

HOSPITAL PHARMACY

Drug Information Services

Dr Meenakshi Chauhan
Lecturer
Delhi Institute of Pharmaceutical Sciences and Research
Sector-III, Pusp Vihar
New Delhi-110017
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The pharmacist's role in providing information on drugs and medicines is not new. When drugs were few in number and generally of relatively low potency the number of inquiries was small and could usually be answered quickly by reference to pharmacopoeias and formularies. In recent years, the number of drugs and medicines has increased enormously which are usually more potent and more selective and also the literature relating to drugs has expanded at a staggering rate. The literature covers a wealth of information on these newer drugs, their actions, clinical uses, unwanted effects, interactions with other drugs, comparative efficacy, etc. A quick reference to pharmacopoeia and formularies is no longer sufficient, in many cases, to provide an adequate answer.

Drug Information

Availability of authentic drug information is the key to promote rational use of drugs, a well-accepted concept in clinical practice in the developed world. The concept is fast catching up in several developing countries because of the sharp rise in the medical costs and increasing instances of medication errors. An important reason for the rising costs of medical costs in developed countries is the marketing exclusivity enjoyed by pharmaceutical companies for their latest life threatening drugs. And the drugs continue to be the major part of the total healthcare costs. With high prices of patented drugs and the strong influence of pharmaceutical companies on medical practitioners, the healthcare costs can only rise in future. Both pharmaceutical companies and the medical practitioners contribute to creating a situation like this. For pharmaceutical companies, pushing up their sales is the sole aim whereas a large majority of the physicians can be easily coaxed into indulges in irrational prescription to serve the interests of these companies. The absence of insurance cover for a large number of poor people both in the developed and developing world also adds to overall healthcare costs. Medication errors by the physicians is another serious problem confronting the patient community today as knowledge level about new drugs and adverse drug reactions (ADR) is extremely poor amongst physicians. Thus, several hundreds of cases of complications and deaths are being reported every year in various parts of the world on account of medication errors. One way to control medical costs and medication errors is to promote the concept of rational use of drugs by providing authentic drug information to doctors, pharmacists, nurses, researchers, other professionals in health care, committees and patients.

Drug information is an essential element in achieving health goals and should, therefore, form a part of any national drug policy. Information is an aid to decision making. The first information center to be set up was at the University of Kentucky Medical Center, USA, in 1962 [Burkholder]. Its objectives were to collect information, to evaluate and compare drugs, to provide an education and teaching aid for health care personnel, to assist clinicians in the selection of safe and effective medication and to enable pharmacists and pharmacy students to develop their abilities in providing information on drugs and medicines. Large hospitals have developed and staffed a new division of the department of pharmacy which is commonly referred to as 'Drug Information Center'. This new concept in hospital pharmacy operation is usually located in a separate section of pharmacy, containing large number of reference texts, journals, reprints and brochures. They are also equipped with electronic data processing equipments and have a full time director and adequate secretarial assistance. Now computers have possible networking of regional drug information centers made located in different hospitals. Networking on regional, national, sub continentals, intercontinental levels had placed Drug Information Services at a global level.

Pharmacy and drug information are synonymous. In 1991 Brodie *et al* identified a multiple theory concept of pharmacy as a drug-use control system, a knowledge service, a clinical profession, and as the interface between humankind and drugs. The description of pharmacy practice was expanded from that of pharmacy as a “knowledge system” to “a system (framework) of concepts dealing with the acquisition, translation, transmission, and utilization of drug knowledge”. As a specific component of pharmacy, the drug information role is characterized by the ability of the pharmacist to perceive, assess, and evaluate drug information needs and retrieve, evaluate, communicate, and apply data from the published literature and other sources as an integral component of pharmaceutical care [Troutman]. The ability to fulfill the drug information role is essential to successful pharmacy practice.

Drug information is both a body of data and information about medications and a set of skills and tools that provide pharmacy professionals with the ability to find, access, understand, interpret, apply and communicate information and acquire knowledge. The body of facts and information pertaining to medications is generally referred to as “the drug literature”. The literature of pharmacy and pharmaceuticals encompasses all aspects of drugs, beginning with isolation or synthesis, including physical analysis, bioactivity, toxicology, clinical research, market research, and economic and social considerations. The drug literature, reflecting all the individuals who create it and use it, such as chemists, biomedical scientists, all the various health care professionals, attorneys, and patients, is vast and complex. Different kinds of publications are available in the library like journals, abstracting and indexing publications, books, compendia, monographs, patents proceedings, reviews, FDA-approved labeling (package inserts), house organs, newsletters, promotional literature, government documents, and analysis by consulting services.

