PATTERN OF ANTIMICROBIAL PRESCRIPIONS IN A GENERAL URBAN HOSPITAL

THESIS

SUBMITTED IN PARTIAL FULFILMENT OF

THE MASTER DEGREE IN INTERNAL MEDICINE

BY

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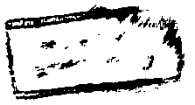

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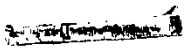

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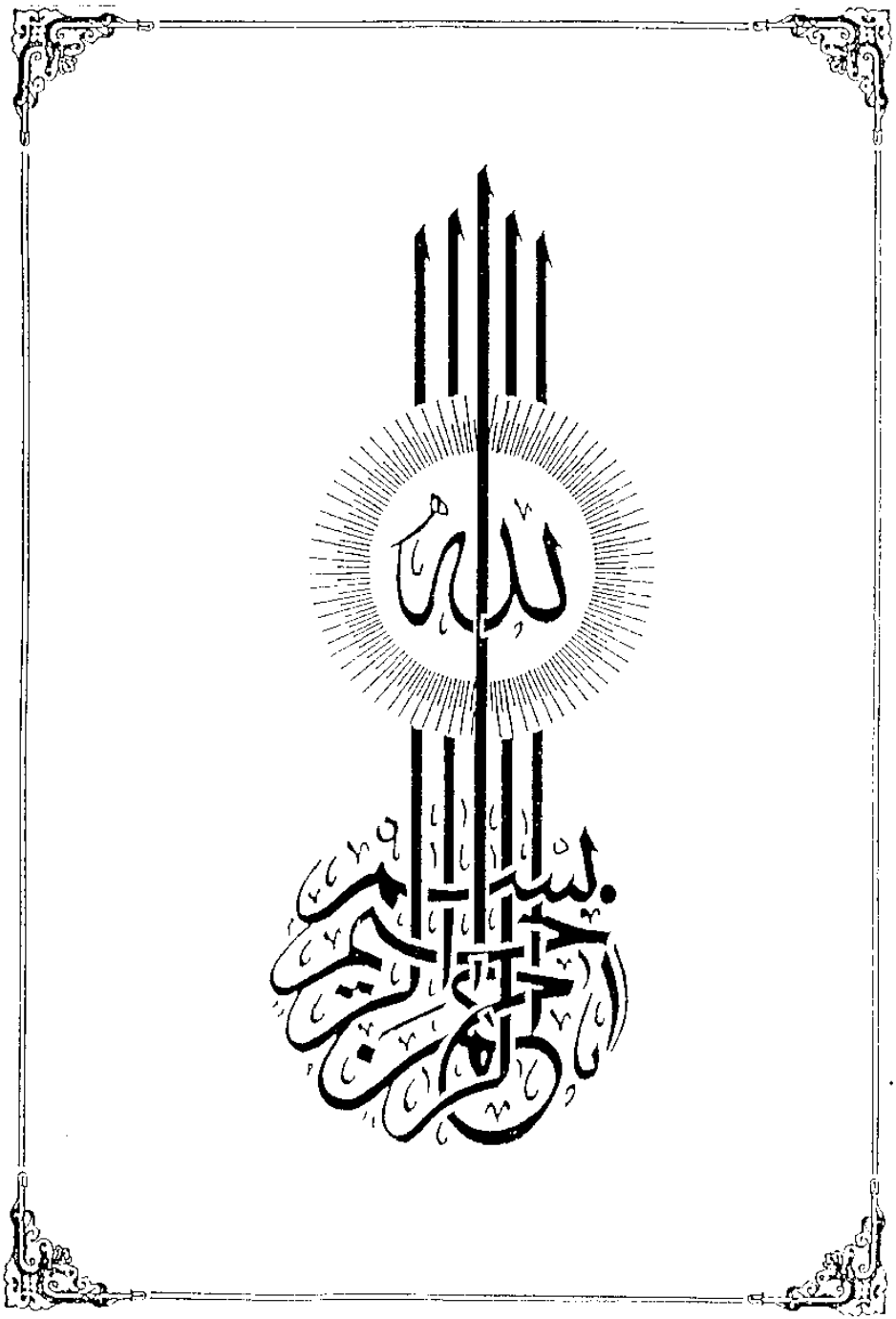
TO MY WIFE



