
  8. Tetracycline loses potency of approximately 10% when it is stored at 37° for 2 months.
  9. Be sure you give the patient the adequate dose and be sure that he is not taking cortisone or antacids with it.
  10. Tetracycline has many side effects, including Gastrointestinal disturbance, vitamin deficiency, increase incidence of infection by Giardiasis, teeth discoloration (in children) photosensitivity, and increased fat in the liver. (29).
  11. Erythromycin can be used as alternative to tetracycline.
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### Instruction for Patient

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1. You should not take tetracycline with milk or buttermilk because these contain magnesium and calcium which decreases absorption of the tetracycline.
  2. Be sure you do not take tetracycline with alcohol because alcohol increase the metabolism of tetracycline.
  3. Be sure do not mix tetracycline with antacid because this will decrease the absorption of tetracycline.
  4. Do not take tetracycline especially if you are pregnant or nursing a child.
  5. Avoid the sunlight especially for a long time because of photosensitivy.
  6. Report any side effects or adverse reactions to your physician or pharmacist.
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## Chapter 4

### SEXUALLY TRANSMITTED DISEASES

There are many sexually transmitted diseases. The route of transmission is the same but the causative agents are different. The most common sexually transmitted diseases are described, and emphasized will be gonorrhoea, being the most common in Saudi Arabia. The incidence of these diseases is different from one disease to another. The most common diseases shown in the following pages are adapted from American Pharmacy, Vol. NS20, No. 8, August 1980, page 35.

The first disease is gonorrhoea; the symptoms of gonorrhoea are different for the male than for the female. In women it is usually asymptomatic; but if there are symptoms they are usually characterized by vaginal discharge and cystitis. In the male symptoms are dysuria, urethral discharge, and pain during urination (30).

The diagnosis of gonorrhoea depends on the microscopic examination and culture of the microorganism. The treatment of gonorrhoea is by antibiotics such as Penicillin G, 4.8 million units by intramuscular injection in two different sites. Probenecid is used orally to enhance or increase the peak serum of penicillin. The alternative is tetracycline--0.5 gm orally, four times daily, for 5 to 10 days.

Gonorrhoea is an infectious disease caused by Neisseria gonorrhoeae. Neisseria gonorrhoeae is gram negative diplococci bacteria. The host of this gram negative bacteria is the human. It causes a frequent purulent urethritis in men and purulent vaginitis in women, purulent conjunctivitis in the newborn child, and gonococcal proctitis in both women and men. Also Neisseria Gonorrhoeae causes salpingitis (pelvic inflammation in women) and also purulent arthritis (31). If the infection is not treated it may cause septicemia with pustular skin lesions, fever, and chronic prostatitis, especially if it disseminates (32).

The symptoms of Gonorrhoea in men are purulent urethral discharge, dysuria, frequent urination, and it may be asymptomatic. This asymptomatic infection is the frequent source of infection and it works as a carrier. The symptoms of gonorrhoea in women are dysuria, frequent urination, an increase in vaginal discharge, abnormal menstrual bleeding, anorectal discomfort, cystitis, and also may be asymptomatic.

The occurrence of purulent urethral discharge for four to ten days after sexual contact is sufficient evidence to make presumptive diagnosis. In women this is very difficult because the asymptomatic is most common.

Diagnosis Gonorrhoea in women depends on:

1. A smear looking for intracellular gram negative bacteria diplococci.
2. Thayer-Montin Media, culture the exudate in enriched chocolate agar with some antibiotics such as vancomycin,

nystatin to eliminate the growth of other bacteria or fungi. The specimen should be taken from the endocervical of the woman.

3. Coagulation test.

4. Serological test especially the tests which distinguish syphilis from gonorrhea.

#### Transmission of the Microorganism--

The major route of transmission is by sexual contact of an infectious person. There is a myth that gonorrhea or other sexually transmitted diseases are transmitted by articles or by the hands (33). The second route of transmission is the infected birth canal. The newborn can be infected especially in the eyes. This may result in gonococcal ophthalmia neonatorum especially if the 1% silver nitrate drops or antibiotic eye ointments are not administered (34).

#### How to Prevent the Infection

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1. Use a condom during sexual contact.
2. Urination immediately following intercourse may be helpful, especially in men.
3. Washing the genitalia with water and soap.
4. Use antibiotics cream or foam for prophylaxis.
5. Some have recommended Penicillin G in a dose of one million units immediately before and after.
6. To prevent the gonococcal ophthalmia neonatorum, apply to the eyes of newborn 1% silver nitrate solution or an antibiotic ointment.

The second disease is syphilis (31), of which there are two types: primary syphilis and secondary syphilis. The primary syphilis is characterized by a painless chancre. Secondary syphilis is characterized by cutaneous and mucous membrane lesion, alopecia, and generalized lymphadenopathy. The diagnosis of syphilis is derived by a VDRL (Venereal Disease Research Laboratory) test or RPR (Rapid Plasma Reagin) or by use of an electron microscope. The treatment of syphilis is by benzathine penicillin G--2.4 million units IM, or procaine penicillin G--4.8 million units (600,000 units IM daily for 8 days).

The third disease is nongonococcal urethritis (NGU). It is characterized by urethral discharge, purulent or mucoid. The diagnosis depends on the clinical picture of the symptoms. It also depends on the microscope and culture to distinguish NGU from the *Neisseria gonorrhoeae*. The usual treatment is tetracycline, 0.5 gm four times daily for 21 days.

The fourth disease is trichomoniasis, a protozoan infection (*T. vaginalis*). It is characterized by erythema and edema of the external genitalia, a greenish-gray vaginal discharge, or it may be asymptomatic. The diagnosis depends on the microscopical examination of the discharge and the treatment is Flagyl, 2 gm orally, or 250 mg three times daily for seven days.

The fifth disease is virus-caused genital herpes. This infection is characterized by vesicular lesions in the



vulva, vagina, and the cervix in the women, or lesions in penis prepuse and scrotum in men. The diagnosis is made by microscopical examination to eliminate other diseases. There is no specific treatment.

The sixth disease is vulvovaginal candidiasis--a mycotic infection. It is a common infectious disease of the vulva. It is characterized by erythematous and edematous vaginal discharge which is characterized by a white, thick color. The diagnosis depends on the culture or by the microscopical examination. The treatment is nystatin vaginal suppositories inserted twice daily for 14 days.

The seventh disease is Corynbacterium Vaginale Vaginitis. This disease is characterized by gray white discharge and vulvular irritation. The diagnosis depends on the clinical picture of the symptoms and also the microscopical examination. The treatment is by ampicillin--500 mg every six hours for 10 days.

Anther problem is pediculosis pubis, known as "Crabs," which is characterized by erythematous, itching papules. Nits, larvae or adult lice stick to the hair around the pubic area or hair around the anus. The diagnosis depends on clinical observation of lice. The treatment is usually 1% gama benzene hexachloride lotion or 25% benzyl benzoate lotion combined with antibiotics to prevent secondary infection.

The next disease is Scabies. This infection is characterized by the red papule which contains the mite. The

scratching may produce excoriation. This is most common on fingers, wrists, elbows, ankles, and waist. It is characterized by night-time itching. The treatment is as for pediculosis.

Genital Warts is a disease characterized by pinkish papillary growth which occurs around the vulva introitus. The diagnosis depends on the clinical appearance and histological observation. The treatment is podophyllin; 10-25% in tincture of benzoin, applied weekly.

Chancroid is a tender ulcer (soft chancre). The base of this ulcer is covered by yellow or gray necrotic exudate. The diagnosis depends on the clinical appearance and on the test which distinguishes the Chancroid from syphilis. The treatment is by sulfisoxazole--1 gm orally four times.

Lymphogranuloma venereum, is characterized by painless vesicles or superficial nonindurated ulcers on the genitalia. This is diagnosed by the clinical picture or by the complement fixation test. The treatment is by tetracycline--500 mg orally four times a day for 2 to 3 weeks.

The disease granuloma inguinale is detected by subcutaneous nodules which erode through the skin producing clean granulomatous beefy red lesions. The diagnosis depends on the clinical picture. The treatment is tetracycline 0.2 gm four times a day for 3 weeks.

Hepatitis Type B is an insidious onset infection characterized by abdominal discomfort, anorexia, nausea, vomiting. If this disease progresses it may lead to jaundice.

### Instructions to the Pharmacist

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1. First of all, do not prescribe any medication to any person who thinks they may have a sexually transmitted disease unless he has first seen a doctor.
  2. Learn the current treatment schedule for uncomplicated gonorrhea.
  3. Tetracycline should be avoided in pregnant women.
  4. Remember there may be drug interactions with tetracycline, such as with antacids or milk products.
  5. Probenicid is used with penicillin to increase the peak serum level of penicillin.
  6. Probenicid may cause nausea, vomiting, precipitate uric acid stone and primary gouty arthritis.
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### Instructions for the Patient

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1. If you have the symptoms of gonorrhea do not hesitate to visit the doctor as soon as possible.
  2. The treatment is usually penicillin. If you are sensitive to penicillin tell your doctor.
  3. Avoid contact with your partner(s).
  4. Personal cleanliness is important.
  5. Avoid the causes which lead to reinfection.
  6. If you have gout tell your doctor because he may prescribe probenicid.
  7. Pregnant women should avoid tetracycline.
  8. Follow the treatment accurately (30, 32).
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## Chapter 5

### PEPTIC ULCER

Peptic ulcer is a term used to represent the ulcerative disorder of the upper gastrointestinal tract. Peptic ulcer includes three different types of ulcers, gastric ulcer, duodenum ulcer, and Zollinger-Ellison syndrome (35). Each of these three ulcers varies in incidence and specific character (37).