Drug information skills coupled with the processes and technology offered by informatics are part of the solution to mastering information overload and maintaining the knowledge system that improves patient care outcomes.

Information Needs

The growth in the role played by science in medicine as reflected in the amount of published work, the number of journals and the vast range of drug products in the market, has meant that practitioners of medicine and pharmacy, in common with other scientific disciplines, have experienced difficulty in keeping up with advances in knowledge. The doctor’s response, increasingly, has been to turn to the pharmacist for help. Most problems presented by the doctor are concerned with a particular patient, his disease-state and therapy. The information requested is usually required within few hours, so that treatment may be changed or started and is needed in the form of data, rather than lists of references or paper reprints. Production of an answer therefore involves selection, interpretation and evaluation of information. The type of information requested may include any of the chemical or biological properties of a compound or a comparison of the suitability of several compounds for a specific case, where for instance, renal or hepatic disease may complicate choice. The pharmacist too, may require immediate information on drugs. This may concern straightforward matters such as dosage or availability but also involve formulation or availability data which may not be found in the manufacturer’s literature. Quality controllers may require an alternative assay or stability data. Nurses need to know the effects and dangers of drug therapy so as to be able to assess the appearance of adverse effects, they must also know enough about preparations to teach patients to use them. Researchers need to retrieve a particular report, or search the literature. Care has to be taken to ensure that they are not asking for information that they should rightly be searching themselves. Committees need information to help them decide policies, produce

hospital formularies and award contracts. Patients need to know how to take the medicines they are given, what they will feel if the drug works, likely adverse effects and what to do about them. Measuring and accurately identifying the nature of the need is, however, not easy. As a prospective undertaking it is virtually impossible and probably futile. Retrospectively it requires constant analysis if changing needs are to be properly met.

Drug Literature

The concept of drug information service or drug information center is an attempt to document drugs by abstracting information about them. The information about drugs is collected from various sources which are available. In 1972 Walton *et al* modeled the drug literature as a pyramid with the primary literature forming the base of the pyramid, the secondary literature interfacing and serving as a bridge from the primary literature to reference works (tertiary literature).

1. Primary Literature

Primary literature contains the first written accounts of original research. In terms of size, the primary literature is probably larger than either the secondary or tertiary literature. It is the original information presented by the author without any evaluation by the second party, for example, articles published in journals, dissertations, conferences, etc.

(i) Prepublication literature: The first communication of research data and ideas may or may not be private. If there is a financial or proprietary interest in the research, the first communication may be in the form of a patent application. Prior to formal publication of the research, the work may be presented as a paper or poster at a professional meeting or conference.

(ii) Journal or serial literature: The current evolution or transition of the journal from a paper-only publication to a paper-and-electronic publication is a second, relatively recent, major change in the journal literature. In the electronic format, the lag time between the submission of a written research report and its publications can be shortened considerably. Electronic preprint, either from the author or from the journal publisher, places an article before the reader several months ahead of paper publication release, albeit without benefit of traditional full peer review.

2. Secondary Literature

In this original information is modified, condensed, commented upon by other persons like review articles, abstracts, text books, etc.

(i) Indexing and Abstracting services: The National Library of Medicine's service, Index Medicus, was first published in 1879 [Day]. Given its size and free availability, it is probably the most used index/abstract service worldwide. Other secondary databases that complement one another's coverage in the chemical, pharmaceutical, and medical areas include Chemical Abstracts, Biological Abstracts, EMBASE, IDIS, IPA, MEDLINE, and Science Citation Index. Each of these bibliographic databases was originally available to the user in a non-electronic format, such as paper or microform. In the mid-1960s the services began appearing in digitized, computer-searchable format from online reference retrieval vendors such as Lockheed Information Systems' DIALOG, System Development Corporation's ORBIT, and Bibliographic Retrieval Services (BRS). CD-ROM technology in the 1980s allowed users to search the index/abstract databases in-house via personal computers. Internet access to these

same bibliographic databases is now enhancing the search-and retrieval process by providing linkage to full text articles.