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THE WORK

FORWARD

During the last decade great progress has been made regarding the appropriate prescription of antimicrobials in prophylaxis and treatment of infectious diseases. It is fortunate that all antimicrobials are relatively non-toxic, however; all have side effects (e.g. allergic reactions, effects on normal bacterial flora and emergence of drug resistant bacteria) (Mills and Jawetz, 1983).

Sabbour et al., (1985) reported that antibiotics have a potential of suppressing host - defence mechanisms and this necessitates intelligent choice and self restraint in prescribing antibiotics for immunosuppressed patients.

AIM OF THE WORK :

To delineate and critically analyse the local pattern of use of antimicrobials in a general urban hospital. (El-Khazendara General Hospital).

HISTORICAL ASPECTS

AND

IN TRODUCTION

Historical Aspects and Introduction :

In 1891, Ehrlich cured experimental malaria in guinea-pigs with methylene blue. In 1904, he controlled trypanosome infections in mice with trypan red. In 1906, Ehrlich's efforts resulted in the introduction of arsphenamine for the treatment of syphilis and it was soon followed by necarsphenamine which was widely used until 1945 when penicillin superseded it (Laurence and Bennett, 1980).

In 1929, Fleming reported his observation that colonies of staphylococci lysed on a plate that had become contaminated with a penicillium mold. In 1935, Domagk reported that a red dye, prontosil, was effective in vivo against hemolytic streptococcal infections. In 1940, Chain, succeeded in producing the first penicillins from culturs of Penicillium notatum. In 1944, Streptomycin was isolated from cultures of Streptomyces griseus. In 1947, chloramphenicol was isolated from cultures of Streptomyces venezuelae. In 1948, chlortetracycline, isolated from Streptomyces aureofaciens, was introduced. In 1952, erythromycin was obtained from Streptomyces erythreus. In 1957, Kanamycin was isolated by Umezawa (Jawetz, 1983). In 1961, " Penbritin " (ampicillin), a semisynthetic penicillin was introduced (Rolinson and Steven, 1961). Lincomycin first appeared in 1963 and clindamycin, a synthetic derivative, was introduced some four years later. (Crossland, 1980). In 1967, Carbenicillin

was first introduced for clinical use by Beecham Research Laboratories (Knudsen et al.,1967). In the mid 1970,the combination of trimethoprim and sulfamethoxazole was introduced. Tobramycin and amikacin were introduced into clinical practice in the 1970_S (Mandell and Sande, 1985), and most widely employed in 1981 - 1982 (Jawetz, 1983).

The history of antimicrobial agents has thus been dynamic, characterized by the constant emergence of new challenges followed by investigation, discovery and the production of new drugs. (Mandell and Sande, 1985).

Definition of Antimicrobials :

The term antimicrobial is used to mean all chemotherapeutic agents used against micro-organisms. The term antibiotic means all substances produced by micro-organisms that, in high dilution, are antagonistic to the growth or life of other micro-organisms. (Laurence and Bennett, 1980).

Classification and Mechanism of Action :

Root and Hierholzer, (1978) reported that systemic antimicrobial drugs can be classified according to class and action as listed in table (1).

Class	Microbicidal	Microbistatic
Antibiotics	B-lactams	Chloramphenicol
	Aminoglycosides	Tetracyclines
	Polymyxin	Erythromycin
	Bacitracin	

	Rifampicin	Lincomycins
	Spectinomycin	
Synthetic anti-bacterial drugs	Nalidixic acid	Sulfonamides
	Nitrofurantoin	Trimethoprim
	Metronidazole	
Antituberculous drugs	Isoniazid	Aminosalicylic acid
	Streptomycin	ethambutol
	Rifampicin	pyrazinamide
Antifungal drugs	Amphotericin B	
	Griseofulvin,Nystatin	
Antiviral drugs	Idoxuridine,Cytarabine	
	Amantadine and others.	