The incidence of peptic ulcer in the male is higher than in the female because of the hormonal protection in the female. The duodenal ulcer is more common than the gastric ulcer, and more common in younger people between 25-50 years; in contrast, gastric ulcer is more common in older people. The differences between gastric and duodenal ulcer are in areas of location, severity, and cause (36). First, the location of the duodenal ulcer is in the first segment of duodenum but the gastric ulcer is found on the wall of the stomach, making treatment more difficult. Secondly, the duodenal ulcer is a benign ulcer, while the gastric ulcer may be malignant. Finally, the amount of hydrochloric acid secretion differs from the gastric ulcer to the duodenal ulcer. The acid secretion associated with a duodenal ulcer is more than the normal which would exist with no ulcer; and in the gastric ulcer, the secretion is normal or may be lower than normal.

There are several causes of the duodenal ulcer. These causes may be endogenous or exogenous. The endogenous causes are increasing vagus nerves stimulation, increasing gastric and secretion or gastric acid overproduction, increasing vulnerability of mucosa, gastric mucosal atrophy and the inflammation of gastroduodenum mucosa (gastritis) (37).

The exogenous causes which may lead to ulceration are stress (which includes emotional stress, stress due to operations), burns, or a type of stress prone personality known as Type A personality. Genetic factors may have an influence such as blood group O. Also, drugs which may induce ulcers are most common, and numerous. Some of the more important drugs are aspirin, phenylbutazone, indomethacin, reserpine, alcohol, caffeine, cigarettes, potassium chloride tablets, and corticosteroids. Reserpine and caffeine increase acid secretion, and alcohol causes gastritis as well as local irritation (37).

The symptoms of peptic ulcer (duodenal ulcer) are epigastric pain, characterized by "heart burn," an increased sensation of hunger, and fullness in the right middle epigastrium especially about 90 minutes after eating. This pain is relieved by food or by using an antacid or even vomiting. Also, there are symptoms of the gastrointestinal tract which include nausea, vomiting, indigestion, constipation, and the vomit may contain blood (coffee ground vomiting) (35, 37).

There are several complications associated with peptic ulcer.

A. A chronic loss of blood causing anemia, i.e., hypochromic microcytic anemia.

B. The ulcer may penetrate the stomach wall and include other organs such as the pancreas.

C. Perforation may occur in which the ulcer eats the gastric or duodenum wall due to erosions to the peritoneum cavity. Food which is contaminated enters the cavity causing peritonitis and septicemia. Besides these, there may be pyloric obstruction with continuous vomiting.

The diagnosis of peptic ulcer is usually made with the first signs and symptoms. The pain which is relieved by food or antacid is evidence or at least a suggestion of duodenal ulcer. Also, there are several x-ray examinations. The barium examinations of the upper gastrointestinal tract, endoscopy, intragastric photography, or the multiple purpose endoscope (36) are used to diagnose this condition.

The treatment of peptic ulcer is basically life-long. The goal of treatment is to prevent the recurrence of the ulcer and to heal the present ulcer, by decreasing gastric acidity and to relieve pain and stress.

First of all, diet is very important. The diet must be nutritious with a restricted intake of gastric irritants; such as alcohol, coffee, tea, chilies, peppers, or other hot foods. It is recommended to take frequent small meals. Using milk to neutralize the acid has some advantage, but

there are disadvantages. Milk has poor neutralizing power, and is also rich in lipids which may increase chances of heart diseases. Also, milk protein increases acid secretion and has a high amount of calcium which influences the heart function.

The second step is the use of antacids. Antacids neutralize acid, but have no healing function or cure. Antacid drugs are selected based upon the neutralization capacity and sodium content. The best antacid is an antacid which has high neutralizing power, and an absence of acid rebound, with no constipation or diarrhea as adverse reactions, or side effects. Also, a good antacid has no influence on the electrolyte balance.

There are several antacid preparations and some of these are: sodium bicarbonate preparations, which are potent and short term, rapidly acting, but may cause systemic alkalosis if a more than 200 m Eq  $\text{NaHCO}_3$  Sodium Bicarbonate to a patient under the age of 60 years old, or if given by 100 m Eq to a patient above 60 years old. The second preparation which frequently described is aluminum hydroxide, and it causes constipation. It may be prescribed alone or with magnesium hydroxide to neutralize the acid and the side effects of aluminum hydroxide. The third preparation is magnesium hydroxide and it is poorly absorbed by the intestine and may cause osmotic diarrhea. It is used usually in combination with aluminum hydroxide. The fourth preparation contains calcium carbonate, and

prolonged use may cause adverse reactions such as producing calculi, acid rebound and hypercalcemia. Anticholinergic drugs such as atropine and probanthine but they are not recommended. This group is not recommended because the amount of drug to neutralize or to inhibit the vagus is close to the toxic dose. The side effects of these medications are dry mouth, blurred vision, confusion, and may cause tachycardia (37, 38, 40, 41).

The next group is H<sub>2</sub> antagonists, or histamine antagonists. Emetidine (tagamet) is an example of this group and the usual dose of cemitidine (tagamet) is 300 mg four times daily. It is used as a prophylactic as well. The side effects may induce mastitis, and maybe mental confusion, especially in old people. The last solution or treatment is surgery. Surgery is not done except if there is a high recurrence rate or frequent complications such as penetration, perforation, or obstruction. Surgery is also done when there is a malignancy (40).

In conclusion, the selection of antacids depends on the situation of the patient and the diagnosis. The patient may have heart failure and need restricted sodium intake. He must be treated by low sodium antacids. Also the treatment complication which is associated with peptic ulcer is very important. It is very difficult to manage a patient with peptic ulcer who also has rheumatoid arthritis or gout. Remember that you should not prescribe any medication without having proper information and background on the patient.



## Instructions for the Pharmacist

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1. Remember that all of the drugs which are used to neutralize acids may have interactions with other drugs.
    - a) Tetracycline should not be administered with an antacid.
    - b) With digitalis it is very important to monitor the dose. Antacid impairs the absorption.
    - c) Naproxen absorption is delayed by an antacid.
    - d) An antacid increases the levodopa absorption.
    - e) An antacid decreases iron absorption, especially magnesium trisilicate.
    - f) Indomethacin is inhibited by an antacid due to decreased absorption.
    - g) An antacid reduces the rate of lithium absorption.
    - h) Oral anticoagulents should not be used with an antacid. If the patient needs to use an anticoagulant, he should use only warfarin.
  2. Remember the list of ulcerogenic drugs such as aspirin, indomethacin, phenylbutazone, cortisone, reserpine, and potassium chloride tablets.
  3. Remember that the patient who has a peptic ulcer may develop hypochromic microcytic anemia (iron deficiency anemia).
  4. Remember that these drugs should be taken 1 hour after a meal except if the physician orders otherwise.
  5. Remember the dose must be reduced if the patient has renal insufficiency.
  6. Selection of the antacid is based upon the neutralizing capacity and also upon the sodium content, especially with a patient who has a peptic ulcer and other disorders, such as hypertension and congestive heart failure.
  7. There are many products. The most common are listed in the following table.

Product	Ingredient	Neutralizing Capacity
Aludrox	Aluminum Hydroxide + Magnesium Hydroxide	42
Amphojel	Aluminum Hydroxide	29
Camalox	Aluminum Hydroxide, Calcium Carbonate, + Magnesium Hydroxide	54
Ducon	Aluminum Hydroxide, Calcium Carbonate, + Magnesium Hydroxide	105
Gelusil	Aluminum Hydroxide, Magnesium Hydroxide, Simethica	36
Maalox	Aluminum Hydroxide, Magnesium Hydroxide	39
Gelusil II	Aluminum Hydroxide, Magnesium Hydroxide Simethica	71
Milk of Magnesia	Magnesium Hydrate	35
Riopan	Magnesium Aidrate	33
Titralic	Calcium Carbonate	35

(Adapted from the Handbook of Clinical Drug Data, p. 377).

8. You may find other preparations which are used to treat Peptic Ulcer especially from Europe, such as licorice derivatives, or antipepsins, or antigastrics.
9. Some use hormones such as estrogen (36).

Instructions for the Patient

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1. Avoid gastric irritant foods such as chilies, alcohol, tea, green chilies, hot peppers, smoking, cola, coffee, or any type of food or activity you feel is a gastric irritant.
  2. Avoid the ulcerogenic drugs such as aspirin, indomethacin, phenylbutazone, reserpine, potassium chloride tablets, and cortisone.
  3. Take rich nutritional food in small meals many times a day.
  4. Use the antacid which your physician prescribed for you and report anything about the drug to your physician.
  5. Report any side effects of tagamet to your physician.
  6. Avoid situations which lead to stress, accept the disease and therapy and learn how to manage it.
  7. Remember that ulcers are never completely healed and may recur. You must use the antacid as long as you live.
  8. Visit your physician regularly (37, 41).
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## Chapter 6

### IRON DEFICIENCY ANEMIA

Iron deficiency anemia is the most common anemia in Saudi Arabia, as it is world wide. It occurs especially in pregnant women and in preschool children, although found in all ages. Iron deficiency anemia is microcytic hypochromic anemia, meaning the red blood cells are small and pale. The hemoglobin is very important for the transportation of oxygen and carbon monoxide from tissue to the lungs. When iron deficiency occurs, the production of the blood cells is less effective and the formation of the hemoglobin content is affected. The red blood cells, being small and pale, reduce the capacity of the blood to maintain normal oxygen transportation (43).

The symptoms of iron deficiency anemia are numerous and depend on the degree of the severity of the deficiency. Most cases are asymptomatic, but if a case is symptomatic, it will be manifested by these symptoms: fatigability, faintness, palpitations, shortness of breath, headache and pallor. Pregnant women as well as children may feel a strange appetite which is called pica; there is often an abnormal appetite for clay, ice and other things that are not fit for food.