(ii) Evaluated Secondary Resources: Choosing or limiting the search retrieval to meta-analysis, guidelines, or systematic reviews will also identify citations with the strongest research methods and design. The goal of guidelines and systematic reviews is to identify relevant research and in addition to classifying the research by strength, also combine the research results statistically to provide a new, global research result. Currently available evaluated bibliographic databases (like ACP Journal Club, Best Evidence, Cochrane Library, Evidence-Based Medicine) depend upon human experts to identify the best citations.

(iii) Internet search engines: Search engines available on the internet function like the traditional index/abstract services discussed above, in that they search and retrieve information to answer questions. They provide access to a staggeringly large number of electronic documents available on the World Wide Web (WWW). Traditional index/abstract database services (DIALOG, MEDLINE, IDIS) search with Boolean logic. Boolean searching matches the terms in the user's search statement with terms appearing in the database. The search is precise, but it is dependent upon the searcher choosing the correct search term to use in the search statement. WWW search engines have made extensive use of probabilistic/statistical search methodologies and natural language processing systems. Probabilistic/statistical methods use the frequency with which the search term(s) appear in the documents and the comparative frequency with which the search term(s) appear in the documents compared to the rest of the database to establish relevance of the document to the search statement [Seaba].

Contrasted to traditional index/abstract database searching WWW searching requires less training and retrieves a broader selection of search results. While many of the documents found on the WWW are free, some search engines direct the user to fee-based resources. WWW search engines are generally free to user. The documents indexed by the major search engines are primarily those available in hypertext markup language (HTML) or plain text format. Documents and files available in other formats, such as Flash, Word, WordPerfect, and Adobe's Portable Document Format (pdf), are generally not indexed. There are several new search engines with the goal of indexing these "invisible" Web files, for example, InvisbleWeb.com, at Uniform Resource Locator (URL) <http://www.invisbleweb.com/>, and Direct Search, <http://gwis2.cire.gwu.edu/~gprice/direct.htm>.

Specialized search engines concentrate their indexing activity on a specific subject. In addition to user submissions and automated robot indexing, content specialists may verify, enhance, and add sites to the specialty database. Specialized search engines are available in the areas of health, medicine, and the sciences and can be found by scanning pointer sites that index the specialized indexes, such as Search Engine Guide, www.searchenginewatch.com/.

3. Tertiary Literature

In this information is gathered from primary and secondary sources and arranged in such a manner to give coupled information. The tertiary literature is a distillation and evaluation of data and information first presented in such primary literature sources as research reports, meeting presentations, and journal articles. Being furthest removed from the primary report, the tertiary literature characteristically is the least current and the most vulnerable to misinterpretations, biases, and inaccuracies. But just as characteristic, the tertiary is the most accessible, easiest to use, and perhaps the most used of all information resources. Information searches generally start with a perusal of books, reviews, and handbooks. Review articles

even though they appear in the “primary” journal literature, belong to the tertiary literature as they present a summarized, organized, and sometimes even an evaluated picture of original research data.

Aggregated and linked references: The computer and subsequent evolution of library resources to an electronic format has spawned a new generation of drug information resources, i.e. aggregated and linked resources. Practitioners and researchers have always needed access to multiple references, regardless of their professional practice site. Digital media allows the aggregation of drug information references that complement one another into single product. The ability to search each reference using the same software and the ability to search all the references (cross search) with a single search statement adds value to the aggregate. Electronic linkages between resources have immeasurably increased the functionality of information resources. The text books is being linked to full text of their references, research article text is linking to the original data of the study; index/abstract databases are linking to the full text articles they index.

(a) MICROMEDEX Systems: MICROMEDEX integrates over 25 texts, monographs, and product databases in the fields of health care, toxicology, and regulatory information. MICROMEDEX and other publishers produce the resources. This system is commercially available in a variety of combinations and formats.

(b) Stat!Ref: Stat!Ref combines more than 30 medical and drug information textbooks from several publishers and allows both individual and cross searching. The texts are commercially available in a variety of electronic combinations.

The compiled information is available for reference purpose and it helps in answering specific queries regarding both old and new drugs from doctors and patients. The information can also be compiled to meet the needs of the deliberations or the training programmes arranged or research projects undertaken. The compiled information also contribute especially in its clinical role.

Information Retrieval Systems

As a drug moves along the path from discovery to the market and into worldwide use, data and information about the agent are created and accumulate. When this information is published, its value and usefulness to scientific, professional, and patient communities becomes known. Publication of research results at each step of the path is essential. There is tendency particularly in clinical research, not to publish “negative” results. When this happens we are left with only research that is favorable to the drug, resulting in a skewed picture of the drug’s place in therapy.