Table (1) : Systemic antimicrobial drugs by class and action.

This classification is arbitary because some drugs are microbistatic or microbicidal according to concentrationand this is particularly true of co-trimoxazole, erythromycin, nitrofurantoin, fusidic acid, lincomycin and clindamycin. Indeed most microbistatic drugs can be shown to be microbicidal at high concentrations (Laurence and Bennett,1980).

Another classification with functional utility is based on the general antimicrobial activity of the various groups of drugs :

(1) Drugs primarily effective against the gram-positive cocci and bacilli, which tend to have a relatively narrow spectrum of activity, include penicillin G, the semisynthetic

penicillinase - resistant penicillins, the macrolides, the lincomycins, vancomycin and bacitracin.

(2) Drugs primarily effective against the aerobic gram-negative bacilli, include the aminoglycosides and polymyxins.

(3) Relatively broad spectrum drugs, that affect both the gram - positive cocci and gram-negative bacilli, these include the broad spectrum penicillins, the cephalosporins,the tetracyclines, chloramphenicol, trimethoprim and the sulfonamides. While this classification has many important exceptions, it does help the physician to remember the antibiotic spectrum of each drug (Sande and Mandell, 1980).

A third classification has been based on chemical structure and proposed mechanism of action, as follows :
(1) agents that inhibit synthesis of, or activate enzymes that disrupt bacterial cell walls to cause loss of viability and, often, cell lysis; these include the penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, and the imidazole antifungal agents (miconazole, ketoconazole, and clotrimazole);

(2) agents that act directly on the cell membrane of the micro-organisms; these include the detergents, polymyxin and colistimethate, and the polyene antifungal agents, nystatin and amphotericin B, that bind to cell wall sterols;

(3) agents that affect the function of bacterial ribosomes to cause a reversible inhibition of protein synthesis, these bacteriostatic drugs include chloramphenical, the tetracyclines, erythromycin, and clindamycin;

(4) agents that bind to the 30S ribosomal subunit and alter protein synthesis, which eventually leads to cell death; these include the aminoglycosides;

(5) agents that affect nucleic acid metabolism, such as rifampin, which inhibits DNA-dependent RNA polymerase, and the quinolones (nalidixic acid and congeners) and metronidazole which inhibit DNA synthesis.

(6) The antimetabolites, including trimethoprim and the sulfonamides;

(7) nucleic acid analogs, such as vidarabine and acyclovir, which bind to viral enzymes that are essential for DNA synthesis and thus halt viral replication. (Mandell and Sande, 1985).

DIFFERENT GROUPS OF ANTIMICROBIALS

SULFONAMIDES

The sulfonamide drugs were the first effective chemotherapeutic agents to be employed systemically for prevention and cure of bacterial infections in man (Mandell and Sande, 1985).

All have the same nucleus to which various R radicals in the amido group ($-SO_2NHR$) have been attached or in which various substitutions of the amino group (NH_2) are made Fig.(1). These changes produce compounds with varying physical, chemical, pharmacological and antibacterial properties (Jawetz, 1983).

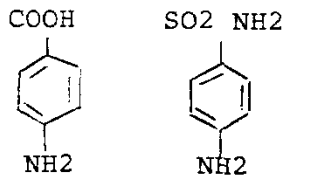

Fig. (1)

The sulfonamides may be classified into 3 groups : (1) agents absorbed rapidly and excreted rapidly, such as sulfisoxazole and sulfadiazine; (2) agents absorbed very poorly when administered orally and hence active in the bowel lumen, such as sulfasalazine; (3) sulfonamides employed mainly for topical use, such as sulfacetamide, mafenide, and silver sulfadiazine (Mandell and Sande, 1985).

These drugs act as competitive inhibitors of the enzyme (dihydropteroate synthase) responsible for the synthesis of dihydropteroic acid, a precursor of folic acid. Sulfonamides are structurally similar to para-aminobenzoic acid (PABA). Only organisms that use PABA to form folic acid