There are several causes of anemia due to iron deficiency (44). The first cause is an imbalance in diet. Iron

is naturally absorbed and the excess is deposited in storage, as the body's reserve, in the hepatic epithelium. The daily iron requirement differs from one individual to another. For example, the normal man and non-menstruating woman need 5-10 mg daily. The menstruating woman needs 7-20 mg daily. The pregnant woman needs 20-40 mg daily. Iron is found in the following kinds of foods: liver, meat, whole grains, potatoes, egg yolks, green vegetables, and fruits (43). It is very important that there be an adequate diet with a good selection of the above for children, especially preschool children. The infant after six months of age will deplete all of the iron storage which he had from his mother. Now he needs iron from external sources. Children often develop milk anemia due to lack of iron in their food. The second cause is the failure to absorb the iron from the food which is ingested. This cause may be secondary to gastrointestinal diseases or malabsorption (45). The third cause is loss of blood. This is the most common cause of iron deficiency anemia. The chronic loss of blood causes the iron deficiency and develops the anemia. This cause can be resultant from several factors.

- a. Ulceration in the gastrointestinal tract, such as peptic ulcer or duodenal ulcer, leading to iron deficiency.
- b. Hookworm infection which will consume the food and also cause internal bleeding. The hookworm produces

chronic bleeding and the iron escapes with the blood.

- c. Drugs, such as aspirin and phenylbutazone, may also induce irritation and bleeding in the gastrointestinal tract.

The fourth case is frequent pregnancy. Pregnancy increases the demand for as well as the loss of iron because of the large amount of blood lost during labor. Infections such as tuberculosis or autoimmune diseases such as rheumatoid arthritis will prevent iron utilization and cause iron deficiency anemia. Finally, lack of hydrochloric acid, or lack of Vitamin B6 may cause anemia (44).

The diagnosis of iron deficiency anemia depends on the severity of this deficiency. When iron storage has been depleted, plasma iron falls and erythropoiesis is curtailed. Red blood cells may be morphologically normal (normocytic).

The results of iron deficiency may be one or more of these:

- a) Plasma iron level is decreased.
- b) Iron binding capacity is increased.
- c) Transferrin saturation is about 5-15% and the normal is usually 10-20%.
- d) Sideroblasts are decreased.
- e) The morphologic shape is normocytic or microcytic hypochromic.

There are some laboratory tests such as a) microscopical examination of smear of marrow aspirate for hemoiderin

granules, b) the plasma levels iron values decreased, and c) if the level is less than 50 mg/100ml then the patient is considered anemic.

#### How to Prevent Iron Deficiency Anemia

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- A) A good diet containing meat, liver, eggs, and green vegetables is very important to maintain adequate iron level.
  - B) Do not depend on one kind of diet such as rice, and do not eat at irregular intervals, or miss breakfast.
  - C) Pay attention to the children and their diet. Give them foods containing iron.
  - D) Pay attention to a child, to see if he has pica, and the pregnant woman should pay attention to her own appetite.
  - E) Correct the causes of the iron deficiency before you treat anemia.
  - F) Vigorous exercise should be avoided if you have anemia.
  - G) Pregnant women should visit the physician regularly during pregnancy (43).
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The treatment of iron deficiency anemia is simple. Just treat the cause by giving iron supplement (47). There are oral preparations which are ferrous salts such as sulfate, gluconate, and fumarate. The usual oral dose is 200 mg daily. The oral iron supplement is preferable to the parenterally supplement.

The parenteral supplement is iron dextran. This injection is not recommended except when there are some factors

which force you to use it. These factors are: oral malabsorption, serious gastrointestinal disturbance, ulceration in the stomach or in any part of the gastrointestinal tract, and gastrointestinal infection.

The iron supplement which is given orally is transported across the intestinal mucosa and it is carried by transferrin to the erythroid marrow. The parenteral iron dextran is metabolized by the liver parenchyma and reticuloendothelial cells. Then the iron containing carbohydrates split, and the free iron is carried by transferrin to the bone marrow.

The dose of ferrous sulfate is 200 mg twice daily for at least three months (44). The side effects of iron preparations may be gastrointestinal irritation, constipation, diarrhea, stained teeth, and sometimes acute poisoning, especially in children (49).



Instructions for the Pharmacist

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- A. All iron preparations should be labeled "Caution! Keep out of reach of children." Acute poisoning is very common among children. A dose of 1 gm can cause acute poisoning.

The symptoms of poisoning:

Gastric irritation, necrosis, nausea, vomiting, shock, pallor, cyanosis, drowsiness, and the stool color is green.

Treatment:

1. Induction of vomiting
  2. Administration of eggs and milk
  3. Gastric lavage
  4. 1% sodium bicarbonate to convert iron to a less soluble compound.
  5. Chelating agent may be used such as deferoxamine.
- B. You will see more than 40 or more oral preparations of iron. Some have intrinsic factors, and some vitamins such as folic acid. There is no advantage to these additions. The simplest and best preparation is ferrous sulfate.
- C. Iron preparations affect a blood test, especially bilirubin. Iron dextran gives falsely positive results.
- D. Iron darkens the urine, due to the sulfide.
- E. Iron dextran is given intravenously. This route is safer than intramuscular. It is given in a dose of 500 mg, by slow administration.
- F. Some drugs inhibit absorption of iron from the gastrointestinal tract. These antacids, tetracycline, vitamin E, pancreatic extract and penicillamine.
- G. Coated tablets decrease the absorption of iron because the best site for absorption of iron is the upper gastrointestinal tract (43, 45, 47, 48).
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### Instructions for the Patient

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- A. The oral iron preparation should be taken with a full glass of water 1 hour before meals or two hours after meals.
  - B. If there is nausea or vomiting, take the oral preparation during the meal.
  - C. If you use an antacid, be sure that you do not take it with iron because antacids decrease absorption.
  - D. Keep out of the reach of children. As acute poisoning is very common. One dose of the medication may be toxic to your child.
  - E. Tetracycline will decrease absorption of iron.
  - F. Do not miss any dose as it will contribute to the failure of the treatment (48, 49).
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## Chapter 7

### RHEUMATOID ARTHRITIS

There are several rheumatic diseases. These are rheumatoid arthritis, osteoarthritis, gout, ankylosing spondylitis, polymyalgia, vasculitis, rheumatic fever, juvenile chronic polyarthritis, and others (51). In the following pages rheumatic arthritis will be discussed as an example of rheumatic disease.

Rheumatic arthritis is considered a chronic disease of unknown causes (52). This disease is evidenced by inflammation of one or more of the joints. It usually begins with simple inflammation, becoming warm and swollen. If the disease progresses it can cause development of granulation tissues, called pannus formation. This granulation begins to destroy the articular cartilage causing pain and erosion of the cartilage. The surface of the cartilage is converted from a smooth surface to a rough one, leading to subluxation or dislocation of the joint. The late stage is characterized by ankylosis (rigidity of the joint), which leads to deformities (52).

Some of the signs and symptoms of rheumatoid arthritis are fatigue and muscle weakness, swollen joints which may be symmetrical, limitation of joint movement or motion, prolonged morning stiffness, and difficulty in walking. Also an increased incidence of colds with low grade fever.

Rheumatoid arthritis is classified into three categories, dependent on diagnostic criteria. Classical rheumatoid arthritis, definite rheumatoid arthritis, and probable rheumatoid arthritis. Those diagnostic criteria include:

- a) the patient may have morning stiffness.
- b) the patient feels pain and he finds that motion is very difficult.
- c) the patient notices swelling in at least one joint.
- d) x-ray findings are positive.
- e) rheumatoid factors are positive.
- f) histological change in nodules or in the synovial fluid.
- g) subcutaneous nodules are present.

It is considered as clinical if most of these symptoms are found in one patient (51, 52). Rheumatoid arthritis is limited to the joints, and is more common in women than in men.

The blood analysis of rheumatic patients is characterized by these findings:

- a) the red blood cells are normocytic hypochromic.
- b) the serum of the patient will show a deficiency in iron concentration.
- c) the white blood cell count will be elevated.
- d) the erythrocyte sedimentation rate is elevated.
- e) the blood protein, especially globulin, is elevated due to increasing synthesis of antibodies IgG, IgM, and IgA.

The diagnosis of the disorder partly depends on the results of laboratory tests such as:

- a) those which measure the erythrocyte sedimentation rate.
- b) serological test, looking for rheumatic factors or antinuclear antibodies.
- c) X-ray findings.
- d) analysis of the synovial fluid.

Rheumatoid arthritis is a very dangerous disorder especially if it progresses. There are some extra articular manifestations of this disease. Those manifestations are:

- a) anemia (normocytic hypochromic anemia). It is considered the most active manifestation of rheumatoid arthritis.
- b) rheumatoid nodules--They are located on the surface of elbows or the external surface of the fingers. These nodules may breakdown and cause the drainage of fluid and become the spot of infection.
- c) nail-fold-thrombi--This may lead to gangrene as well as ulceration.
- d) pulmonary fibrosis--This is characterized by interstitial fibrosis, and nodules in the parenchyma.
- e) pericarditis, splenomegaly, and lymphadenopathy are involved in the late manifestation of rheumatoid arthritis.

## What to do if you have Rheumatoid Arthritis

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1. The earlier you begin treatment, the more benefit you will get from it.
2. It is important to know a little bit about this disease to build a positive attitude regarding this disease.
3. The physical therapy including training procedures and the use of heat can help to relieve pain.
4. Be aware of possibility of developing anemia.
5. The treatments by medications are important, and remember those drugs, which are usually used.
6. Maybe the doctor will prescribe to you corticosteroid or gold salts or penicillamine.
7. Surgery may be done if needed.