The path of drug development and marketing offers a structure that is useful to scientists and practitioners concerned with compounds of potential therapeutic value. The resources themselves are classified as primary (original research), secondary (indexing and abstracting services), and tertiary (textbooks and evaluated information). Individual resources are now generally available in more than one physical format; for example, a journal may be available as a paper publication or as an electronic publication (either individually or as part of a publisher’s electronic journal collection or content collection). Primary, secondary, and tertiary resources are available for each step in the path of drug development, but reporting time increases from each step to the next.

(1) Preclinical Drug information

At this point a compound is recognized and then considered for potential pharmaceutical or therapeutic usefulness; researchers will be both consumers of and contributors to the data-information-knowledge cycle that characterizes science. Initially, in the synthesis and purification phase of drug development, information about the compound's chemistry and physical properties may be both sought and created. Whether or not the compound has been of interest to other researchers may be determined by searching public records of grant and contract awards and also by searching resources that cover preliminary and early research results. The patent status of the compound may need to be established.

(a) Physical and chemical data:

- i) **AIDSDRUGS:** Published by the US National Library of Medicine, AIDSDRUG is a dictionary of chemical and biological agents currently being evaluated in the AIDS clinical trials covered in the companion AIDSTRIALS database.
- ii) **Beilstein:** Beilstein, a structure and factual database covering organic chemistry.
- iii) **CAS Registry:** CAS Registry, is a substance database containing structures and chemical names.
- iv) **Chemyclopedia:** It is an annual supplement to Chemical and Engineering News (C&EN), provides a listing of chemicals, trade names, packaging, special shipping requirements, potential applications and CAS Registry Numbers.
- v) **ChemFinder:** ChemFinder WebServer is a WWW search engine that works from a single master list of chemical compounds covering all areas of chemistry and also provide information on physical property and two-dimensional chemical structures.
- vi) **Chemical Abstracts:** Chemical Abstracts is a collection of chemical information with nearly 16 million abstracts of journal articles, patents, and other documents.
- vii) **ChemIDplus:** Published by the US National Library of Medicine, it's a web based search engine, <http://chem.sis.nlm.nih.gov/chemidplus/>, that provides free access to structure and nomenclature authority files used for identification of chemical substances cited in National Library of Medicine databases.
- viii) **Chemindex plus:** Database contains 8000 pharmaceutical ingredients linked to 300,000 preparations.
- ix) **Ei CompendexWeb:** It's a comprehensive bibliographic database of engineering research literature containing references to over 5000 engineering journals and conferences.
- x) **The Merck Index:** The Merck Index is an encyclopedia of chemicals, drugs, and biologicals that contains more than 10,000 monographs.
- xi) **NIST Chemistry WebBook:** The National Institute of Standards and Technology (NIST) Chemistry WebBook provides free access to chemical and physical property data for chemical species via the internet, <http://webbook.nist.gov/chemistry/>.
- xii) **RTECS:** The Registry of Toxic Effects of Chemical Substances (RTECS) is a database of toxicological information compiled, maintained, and updated by the National Institute for Occupational Safety and Health (NIOSH).

- xiii) **The USP Dictionary of USAN (U.S. Adopted Names) and International Drug Names:** The USP Dictionary provides comprehensive information on chemical and brand names of drugs. It includes USAN and International Nonproprietary Names (INN). It also lists drug manufacturers, therapeutic uses, and molecular and graphic formulas.

(b) Patents: Through the granting of a patent the U. S. Patent and Trademark Office (PTO) provides intellectual property protection to the inventor for 20 years. U. S. Patent and Trademark Office Web Patent Databases offer free WWW access, <http://www.uspto.gov/main/patents.htm>, to a bibliographic patent database that uses the most current patent classification system.

The Delphion Intellectual Property Network (IPN) is a research tool for patent information. Derwent World Patents Index (DWPI) is a comprehensive database of patent documents published worldwide. IMSworld Drug Patents International database provides access to the patent status of over 1200 molecules. The database contains information on patents due to expire (over a given time period), patents by therapy class, and patents by country.