The treatment of rheumatoid arthritis depends on the stage of the disease and the response to the medications. There are several lines which the physician must follow.

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The first line of treatment:

Aspirin in large doses.

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Second line of treatment:

A rapid-acting non-steroid anti-inflammatory such as

Ibuprofen - (Mortin)  
Naproxen - (Naprosyn)  
Fenoprofen - (Nalfon)  
Tolmetin - (Tolectin)  
Sulindac - (Clinoril)

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Third line of treatment:

Slow-acting non-steroid anti-inflammatory such as:

Indomethacin  
Phanylbutazone

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Fourth line of treatment:

1. Gold Salts
  2. Penicillamine
  3. Anti-Malaria drugs
  4. Immune suppressives such as
    - a) cyclophosphamide
    - b) azathioprine
- 

Corticosteroids:

1. orally
  2. ACTH injection
  3. intra-articular injection (51)
- 

The first line of therapy is aspirin. It is the drug which the physician usually prescribes. The physician usually does not go to another drug until there is no response to the aspirin or side effects of the drug appear. Aspirin is acetylsalicylic acid. It is a weak organic acid. It has antipyretic analgesic and anti-inflammatory properties. The lower doses of aspirin do not produce anti-inflammatory action as do large ones. Aspirin is absorbed directly from the stomach and upper intestinal tracts, being distributed throughout the body. It will pass through the placenta (53). Aspirin also is found in the cerebral spinal fluid. It is bound to the blood protein especially albumin. Its excretion in the urine is influenced especially by the pH level of the urine. The clearance of aspirin increasing if the urine is alkaline.

The major side effects of aspirin are headache, dizziness, tinnitus, gastric irritation, gastrointestinal bleeding, and ulceration, (especially peptic). The platelet

aggregation is decreased and may cause a bleeding disorder. There may be a hearing loss due to chronic use of aspirin (54).

There are no differences or advantages to using one brand of aspirin over another or from using the buffered kind, if you take aspirin with large amounts of water or after eating meat. All of the brands contain aspirin and vary in their other additives. Bufferin contains 480 mg of aspirin with buffered aluminum glycinate and mg carbonate. Excedrin contains aspirin (280 mg) plus acetaminophen (250 mg), and caffeine (65 mg). APC is aspirin, phenacetin, and caffeine, and it is not recommended.

The other medications are non-steroid anti-inflammatory such as phenylbutazone (Butazolidin) and oxyphenylbutazone (Tanderil). They are effective in reducing the synovitis of active rheumatoid disease. It should be used in short term therapy only because of side effects such as salt retention, peptic ulceration, rashes, and also hematologic abnormalities and disorders. Another drug is indomethacin (Indocin). It has major side effects which are headache, confusion, and peptic ulceration. If neither the aspirin nor the non-steroid anti-inflammatory (such as phenylbutazone or indomethacin) is effective fail, the gold salts may be used (55).

The preparations of gold salts are: gold sodium thio-sulfate, gold sodium thiomalate, gold thioglucose, and gold thioglyconate. However, these can have side effects or cause adverse reactions, such as skin rash. Corticosteroids



may be used as systemic administration or topically, but they have contraindications and may cause adverse reactions such as depressed immune response (51).

In Saudi Arabia, most medication can be obtained without a prescription except narcotics and tranquilizers. This causes a major problem among the population. This problem may cause drug-drug interactions.

Aspirin is found in many homes and the use of aspirin for headache or arthritis is very common. The major drug interactions of aspirin and other drugs are:

1. Alcohol causes gastrointestinal irritation. Aspirin with alcohol increases the risk of ulceration.
2. Aminosalicyclic acid potentiates aspirin and causes salicylism.
3. Ammonium chloride increases the salicylate level due to the decreasing of the clearance.
4. Ascorbic acid (Vitamin C) will increase the plasma level of aspirin.
5. An anticoagulant such as Warfarin of which the major side effect is gastrointestinal bleeding and the use of aspirin will increase the risk of hemorrhage.
6. Aspirin will increase the effect of oral antihyperglycemic agents and may cause hypoglycemia.
7. Aspirin is to be avoided in the presence of gout because aspirin will increase the uric acid level (57).

## Instructions to the Pharmacist

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1. Aspirin is hydrolyzed to acetic acid and salicylic acid when moist. Remove the product from your pharmacy if you notice an odor of acetic acid.
  2. Aspirin is not recommended for an infant under one year.
  3. Aspirin is used with caution in a patient with renal impairment.
  4. Be sure you understand the drug-interaction of aspirin as there is a high chance of interactions.
  5. Aspirin interferes with the lab measurement of uric acid.
  6. Avoid dispensing phenylbutazone to a patient with congestive heart failure.
  7. A patient who is taking phenylbutazone should be warned to report any abdominal pain, fever, rashes, or swelling of the ankles.
  8. The treatment of the toxicity of phenylbutazone is by emptying the stomach and by giving sodium bicarbonate.
  9. All of these medications must be protected from light.
  10. There are now medications which are non-steroid anti-inflammatories. They have less side effects, but they should not be used until there is aspirin failure.
  11. Be aware about the widespread availability of corticosteroids (53).
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Instructions for the Patient

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1. Aspirin may cause peptic ulcer and gastrointestinal bleeding. Take aspirin after meals and drink water with it.
  2. If you drink alcohol, do not take aspirin with it because there is high risk of gastrointestinal bleeding.
  3. Do not mix antacids with aspirin, as they decrease the aspirin's effectiveness.
  4. If you are a diabetic person and you are taking an oral hypoglycemic, do not take aspirin because aspirin may increase the hypoglycemic effect of these agents.
  5. Tell your doctor about any extra medications you are using.
  6. Aspirin is contraindicated in pregnancy, gastric ulcer, or any bleeding of the gastrointestinal tract.
  7. Do not prescribe aspirin for yourself to treat arthritis. You could, for example, have gout and aspirin would be contraindicated.
  8. Be aware if you take phenylbutazone. It must be used for a short period of time, and it should be taken after meals.
  9. Avoid indomethacin (Indocin) if you are taking an antiepileptic drug.
  10. Avoid taking aspirin, indomethacin or phenylbutazone if you have a peptic ulcer, or bleeding.
  11. There are always new drugs, so be sure that you are informed about your medications and report any difficulties to your doctor.
  12. Keep all medications out of the reach of children.
  13. Always report medications, symptoms and complications to your doctor.
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## Chapter 8

### DIABETES MELLITUS IN ADULTS

Diabetes mellitus is a chronic disease characterized by a disorder of the metabolism of carbohydrates, protein, and fat. Diabetes is associated with hyperglycemia due to the absolute absence of insulin or the reduction of the effectiveness of insulin. These are two types of diabetes: the juvenile onset and adult onset diabetes (58). The normal metabolism of carbohydrates, fat, and protein, however, should be discussed before the discussion of abnormal metabolism. After the normal person (non-diabetic) digests and absorbs sugar, the glucose goes into the circulation through the influence of the insulin which is secreted from the pancreas. It is utilized in different areas of the body excluding the brain, which utilizes glucose without the need for insulin. Insulin converts glucose to glycogen in the liver and the muscles; it increases glucose intake across muscle cells; it increases glucose utilization via the Krebs cycle in order to produce energy; it decreases the breakdown to the amino acids and the fatty acids to glucose; additionally, it increases the synthesis of fatty acids and triglycerides. Insulin increases glycogen synthesis and decreases other catabolic processes such as glycogenolysis, ketoacidosis, gluconeogenesis.

If the person does not eat, there is no exogenous sugar in the blood and the glycogen in the liver is converted to glucose. At the same time, the other mechanism, such as gluconeogenesis (synthesis of glucose from amino acids or another source rather than carbohydrates), has begun. Lack of glucose causes wasting the muscle, fat, and protein, and the body depends on its own storage of glycogen, protein, and fat to produce glucose, an essential source of energy.

In the diabetic patient, there is glucose in the blood which cannot be utilized and the mechanisms upon which the fasting person depends to produce glucose are activated. Accumulation of blood-glucose (hyperglycemia) is responsible for many of the symptoms of diabetes (59).

The major symptoms of diabetes are weakness, fatigue, weight loss, and polyuria, polydipsia, and polyhagia. Also, the diabetic may experience blurred vision, pain, muscle cramps, intensive itching, and slow wound healing.

The following table is a comparison between the two types of diabetes mentioned earlier: juvenile onset and adult onset (60).

Juvenile Onset Diabetes	Adult Onset Diabetes
Insulin dependent	Insulin independent
Ketosis prone	Ketosis resistant
Hyperosmolor resistant	Hyperosmolor prone
Rapid onset	Gradual onset

Juvenile Onset Diabetes	Adult Onset Diabetes
Rapid onset	Gradual onset
More severe	Less severe
Greater insulin deficiency	Normal insulin, or higher than normal
Patient is thin	Obese patient
Diet alone is inadequate	Diet may be adequate
No response to oral hypoglycemic agents	Oral hypoglycemic agents are effective (59).

The diagnosis of diabetes is based upon clinical tests. The diagnostic test is the oral glucose tolerance test. This test depends on determining the fasting blood sugar level two hours after administering 100 mg of glucose. If the person is non-diabetic, the blood sugar returns to a normal level within two hours after glucose loading. If the patient is diabetic he needs more time to return to normal. There are a number of other tests for screening and aids to diagnose, such as testing for glucose in the urine, or 2 hour postprandial blood sugar (58).

If the person does not begin treatment for diabetes, there may be many complications associated with increasing blood sugar level. There are some complications which are acute, such as ketoacidosis and non-ketotic hyperosmolar coma.

The later complications are increased tendency for

myocardial infarction, congestive heart failure, tendency to myocardial rupture, and increase in the risk and severity of coronary artery diseases. Patients with diabetes are more liable to coronary disease than non-diabetics. Diabetics also may have decreased or lack of circulation in the extremities, particularly the feet, which may lead to gangrene. High blood sugar level increases the tendency to cerebral vascular accident and hemorrhage. A change in the metabolism of lipoprotein leads to the increase of the total lipid and cholesterol, and a decrease of triglyceride clearance, which lead to hypercholesterimia hyperlipidemia, a condition closely associated with atherosclerosis.

Second, diabetes affects the retina in the eye, causing a chronic progressive disease which may lead to blindness. Diabetes is considered the most important systemic disease which causes blindness.

Third, nephropathy is another dangerous complication which can lead to death due to kidney failure. In this case, there is glomerulosclerosis and a hyaline mass in the glomeruli. Also, there may be glomerulosclerosis which is characterized by glomerular basement membrane thickening. As a result, this causes diabetic glomerulosclerosis of the nodular or diffuse varieties of arterial and arteriolar nephrosclerotic pyelonephrytis. The first clinical pictures are porteinuria, edema, azotemia, and also hypertension. The first sign of nephropathy is edema. There is a possibility of silent myocardial infarction, papillary necrosis, and infections. (61).

In general, the management of diabetes is the balance between diet, exercise and therapy. The diet in insulin-independent diabetes is the keystone. Diet is considered the first step to control diabetes in obese patients. If the patient reduces his weight and the blood sugar is not controlled, other treatments must be initiated. When the symptoms of the disease are adequately controlled by reducing weight and the regulation of the diet, no other therapy is indicated, but if the obese patient cannot control his weight, then oral hypoglycemic agents or probably insulin is required. The diet adjustment must depend on several variables which include the kind and amount of physical activities, occupation activity, body weight, race, and other factors. The diet is calculated on the amount of calories required. A maintenance diet is calculated by multiplying the patient's weight in kilograms by 30, a reducing diet is calculated by multiplying the body weight in kilograms by 20 which will give the daily caloric intake.

The ideal diet is composed of 40% carbohydrates, 20% protein, and 20% fat. These percentages need to be modified upon if there is liver disease, renal disease, and excess body weight. The daily food intake should be divided into five or more meals instead of three meals. Also, the intake of unsaturated fats should be reduced. A vitamin supplement is required, especially in older people and for those consuming a malnutritional diet (62).



The second step of management, if diet alone does not control the blood sugar level, is the use of oral hypoglycemic agent. These agents are the sulfonylureas. They act as stimulants to release insulin from the pancreas, and also they may enhance the effectiveness of insulin at the receptor sites. They also increase the affinity of insulin for the receptor site. Sulfonylureas are used in adult onset diabetes. Those agents which are usually used are listed in the following table (63).

Oral hypoglycemics have an advantage in that they are easy to use, and also they are good for the non-insulin dependent patient, and they stimulate the release of endogenous insulin. The disadvantage is dependence upon the patient to monitor himself when using these agents. There may be some adverse reactions.

The first adverse reaction is hypoglycemia. This is a clinical condition associated with a low level of glucose in the blood. During hypoglycemia the glucose blood level is less than 50mg/100ml. The symptoms and signs of hypoglycemia are feelings of fatigue, heaviness, a tremor in the hands, confusion, nervousness, and sometimes delusions. The usual causes of hypoglycemia are due to:

- a) dietary changes or inadequate nutrition
- b) weight reduction, and the same time using the same doses of oral hypoglycemic.
- c) increasing physical activity above the normal level

AGENT	DURATION	DOSE	FREQUENCY	TABLETS OR CAPSULES	PHARMACOLOGICAL COMMENTS	COMMENTS
Tolbutamide (Orinase)	8 hours	1000- 3000 mg	2 x a day or 3 x a day	500 mg	inactive metabolic products excreted	drug of choice
Acetohexamide (Dymelor)	12-24 hrs.	500-1500 mg	once daily or 2 x a day	250 mg and 500 mg	metabolic pro- duct is more potent as a hypoglycemic effect than the original	the second choice or alternative to Orinase
Tolazamide (Tolinase)	16-24 hrs.	100-1000 mg	once daily or 2 x a day	100-250 mg	has 6 metabo- lite products	intermediate duration of action
Chlorpropamide (Diabinese)	24-36 hrs	125-500 mg	once daily	100-250 mg	excretion unchanged	avoid in renal disease and elderly people

- d) removal of stress, emotional stress or the stress due to a surgical operation
- e) termination of a pregnancy
- f) correction of hyperendocrinopathy such as Cushing Syndrome
- g) omission of meals, or forgetting to take a meal.

There are many factors associated with hypoglycemia due to oral hypoglycemic agents. These factors include inappropriate dosage, a person uses more of the medication than is required, impaired renal functions leading to a prolonged hypoglycemic effect, or by administration of other drugs, which exacerbate the hypoglycemic effects. Also, if the hypoglycemia appears, sometimes syrups, juice, or milk may reverse the situation. The patient may require intravenous hypertonic glucose solution for severe hypoglycemia (58).

There are many drugs which interact with the oral hypoglycemic agents. There are those drugs which may increase the effect and drugs which may reduce the effect leading to hyperglycemia. Anabolic steroids alone may decrease blood glucose level in some diabetes patients. It increases the hypoglycemic response to tolbutamide. Chloramphenicol inhibits hepatic microsomal enzymes activity, the result is an increase in the half life of oral hypoglycemic agents and an increase in the activity of the hypoglycemic effect. Also, monoamine oxidase inhibition interferes with compensatory adrenergic response to hypoglycemic agents. It enhances or prolongs the hypoglycemic response. Phenylbutazone prolongs

the half life of the active metabolite of chlorpropamide and enhances the hypoglycemic response. Probenicid will inhibit the renal tubular secretion of chlorpropamide and enhances the hypoglycemic effect.

On the other hand, alcohol, salicylates, thiazide diuretics, glucagon, epinephrine, and oral contraceptives antagonize the effect of hypoglycemic agents indirectly and may cause hyperglycemia.

#### Instructions to the Pharmacist

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1. Oral agents should not be given until the patient knows how to balance a diet and exercise, and after the failure of the diet alone.
  2. Oral agents are contraindicated in a history of ketoacidosis and insulin dependent cases. Also it is contraindicated with oral contraceptives.
  3. The patient who is sensitive to sulfa drugs may be allergic to sulfonylureas.
  4. Hypoglycemic side effects of oral agents are rare, but it may happen.
  5. If oral hypoglycemic agents and the diet combination fails, the next step is insulin therapy.
  6. Alcohol and oral hypoglycemic agents are contraindicated because alcohol and oral agents produce an antibuse-like reaction.
  7. Alcohol increases the glucose level and causes hyperglycemia. It decreases the effect of the oral hypoglycemic agents (63).
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## Instructions to the Patient

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1. Your medication will not work if you exceed your recommended diet by eating too much starch or carbohydrates.
  2. You must completely avoid table sugar, dates, and candy.
  3. If you take rich foods (nutritional food) you do not need to take vitamins unless your doctor recommends it.
  4. Salt should not be restricted from your diet except for other conditions which need salt restriction.
  5. Remember the fact that your diet should contain protein, fat, and carbohydrates (a complete nutritional diet).
  6. It is recommended to eat on a regular schedule. Make a table of times and follow the schedule carefully.
  7. Do not hinder your social life by refusing invitations to parties or dinners; go, but remember that you must choose the foods which are good for you.
  8. To be safe, follow the diet strictly at all times.
  9. If you are doing more exercise, it is recommended to eat more snacks.
  10. Remember that oral hypoglycemic agents may have adverse reactions, and if this happens see your doctor.
  12. Take care and clean your feet, and do not wear tight shoes; be careful of your feet and protect them from injury or infections.
  13. Visit your ophthalmologist regularly to take care of your eyes.
  14. Remember that you must continue to take your medication all of your life (62, 63, 64).
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## Chapter 9

### ESSENTIAL HYPERTENSION

Hypertension occurs when the diastolic arterial blood pressure rises above 105mmHg. Age, sex, race, and environment are important factors in the etiology of hypertension. The mortality can be reduced by adequate therapy. It is a chronic disease that requires treatment all of the patient's life. There is no known cure for this disease.

There are many factors associated with the increase in risk, as well as being considered precipitating causes for hypertension, such as age, obesity, smoking, high cholesterol levels, and race. The cause of essential hypertension is unknown; but the family history and race play a role in this disease (65).

The signs and symptoms of hypertension vary from one person to another. There may be no overt symptoms and the disease may be identified only by physical examination. Other patients may have symptoms which indicate an elevation of blood pressure, hypertension vascular disease or underlying diseases. The symptoms may include headache (especially in the occipital region), dizziness, palpitation, and fatigue. Also, there are symptoms related to vascular disease which include epistaxis, hematuria, blurred vision, angina pectoris, and dyspnea. If untreated it may lead to heart failure, polyuria, polydipsia, and muscle weakness

which are secondary to hypokalemea.

The diagnosis depends on the symptoms seen, the blood pressure and the laboratory tests which include: a urine test for protein, a blood test for glucose, hematocrite serum potassium, serum creatinine, blood urea nitrogen, and an electrocardiogram test for irregularities.

The goal of treatment of hypertension is to maintain blood pressure in the normal range level and to decrease the mortality associated with rising pressure (65). The first general method of treatment is weight reduction. It is very important to reduce the weight because it is a major risk factor (66). The second step is sodium restriction. The amount of sodium chloride ingested must not exceed 4-6gm. per day. The third step is improving the physical condition, especially by isometric exercises such as running. The physical activity will both reduce body weight and lower the blood pressure (65). The fourth step is removing the physiological stresses and remembering that tension and anxiety will only raise the blood pressure (66).