(2) Phase IV Studies and Post Marketing Drug Information

During the Phase IV Studies and Post Marketing Drug Information stages a thorough literature search is required to find material relevant to the clinical use of the drug. This will require not only searching the basic bibliographic databases such as Biological Abstracts, EMBASE, IDIS, IPA, MEDLINE, and Science Citation Index, but also searching the patent literature, using Patent and Trademark Office Web Patent Databases. The following bibliographic databases provide access to the full span of life-science periodical literature, including all stages of a compound's development from early brief reports to comprehensive assessments after years of clinical use.

(i)BIOSIS: BIOSIS processes approximately 5,50,000 items each year, from primary research and review journals, books, monographs and conference proceedings. It is available in several formats. These include Biological Abstracts/RRM (Reports, Reviews, Meetings), the companion reference to Biological Abstracts.

(ii)EMBASE: EMBASE, the Excerpta Medica database is a biomedical and pharmacological bibliographical database that provides access to medical and drug related subjects from over 4000 biomedical journals from 70 countries. The EMBASE database combined with unique MDLINE records back to 1966 are available in EMBASE.com.

(iii)International Pharmaceutical Abstracts: IPA published semimonthly, is an abstracting/indexing publication which covers all pharmaceutical literature.

(iv)MEDLINE: MEDLINE (Medical Literature Analysis, and Retrieval System Online) contains over 11 million references to journal articles in life sciences with a concentration on biomedicine from 1966 to the present. MEDLINE is available on internet through the National Library of Medicine (NLM) home page at <http://www.nlm.nih.gov> and can be searched free of charge.

(v)Pubmed Central: Pubmed Central (PMC) which encompasses Medline is a web-based archive of journal literature for all of the life sciences. Access to PMC is free and unlimited.

(vi)Science Citation Index: Science Citation Index (SCI) provides access to current and retrospective bibliographical information, author abstracts, and cited references found in various scholarly science and technical journals covering more than 150 disciplines.

Table 1: Important resources/internet websites for Drugs related Information

S. No.	Resources/sites for Drug Information and related information	Information provided
1	www.ashp.org/s_ashp/sec_drug_shortages.asp	American Society of Health-System Pharmacy – Shortages: Drug Shortage Resource Center with updates/ management of shortages
2	www.cdc.gov	Centers for Disease Control: Public health guidelines, vaccine and travel information, and CDC publications
3	www.fda.gov	Food and Drug Administration: Drug and Biologics information (approvals, shortages, Orange Book, news, etc.). Be sure to click CBER for biologics and CDER for drug information.
4	www.home.mdconsult.com	Full-text books and journals, drug information, news, CME, and patient leaflets. Requires fee and password
5	www.guidelines.gov	National Guidelines Clearinghouse : Public resource for evidence-based clinical practice guidelines established by the governments Agency for Healthcare Research and Quality.
6	www.health.nih.gov	National Institutes of Health: Information on disease states, research, and federal health programs from the NIH
7	www.ncbi.nlm.nih.gov/entrez	National Library of Medicine: PubMed - a searchable listing of abstracts of medical literature
8	www-medlib.med.utah.edu	Spencer S. Eccles Health Sciences Library: Library catalog, full-text journals, searchable databases, etc.
9	www.uuhsc.utah.edu/pharmacy/druginfo	The University of Utah Hospital & Clinics Drug Information Service: Information about our service, publications, and drug shortage updates. Many links are for internal use only.
Pharmacy Calculations and Kinetics		
10	www.boomer.org/c/p1/	A First Course in Pharmacokinetics and Biopharmaceutics : General overview of definitions and basic concepts
11	www.cardinalpharmacy.com/calculators.htm	Health and fitness calculators for the general public
12	www.globalrph.com	Sells dosing and pharmacokinetic programs for desktops and PDAs with demos
13	www.goodgrade.com/pha/pharmacy.htm	Provides a variety of free conversion calculators
14	www.martindalecenter.com/Calculators1B.html	Martindales's The Reference Desk : 16,535 online calculators for a variety of mathematical applications including SI conversion, measurement conversions, and complex mathematical equations.
15	http://pharmcal.tripod.com/index2.htm	Pharmaceutical Calculations : Provides several conversion calculators and equations free of charge
16	www.boomer.org/pkin/soft.html	Pharmacokinetic Software: Links to different program sites with information about lab and