After all of the above, drug treatment is the next step. The therapy is usually begun with diuretics. The drug therapy is very important because the anti-hypertensive affect reduces the risk of hypertension complications, such as congestive heart failure, stroke, and renal damage (67). The complications of untreated hypertension are numerous, but the most important of them is hypertension encephalopathy. The clinical picture is headache, nausea, mental

confusion, stupor, convulsions, and death if it is not treated. There may also be edema and thrombi in the brain if this condition is not treated. Hypertension can be complicated by hemorrhagic stroke, cerebrovascular insufficiency, and acute left ventricular failure (66).

It is important to begin treatment early to manage high blood pressure. The first step is the use of diuretics. Diuretics are used in mild, moderate, and severe hypertension. Sometimes the diuretics and salt restriction is enough for some patients. Diuretics produce a negative salt and water balance by preventing sodium retention. Since the anti-hypertensive effect of diuretics depends on adequate natriuresis, the effect could be reduced or abolished by excessive sodium intake, or by reducing the glomerular filtration. Diuretics are of different types, classified by the site they effect: the filtration diuretics, such as cardiac glycosides, proximal tubular diuretics, such as osmotic agents, and carbonic anhydrase inhibitors. A loop diuretic such as furosemide prevents the reabsorption of sodium. Aldacton (spironolactone) acts directly on the sodium pump and decreases aldosterone production. Thiazide has a diuretic effect and inhibits sodium reabsorption causing saluresis, which produces hyponatremia. Thiazides decrease calcium clearance, causing hypercalcemia, and decrease uric acid clearance, causing hyperuricemia. Thiazide also decreases creatinine clearance which causes azotemia. Also thiazide causes hypokalemea as well which



leads to hyperglycemia. Aldactone, a potassium sparing agent, does not produce the above side effects, but may cause amenorrhea in women and may cause gynecomastia in men.

Thiazide diuretics should not be used in renal function impairment and the drug of choice is furosemide (Lasix). It is a potent diuretic which blocks chloride reabsorption in the ascending limb of the loop of the Henle in the patient with renal failure (67).

The second step involves beta-blocking agents such as propranolol (Inderal). Some claim that propranolol can be used as the first drug, but the combination of diuretics and beta-blockers just is more effective. Propranolol will inhibit renin activity and reduces cardiac output. Beta-blocking agents such as propranolol are contraindicated in person with asthma. Also, beta-blockers must never be given to a patient without first ascertaining that there is no tendency for heart failure, or second degree heart block (68). The second step includes the sympatholytic agents (sympathetic depressants) such as methyldopa (Aldomet) which forms false transmitter  $\alpha$ -methyl noradrenaline and causes some depletion of axonal stores of noradrenaline and has some adrenergic neurone blocking action. Major side effects of methyldopa are fever, a positive Coombs test, and also may induce hepatotoxicity (hepatitis) and rarely hemolytic anemia. The adverse effects of methyldopa are sedation, fatigue, dry mouth, and salt and water retention, and sexual dysfunction (67).

Another drug is reserpine. It depletes the catecholamines and serotonin. It causes peptic ulcer, depression, nasal congestion, and possibly breast cancer (70).

Clonidine (sympathetic inhibitor) reduces sympathetic outflow by stimulating  $\alpha$ -adrenoreceptors. Adverse reactions to this drug are sedation, dry mouth, salt and water retention, sexual dysfunction, bradycardia, heart block and withdrawal syndrome. The last drug in step two is guanethidine which depletes axonal stores of noradrenaline and prevents storage and release of catecholamines. It has adverse reactions such as orthostatic hypotension, sexual dysfunction, diarrhea, salt and water retention, and intestinal cramping.

Step three is arteriolar vasodilation. The vasodilators which are used are hydralazine, prazosin, diazoxide and nitroprusside. Hydralazine reduces blood pressure through direct relaxation of arteriolar smooth muscle. Adverse effects of hydralazine are related to the reflex sympathetic stimulation or its direct vasodilation. These include headache, flushing, nasal congestion and dizziness.

## Instructions to the Pharmacist

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1. Diuretics must be given in an adequate and standard dose to achieve the effect.
  2. It is not used if the glomerular filtration rate is less than 35 ml.
  3. If there is no response to diuretics there are two possible reasons why not:
    - a) vasoconstrictive type hypertension rather than volume dependent
    - b) the diuretic does not induce adequate sodium diuresis.
  4. Diuretic therapy may cause hypokalemia. The patient may need a potassium supplement. The pharmacist should advise the patient to take food rich in potassium.
  5. If the patient is taking aldactone, no potassium supplement is needed, because it is potassium sparing (68).
  6. Restriction of sodium is important because excessive sodium intake renders the effect of diuretics useless.
  7. Thiazide causes hyperglycemia. It may be due to inhibition of insulin or due to hypokalemia. The patient who takes oral hypoglycemic with thiazide should be monitored carefully.
  8. Thiazide interferes with many blood tests such as uric acid, amylase, blood ammonia.
  9. Thiazide may cause hypokalemia if the patient also takes digitalis; the possibility of digitalis toxicity may be enhanced (69).
  10. Inderal is contraindicated in asthma because inderal has bronchoconstriction and aggravates the asthma.
  11. There are drug interactions between inderal and aminophylline.
  12. Antacids such as aluminum hydroxide inhibit absorption of inderal.

## Instructions to the Pharmacists (continued)

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13. Digitalis and inderal may aggravate each other, and produce bradycardia.
  14. Barbiturates and phenytoin induce microsomal enzymes and enhance the metabolism of inderal.
  15. Phenytoin and inderal may increase the effect (synergis effect) and may depress the myocardium.
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16. A combination of two drugs with the same class and the same mechanism may aggravate the side effects and there will be no significant effect, for example, guanethidine plus reserpine.
  17. Tricyclic interferes with the guanethidine effect by blocking its uptake to adrenergic neurons.
  18. Anesthesia, procainamide, quinidine, or inderal exaggerate the lowered blood pressure induced by specific antihypertensives (69).
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Instructions to the Patient (68, 69, 70)

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1. Continue your medication and do not miss any day. Report any side effects to your physician.
  2. Drug therapy can make a difference and that can save your life.
  3. Remember there is no ideal drug for hypertension. Each one may produce side effects. Report these to your doctor.
  4. Diuretics increase the excretion of sodium, so sodium intake must be restricted.
  5. You must eat food rich in potassium as diuretics will decrease your potassium level.
  6. If there is reserpine in your medication it may cause peptic ulcer. Do not exceed the dose which is recommended to you.
  7. Remember that taking of clonidine should not be discontinued suddenly, as it can cause a withdrawal syndrome.
  8. The first dose of prazosin may cause syncope. This is an episode of sudden collapse and unconsciousness which can occur in the patient taking 2 mg or more for the first time.
  9. Begin a quiet life far away from those factors which aggravate your problem. Stop smoking if you do, and reduce your weight if you are overweight.
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## Chapter 10

### GRAND MAL EPILEPSY

Epilepsy itself is not considered a disease. It is a sign of other diseases or an alteration of physiological reactions of the central nervous system function. The seizure is considered a sudden change of the central nervous system due to a paroxysmal high frequency or synchronous low frequency, or a high voltage electrical discharge.

The signs and symptoms of seizures depends on how the seizure originated or which region of the brain is involved. The seizure by conduction mechanism spreads to the brain-stem center which controls the spinal motor neurons, then moves to involve all of the brain. The autonomic system is involved as well and the influence of this system in the body appears such as dilation of pupils, salivation, etc. After seizures continue, the tonic muscular activity changes or progresses to clonic movement. Then the patient falls into a coma, followed by confusion and lethargy eventually returning to a normal state slowly (71).

Grand mal epilepsy is characterized by four phases. The first phase is the prodromal phase; this is the aura phase in which the patient is aware of remembering past experiences, strange visual sensations, migraine headache, crying, and seeing or pointing to something. The second phase is the tonic phase. This phase is characterized by

muscle rigidity, and the airway is closed off by the vocal cord causing an epileptic cry. The third phase is the clonic phase. The convulsion is generalized with a tonic-clonic spasm of the extremities. The last phase is the postictal or relaxation phase in which the patient may sleep several hours and wake up with a headache, and sometimes a sore tongue. And, also the patient may have urinated in his clothes, his bladder having emptied during the seizure or during sleep. Due to the stimulation of the autonomic nervous system the patient is bathed in sweat, the pupils of the eye are constricted, and there is salivation and foaming of the mouth accompanied by respiratory difficulties (71, 72).

The causes of epilepsy, in a general statement, is idiopathic, but there are some suggestions of causes leading to the convulsions. Some are severe perinatal injury (especially in the newborn). Metabolic defects such as acidosis, alkalosis, congenital malformations, infections, genetic disease, myoclonic syndrome, postnatal trauma, brain tumor, vascular diseases, and myclonus epilepsy. There is no clear proof that epilepsy is inherited, but the evidence for inheritance is strong if the patient's seizures start at an early age (71). Diagnosis of epilepsy depends on clinical manifestations, family history, signs and symptoms, an EEG to determine if there is a brain tumor, a spinal puncture to study spinal fluid, and brain scan to determine where the foci are (72).

What to do for the patient who is in a convulsive state:

1. Put the patient in a wide place and away from hard objects; put the patient in bed, or prevent the patient from falling down.
2. Put something in his mouth such as clothes, or a hard thing between his jaws to prevent him from biting his tongue.
3. Put the patient on his side, and avoid putting the patient on his back or on his abdomen because there is a chance of vomiting.
4. Loosen his clothing to avoid choking.
5. Do not give the patient his medication orally and do not give him water or food.
6. Check the breathing. If the breathing has stopped, give him artificial respiration.
7. Watch carefully and call an ambulance.