		clinical pharmacokinetics
17	www.pharmacyexam.com/rc_sample6.asp	Pharmacyexam.com: Lists sample NABPLEX questions, and sells tutorial materials.
18	www.rphonline.com	RPhOnline.com: Provides a few pharmacy calculators and kinetics programs. Interaction calculators and CE are available
19	www.rxkinetics.com/	RxKinetics: Free trial for palm program for calculating adult and pediatric antibiotic kinetics.
20	www.eduserv.hscer.washington.edu/pharmacy/pharm309/calculations/#lesson	Provides an overview of pharmacy calculations with a tutorial and practice questions.
21	www.lapk.org	USC Laboratory of Applied Pharmacokinetics: Offers software for population modeling, clinical programs, programs for ID or cardiology.
Resources for finding statistics on diseases and demographics		
22	www.cdc.gov/scientific.htm	CDC: Data and Statistics: Links to scientific data on statistics and scientific laboratory data.
23	www.healthatoz.com	Search engine for consumer health and medicine information
General Drug Information		
24	www.medlineplus.gov	Site links to patient drug category and health monographs, medical dictionaries, health professional directories and other resources such as organizations and health libraries.
25	www.health.nih.gov	National Institutes of Health: Information on disease states, research, and federal health programs from the NIH
26	www.Csmwm.org	Specialize in Depression Help , Drug Reaction , Depression Drugs , Allergy Medicines , Drug Safety and an array of other products and services
Investigational Drugs		
27	www.clinicaltrials.gov	National Institutes of Health--Clinical Trials: Directory of clinical trials in progress. Can search by disease state or specific agent.
28	www.phrma.org/newmedicines/	Information on drugs in the pipeline. Can search by disease state and therapeutic categories. Good summary articles on topics related to drug development.
29	www.cancer.gov/clinicaltrials	National Cancer Institute: Specific for clinical trials to treat cancer
30	www.patientadvocate.org/	Patient Advocate Foundation : Patient resource i.e. it means to participate in clinical trials and use investigational drugs.
31	www.bioscorprio.com	Lists of investigational drugs in pipeline by disease state. Major limitation is must pay for additional information.
32	www.centerwatch.com	Provides trial data and email-notification services to patients interested in participating in clinical trials. Professional investigation drug information can be found after subscribing to the service for a substantial fee.

Disease Treatment

Treatment of disease in the affected individual is twofold in nature, being directed (1) toward restoration of a normal physiological state and (2) toward removal of the causative agent. The diseased organism itself plays an active part in both respects, having the capacity for tissue proliferation to replace damaged tissue and to surround and wall off the noxious agent, as well as defense and detoxification mechanisms that remove the causative agent and its products or render them harmless. Therapy of disease supplements and reinforces these natural defense mechanisms.

Metabolic faults also may sometimes be corrected—for example, by the use of insulin in the treatment and control of diabetes—but more often specific therapeutic measures for idiopathic diseases are lacking. However, advances in gene therapy may be able to correct defective genes that result in disease.

When disease is produced by environmental factors, there is commonly no specific treatment; only removal of the affected individual from exposure to the agent generally allows normal detoxification responses to take over. Again, there are notable exceptions, as in the treatment of lead poisoning with ethylenediaminetetraacetic acid, an agent that forms complexes with lead that are excreted by the kidney.

Treatment of infectious diseases is more effective in general; it assumes several different forms. Treatment of diphtheria with antitoxin, for example, neutralizes the toxin formed by the microorganisms, and host defense mechanisms then rid the body of the causative microorganisms. In other diseases, treatment is symptomatic in the sense of restoring normal body function. An outstanding example of this is in cholera, in which disease symptoms result from a massive loss of fluid and salts and from a metabolic acidosis; the highly effective treatment consists of restoring water and salts, the latter including bicarbonates or lactates to combat acidosis. More often, however, therapy is directed against the infecting microorganism by administration of drugs such as sulfonamides or antibiotics. While some of these substances kill the microorganisms, others do not and instead inhibit proliferation of the microorganism and give host defenses an opportunity to function effectively. For other infectious diseases there is no specific therapy. There are, for example, very few antiviral chemotherapeutic agents; treatment of viral diseases is mainly directed toward relief of discomfort and pain, and recovery, if it ensues, is largely a matter of an effective cellular immune response mounted against the invading virus by the host.

Medication Errors

The problem of medical errors, and in particular medication errors, has prompted a strong response by the health care industry, purchasers, and by state and federal governments. Medical errors are the eighth leading cause of death in the United States, with the number of deaths exceeding those associated with motor vehicle accidents, breast cancer, or AIDS. Medication errors represent the largest single cause of errors in the hospital setting, accounting for more than 7,000 deaths annually—more than the number of deaths resulting from workplace injuries. Approximately 1.3 million people are injured annually in the United States following medication errors.

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) defines a medication error as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional

practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use." The National Coordinating Council for Medication Error Reporting and Prevention is an independent body comprised of 22 national organizations. In 1995, USP spearheaded the formation of the National Coordinating Council for Medication Error Reporting and Prevention. Leading national health care organizations are, for the first time, meeting, collaborating, and cooperating to address the interdisciplinary causes of errors and to promote the safe use of medications. USP is a founding member and the Secretariat for NCC MERP.

Almost everyone in the modern world takes medication at one time or another. According to one estimate, in any given week four out of every five U.S. adults will use prescription medicines, over-the-counter drugs, or dietary supplements of some sort, and nearly one-third of adults will take five or more different medications. Most of the time these medications are beneficial, or at least they cause no harm, but on occasion they do injure the person taking them. Some of these "adverse drug events (ADEs)," as injuries due to medication are generally called, are inevitable, the more powerful a drug is, the more likely it is to have harmful side effects, for instance but sometimes the harm is caused by an error in prescribing or taking the medication, and these damages are not inevitable. They can be prevented.

In hospitals, errors are common during every step of the medication process—procuring the drug, prescribing it, dispensing it, administering it, and monitoring its impact—but they occur most frequently during the prescribing and administering stages. When all types of errors are taken into account, a hospital patient can expect on average to be subjected to more than one medication error each day. However, substantial variations in error rates are found across facilities. An ADE arising from an error is considered preventable. It is difficult to get accurate measurements of how often preventable ADEs occur. These medication errors are undoubtedly costly to patients, their families, their employers, and to hospitals, health-care providers, and insurance companies, but there are few reliable estimates of that cost.

Drug errors are far from new, but with more than 12 million chemical substances now available, taking medications has become an increasingly dangerous proposition. In 1999, a report called *To Err Is Human* by the Institute of Medicine of the National Academy of Sciences, estimated that as many as 98,000 hospital patients die every year as a result of preventable errors, including medication mistakes. These findings prompted the Clinton administration and Congress to call for urgent reforms. Both academics and entrepreneurs are proposing an array of systems and gadgets designed to prevent errors or catch them before they can harm the patient.

Medication errors that lead to iatrogenic injuries are a well-known worldwide phenomenon and are common, costly, and clinically important [Lesar, et.al., Classen ,et.al.]. In 1910, Richard Clark published the first study that looked at error rates in clinical diagnosis [Gore]. Since then, several studies have looked at the problem of medication errors. Incidence rates of adverse drug events amongst adults admitted to the hospital have ranged from 2 to 7 per 100 admissions [Bates, et.al., Jha,et.al.]. Approximately, 28% of adverse drug events are related to medication errors and are, therefore, judged to be preventable [Bates, et.al.]. This issue has also received considerable attention in the lay press. Over a period of time, there has been a transition from an era where medical practice and its practitioners were revered to a time when doubt and fear is expressed and legal suits are pursued by aggrieved patients [Ferner].

Against this background, the Centers for Medicare and Medicaid Services requested that the Institute of Medicine study the prevalence of such medication errors and formulate a national agenda for reducing these errors. The resulting report, Preventing Medication Errors, finds that medication errors are surprisingly common and costly to the nation, and it outlines a comprehensive approach to decreasing the prevalence of these errors. This approach will require changes from doctors, nurses, pharmacists, and others in the health care industry, from the Food and Drug Administration (FDA) and other government agencies, from hospitals and other health-care organizations, and from patients.

In 1992, the FDA began monitoring medication error reports that are forwarded to FDA from the United States Pharmacopoeia (USP) and the Institute for Safe Medication Practices (ISMP). The Agency also reviews MedWatch reports for possible medication errors. Currently, medication errors are reported to the FDA as manufacturer reports (adverse events resulting in serious injury and for which a medication error may be a component), direct contact reports (MedWatch), or reports from USP or ISMP. FDA receives medication error reports on marketed human drugs (including prescription drugs, generic drugs, and over-the-counter drugs) and non-vaccine biological products and devices.