Grand mal epilepsy have regular intervals but the interval may be close enough that they occur more than once in 24 hours. Status epilepticus needs emergency treatment and medication by intravenous route is necessary for treatment.

The treatment goal is complete suppression of the seizures, at a dose level which will produce this effect without signs and symptoms of drug side effects or toxicity. The drugs that are commonly used to treat grand mal epilepsy include phenytoin (which is the drug of choice). Pheno-barbital, primidone and carbamazepine are the alternatives. Also, there are combinations of these drugs. In the following tables the drugs commonly used with some of their respective characteristics are listed (73).



Drugs that are used in the treatment of Grand Mal Epilepsy (73)

AGENT	BRAND NAME	ADULT DOSE	CHILD DOSE	SERUM CON-CENTRATION	HALF-LIFE	TIME TO REACH THE PLATEAU	COMMENTS
Phenytoin (PPH)	Dilantin	300-400 mg	4-7/ kg	10-20 Mg/ 100ml	7-42 hrs	5-10 days	the drug of choice
Phenobarbital (PB)	Luminal	150-250 mg	3-8/ kg	10-35 Mg/100 ml	2-4 days	14-21 days	alternative
Primidone	Mysoline	500-1500 mg	10-25/ kg	6-12 Mg/100ml	3-12 hrs	4-7 days	alternative
Carbamazepine	Tegretol	600-1200 mg	15-30/ kg	6-8 Mg/ 100 ml	7-30 hrs	2-4 days	alternative

When the patient is in status epilepticus, the intravenous route is used. Intravenous diazepam is the drug of choice often but sometimes phenytoin is preferred. Phenytoin has brand names such as dilantin, dilabid, ditiycon, and dilan. It has been used for forty years and still is the most popular drug to treat grand mal epilepsy. Ninety percent (90%) of this drug is bound to protein and is metabolized in the liver. The half life of phenytoin is 24-30 hours and the steady state is reached in four to five days. It has side effects such as ataxia, diplopia, vomiting, and hypersensitivity reactions such as skin rashes and fever. Also, phenytoin may produce liver dysfunction, such as hepatitis. Also, chronic use may produce hypertrophy of the gums. It causes folic acid deficiency with or without microcytic anemia. Also it interferes with Vitamin D metabolism with thyroid functions. It will also cause nystagmus (74, 75). At blood level greater than 30 mg/ml ataxia and dysarthria can occur. Additionally, Vitamin K level may be depressed and bleeding disorders have been reported. Phenytoin is teratogenic which may cause congenital abnormalities (75).

Phenytoin has an affect on membrane cell stabilization. It will stabilize the exciting membrane and prevent the spread of the seizures. It will reduce sodium and calcium influx into the nerves and prevent post-tetanic potentiation and post-tetanic hyperpolarization, as well as decreasing the neurotransmitter from the nerve endings (77).

The second drug is phenobarbital. Phenobarbital is used as an alternative to phenytoin, and it is a widely used and effective drug. It may be used in combination with phenytoin and carbamazepine. The side effects of phenobarbital, or the unwanted effects, are sedation, nystagmus, ataxia, and osteomalacia. Also in young children, hyperactivity or restlessness may occur. Addiction to phenobarbital is common (75) and it may also interfere with learning ability (76).

Phenobarbital is a potent anticonvulsant, more so than other barbiturates. There are some qualitative similarities with phenytoin. They block the sodium conduction, stabilize the nerves, and decrease calcium influx into the depolarized nerve endings. It will depress the sympathetic transmission at a number of different sites (71).

The third drug is primidone (mysoline) and it is also effective in grand mal epilepsy. It is absorbed quickly. The half life is about 12 hours. It is converted to two active metabolites, which are phenobarbital and phenyl ethylmalonamide. The side effects include ataxia, nausea, and irritability in children. It is absorbed from the stomach and the intestines and most of its effect is due to its metabolite phenobarbital. The most common side effect is drowsiness and the mechanism of action is similar to phenobarbital (76).

Finally, carbamazepine (Tegretol). It is useful in the treatment of generalized tonic-clonic seizures, but more

effective especially in the treatment of partial seizure. The drug has side effects including dizziness, ataxia, diplopia, drowsiness, impaired hepatic function, and bone marrow suppression. It is structurally related to the tricyclic antidepressants (76), but its major effect is as an anti-convulsant. The adverse effects include hepatitis, aplastic anemia, heart block, ataxia, diplopia, and skin rash.

It is very important to know the drug interactions with anticonvulsants. The drugs which are used in grand mal epilepsy are phenytoin, primidone, phenobarbital, and carbamazepine. In general, tricyclics may produce epileptic-form seizures in susceptible patients and the patient must be monitored closely. Also, oral contraceptives induce fluid retention and may precipitate seizures. It is recommended that epileptic patients use another birth control rather than an oral contraceptive. It is important to know this information about phenytoin drug interactions, and also the complications of treatment and overdoses, and how to treat it (71, 78).

## Instructions to the Pharmacist

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1. Patients with epilepsy and glaucoma using acetazolamide will have increased side effects of the anticonvulsant, and osteomalacia may be induced.
  2. Alcohol enhances the metabolism of phenytoin and seizure control is reduced.
  3. Antihistamine preparations enhance the phenytoin plasma level and may increase toxicity.
  4. Barbiturates induce microsomal enzymes and increase the metabolism of phenytoin and the serum therapeutic level is decreased.
  5. Benzodiazepines increase the blood level of phenytoin.
  6. Phenytoin enhances the metabolism of corticosteroids.
  7. Diazoxide enhances phenytoin metabolism.
  8. Phenytoin enhances the metabolism of digitalis.
  9. Folic acid, when given, will decrease the phenytoin level in the blood and phenytoin will also cause folic acid deficiency.
  10. In general, the basic drug interactions are due to alteration of absorption, interference with protein binding, or with the metabolism.
  11. Acetazolamide reduces the gastrointestinal absorption of primidone.
  12. Primidone is converted to two metabolites. Giving barbiturates plus metabolites will increase the blood level.
  13. Propoxyphene inhibits the metabolism of carbamazepine.
  14. Barbiturates stimulate the metabolism of carbamazepine.
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### Instructions to the Patient

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1. Do not treat yourself by the ways or methods the public describes to you.
  2. The treatments which are used in the hospital are the ideal method for your problem.
  3. Do not discontinue the treatment for any reason and be careful not to take an overdose.
  4. Refill your prescription before your medication is finished and visit your physician regularly. Report any side effects to your physician.
  5. It is recommended to avoid driving a public vehicle or work with sharp or dangerous machines.
  6. Do not travel without enough medication.
  7. It is recommended when traveling that you take with you your certificate which shows that you are using the medication legally.
  8. If you have an illness other than epilepsy and you need to take another drug, tell your physician about your medication to avoid drug interactions, or an alteration of the serum level of your medication.
  9. Remember that you are not alone in this world, but there are millions of people you who have epilepsy (73, 75, 78).
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## Chapter 11

### GLAUCOMA

Glaucoma is most common in older people and is a very complicated disease which needs very careful management.

Glaucoma is a chronic disease with multiple etiological causes. Sometimes glaucoma is asymptomatic and causes irreversible destruction of the visual field. The treatment is very important to prevent progression of the disease and hence, loss of vision. It should be detected early to begin treatment, and the patient must continue using the medication all of his life (79).

The definition of glaucoma is a rise in the intraocular pressure of the eye. Normally there is a constant production of clear fluid within the front part of the eye, which is drained away as fast as it is produced. In glaucoma, there is interference with the drainage of this fluid which leads to increased pressure. Thus, in glaucoma, there is an increase in the intraocular pressure which leads to a change in the optic disk and gradually a loss of the visual field. This increases the intraocular pressure due to obstruction to the outflow of the aqueous humor. The aqueous humor is produced primarily in the ciliary body with drainage from the posterior chamber via the pupil into the anterior chamber of the eye. It discharges from the eye through the canal, called Schlemm, at the angle of the eye, to the veins (80).

In the following table are listed the types and kinds of glaucoma. This classification divides glaucoma into four categories depending on the causes and characterizations of each type.

- I. Primary Glaucoma
  - 1) Open angle glaucoma
  - 2) low tension glaucoma
  - 3) Primary closed angle glaucoma
  
- II. Variants of Primary Glaucoma
  - 1) Pigmentary glaucoma
  - 2) Foliation glaucoma
  
- III. Developmental Glaucoma
  - 1) Primary
  - 2) Infantile
  - 3) Glaucoma associated with heredity
  
- IV. Secondary Glaucoma
  - 1) Inflammatory glaucoma
    1. Uveitis of types
  - 2) Phacogenic glaucoma
    1. Angle closure with cataract
    2. Phacoanophtalactic glaucoma with rupture of the lens
  - 3) Glaucoma secondary to intraocular hemorrhages
    1. Hyphema
    2. Hemolytic glaucoma
  - 4) Traumatic glaucoma
    1. Traumatic recession of chamber
    2. Post-surgical glaucoma
  - 5) Drug induced glaucoma
    1. Corticosteroids
    2. Anticholinergic
  - 6) Miscellaneous glaucoma
    1. Tumor
    2. Chemical burns
    3. Irish atrophy

The symptoms of glaucoma are various. If the patient has open angle glaucoma, there are no symptoms (Silent). The disease progresses slowly. It may become advanced before the patient recognizes it, but some indications such as the need for changing glasses, mild eye aches, may indicate open angle



glaucoma. The second type which is characterized by severe headache, pain, nausea, vomiting, and decreased visual activity, halo and rainbow vision is an indication of closed angle glaucoma (79, 80).

If the patient does not have glaucoma treated, the chronic elevation of intraocular pressure will effect the nerve fibers by influencing the vessels which supply the nerve fibers. Increasing the pressure will cause ischemic impairment and reduce the nutrition supply, impair axoplasmic flow (protoplasm of the axon) and hence, gradual and irreversible destruction, leading to blindness. The greater the rise in intraocular pressure, the more serious the complications (79, 80).

There are three factors which influence the pressure: the rate of aqueous production, the rate of aqueous outflow, and the volume of other tissues within the eye. There is equilibrium under normal pressure but with glaucoma there is no equilibrium. The normal intraocular pressure is 12 to 21 mmHg. The visual field diminishes within five years in 3.5 percent of patients with intraocular pressure between 21 and 30 mmHg. The more the ocular pressure increases, the greater the risk for loss of vision (79).

The goal of the treatment of glaucoma is to reduce and sustain the intraocular pressure in order to prevent deterioration of the optic nerve and loss of visual function. The drugs which are used are divided on the basis of mechanism of action. Some drugs cause an increase in the elimination of aqueous humor; others decrease the production of aqueous

humor. The basis of treatment of glaucoma is:

- A. Increasing elimination of aqueous humor by a drainage system. Such drugs are parasympathomimetics and sympathomimetics.
- B. Drugs which decrease the formation of aqueous humor by the ciliary process. Those drugs are sympathomimetics and carbonic anhydrase inhibitors.
- C. There are drugs which reduce the volume of aqueous humor in the anterior chamber. Those drugs are hyperosmotics, such as mannitol.

The drug therapy is to manage open angle glaucoma, but it is necessary to use surgery for closed angle glaucoma (81). The drugs which influence the outflow and increase the elimination of aqueous humor are parasympathomimetic drugs which include direct acting cholinergics such as pilocarpine and carbachol. Also cholinergic esterase inhibitors such as physostigmine (Eserine) and sympathomimetic agents such as epinephrine. Sometimes beta adrenergic blocking agents are used such as Timoptic. There are drugs which reduce the overproduction of aqueous humor, which are sympathetic, such as epinephrine and carbonic anhydrase inhibitors, and Diamox (acetazolamide). Also, hyperosmotic agents, such as mannitol, are given intravenously (32).

The medications are used essentially to treat open angle glaucoma. The medications are eye drops such as pilocarpine, epinephrine, anticholinergic esterase, echothiophate iodine drops, and demecarium bromide. Also, systemic medication

such as carbonic anhydrase inhibitors, e.g. Diamox (80).

The first line of treatment is a parasympathomimetic, pilocarpine, for example, which have direct cholinergic effect. Pilocarpine is considered the drug of choice. It will increase the elimination of aqueous humor, and induce miosis. Pilocarpine causes contraction of the ciliary muscles and dilation of the aqueous veins into which the schlemm canal empties. The official preparations are pilocarpine chloride, and pilocarpine nitrate. They are available in ophthalmic drops and ointment. The side effects and toxicity of pilocarpine are due to the toxicity of the parasympathomimetic activity which is treated with atropine (83). Those drugs which include pilocarpine and carbachol are called miotic agents (84). The other types from this class are cholinesterase inhibitors which have miotic effect but are rarely used. The following table shows the characterizations of the two most important agents in this group which are pilocarpine and carbachol (82).

#### Direct-Acting Cholinergic Drugs

CHARACTERISTICS	PILOCARPINE	CARBACHOL
Indications	Open angle glaucoma	Open angle glaucoma
Class	Parasympathomimetic	Parasympathomimetic
Brand Names	Almocorpine, Pilocar	Esoptocarbachol, Miostat
Dose	0.5%-4% solution, instill 2 drops four to six times in eye daily	0.75% - 3% one drop two to three times daily

## Direct-Acting Cholinergic Drugs (Cont'd)

CHARACTERISTICS	PILOCARPINE	CARBACHOL
Mechanisms	Increases the rate of elimination of outflow of aqueous humor (for both)	
Local Side	Conjunctival, congestion, irritation, myopia, and poor night vision (for both)	
Systemic Side	Nausea, diarrhea, bradycardia, and excitation (for both)	
Inactivation by Acetyl Cholinesterase	More prone	Less prone
Activity	Less Active	More Active
Absorption	More absorbed	Less absorbed
Comments	Drug of choice	Alternative (79, 82, 84, 85).

There are also other agents from this group which increases the rate outflow. These are cholinesterase inhibitors such as eserine, (Physostigmine), neostigmine demecarium, echothophate iodide. The following table lists the characteristics of those agents. This table is extracted form U.S. Pharmacist, 4, April 1979 (82).

Other drugs which increase the outflow are sympathetic amines such as epinephrine and phenylephrine. The epinephrine brand names are Adrenaline, Epifrin, and Epitrate. The solution concentration is 1%-2% and is applied twice or thrice daily. The other drug is phenylephrine for which the solutions concentration is 10%. The sympathetic drugs will increase the outflow

and reduce the pressure of aqueous humor (82).

The second class which reduces the rate of aqueous humor production consists of sympathetic and carbonic anhydrase inhibitors. Carbonic anhydrase inhibitors include several drugs, but the one most commonly used is acetazolamide (Diamox). The usual adult dose is 250mg four times a day. The major side effects of Diamox are gastrointestinal disturbances, thirst, drowsiness, confusion, paresthesia, depression, hypokalemia, hyperuricemia, acidosis and kidney stones. Diamox is a mild diuretic which reduces the production of aqueous humor, not from the diuretic effect but by blocking the ocular carbonic anhydrase. Hyperosmotic agents such as mannitol, urea, glycerol, and isosorbide are used to reduce the ocular pressure by increasing the osmolality of the blood relative to the fluid of the eye. The result of that is that they create an osmotic gradient between the two compartments. The most common one used is mannitol which is used at 1gm/kg intravenously over 30 to 45 minutes. The major side effects are circulatory overload, edema, cellular dehydration, urinary retention and electrolyte imbalance. They are used especially in preoperative management of acute closed angle glaucoma (82, 83, 85).

### Cholinesterase Inhibitors

	PHYSOSTIGMINE (ESERINE)	NEOSTIGMINE	DEMECARIUM BROMIDE
Dosage	0.25% to 0.%, one drop to two drops, three times daily	5% solution, one to two drops every 4-6 hours	0.125% or 0.25%, one to two drops
Duration of Action	12-30 hours	6-24 hours	1-7 days
Vehicle	water	water	water
Stability	months	weeks	months
Strength of increased outflow	+	+	+
Class	Cholinesterase Inhibitors (all)		
Indications	Open Angle Glaucoma (all)		
Mechanism	Increases the rate of outflow of the aqueous humor (all)		
Local Side Effects	Pupillary and accommodative spasm, twitching of the eyelids, pigmentary changes in the iris, cataracts, conjunctival thickening, refractive changes		
Systemic Side Effects	Nausea, diarrhea, bradycardia, sweating, and central nervous system excitation (79). (for all)		

Instructions to the Pharmacist

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1. There are many drugs which may induce glaucoma, or are contraindicated for a patient with glaucoma.
    - A. Nitroglycerin should not be used in a patient with glaucoma, because nitroglycerin which is used in angina will increase intraocular pressure.
    - B. Beta blocking agents such as inderal sometimes reduce intraocular pressure.
    - C. Oral contraceptives may induce glaucoma.
    - D. Corticosteroids will increase the intraocular pressure of the eye.
    - E. There is a misconception that systemic anticholinergics aggravates or induce open angle glaucoma, but in a patient with abnormal narrow angle glaucoma this may be true.
  2. Therapy is started by using the smallest dose of pilocarpine that will control the pressure of the eyes and increase the dose if there is no, or an inadequate, response. If the patient is unable to tolerate pilocarpine, the alternative is carbachol.
  3. Epinephrine in some patients may be used to initiate therapy.
  4. A combination of drugs may be used depending on the response of the patient.
  5. Carbonic anhydrase inhibitors are available in two forms; normal form and sustained released.
  6. Combinations which are recommended are usually from a different class, and have a different mechanism.
  7. Monitor the patient closely.
  8. Treatment of closed angle glaucoma is surgery.
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Patient Instructions

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1. It is recommended that the person above 40 years of age should visit the physician and have a routine examination of his eyes, because there is a type of glaucoma which is asymptomatic (silent).
  2. Carefully follow the directions which your doctor recommended to you, and follow the treatment. Report any side effects to your doctor.
  3. Open angle glaucoma is considered a chronic disease and there is no cure for this kind of glaucoma. You must use your medication all of your life.
  4. If you have more than one kind of eye drops, it is recommended to give each drop the time to be absorbed by applying the first drops, and then waiting 10 to 15 minutes before applying the other ones.
  5. Ask your pharmacist or your doctor about any medication which you use other than your eye drops. It may be contraindicated.
  6. Remember that if you do not use your medication as recommended the pressure of your eye will rise and could lead to blindness (82, 85, 86).
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## CONCLUSION

For the Pharmacist: It is also true that you are facing a lot of people every day and your time is limited, but try to be helpful in your field and your responsibility as a consultant about the medication. Be sure that you can give the patient the correct doses and the correct medication, and give the patient the best instructions or advice. Your good communication with the physician will increase the level of the job you are doing and the level of treatment.

For the Patient: It is also too often true that a doctor, especially in an Outpatient Clinic in any hospital, has a limited amount of time to spend with you. Therefore, to spend the time wisely and to understand carefully the instructions from your doctor will help you increase the chance for your recovery. If you are confused or not sure, do not be shy, and do not be afraid to ask again. Be cooperative with your physician and the pharmacist. All of them want to help you to understand your disease state and medications.

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