1. Common Medication Errors

In a study by the FDA that evaluated reports of fatal medication errors from 1993 to 1998, the most common error involving medications was related to administration of an improper dose of medicine, accounting for 41% of fatal medication errors. Giving the wrong drug and using the wrong route of administration each accounted for 16% of the errors. Almost half of the fatal medication errors occurred in people over the age of 60. Older people may be at greatest risk for medication errors because they often take multiple prescription medications.

Medication errors come in many forms: Patients can be given the wrong drug or dose because of an error in reading or writing a prescription. Doctors can fail to find out if a patient is allergic to a particular drug or has a condition that can be worsened by a medication. Different drugs may interact with each other to trigger a problem. Or, as in my case, two drugs with similar side effects can amplify the extent of that side effect synergistically. These errors are costly, in dollars as well as lives. Prescription errors are the second most frequent and expensive cause of medical malpractice claims, costing \$219 million a year, according to the Physicians Insurance Association of America.

The American Hospital Association lists the following as some common types of medication errors:

- incomplete patient information (not knowing about patients' allergies, other medicines they are taking, previous diagnoses, and lab results, for example);
- unavailable drug information (such as lack of up-to-date warnings);
- miscommunication of drug orders, which can involve poor handwriting, confusion between drugs with similar names, misuse of zeroes and decimal points, confusion of metric and other dosing units, and inappropriate abbreviations;
- lack of appropriate labeling as a drug is prepared and repackaged into smaller units; and
- environmental factors, such as lighting, heat, noise, and interruptions, that can distract health professionals from their medical tasks.

There are many reasons for the growing incidence of prescription errors. Thanks partly to pressure from managed care, doctors have little time to spend with patients, often see patients they don't know, and are forced to make snap judgments. Patients' files are frequently unavailable, especially in emergency rooms and county hospitals. And pharmacists under pressure to fill prescriptions quickly may make mistakes.

2. Prediction and Prevention of Medication Errors

Information is only part of the problem of improving the safe use of medicines. The psychological theory of errors recognizes that in performing a habitual act we follow a 'schema' that specifies the nature and order of the steps required to perform the act [Reason]. When we tie our shoe laces, or write a cheque, or give an injection of benzyl penicillin, we follow such a schema. Sometimes we err. We write '3 Jan 2006' on our cheques on 3 Jan 2007. or we are presented with a prescription 'Lamisil' (terbinafine, an antifungal) but read 'Lamictal' (lamotrigine, an antiepileptic agent). Or we automatically draw up penicillin powder and use the potassium chloride solution in the nearest ampoule without realizing it. Such errors, in which steps in the schema are omitted, duplicated, or subverted by those of another schema, are the price we pay for 'automatic', learned, behavior. These slips are unconscious, so that exhortation will not prevent them. Their frequency is increased by distractions, simultaneous and competing demands, and tiredness: just the circumstances of hospital medicine.

(i)Predicting look-alike and sound-alike medication errors: Look-alike or sound-alike (LA/SA) health products refer to names of different health products that have orthographic similarities and/or similar phonetics (i.e. similar when written or spoken). These similarities may pose a risk to health by contributing to medical errors in prescribing, documenting, dispensing or administering a product. These medication errors may be more likely to occur because of contributing factors such as identical doses, dosage forms or routes of administration, similar packaging or labeling, incomplete knowledge of drug names, illegible handwriting, verbal order errors and even lack of an appropriate knowledge-base. Some of the brand names may not sound-alike when read out or look-alike when in print, but when hand written or communicated verbally they can cause confusion. Confusion regarding drug names is thought to account for 25% of all medication errors [Lambert, et.al.]. However, while each category listed by Rataboli *et al* represents an area for potential error, the number of drugs listed in each category is small and merely representative. One test, the Levenshtein distance, has been used to predict error pairs. An example of how this works is given by comparing Lamictal (lamotrigine) and Lamisil (terbinafine) [Lambert]. To transform Lamisil into Lamictal, the S is changed to a C, the I is changed to an A and the T is added. Three edit operations are required, giving a Levenshtein distance between the two names of three. The lower the distance, the more similar the drug names are. A threshold for Levenshtein distances has been proposed as greater than 5, therefore this test may have predicted the problems associated with Lamisil and Lamictal.

As mentioned above many medication errors are caused by look-alike and sound-alike medication names, yet few procedures exist to ensure the safety of new drug nomenclature or to identify confusingly similar names from within existing databases. A model for predicting medication name confusion has been described in one of the studies. Three automated, quantitative measures of orthographic similarity (i.e., similarity in spelling) were identified (bigram similarity, trigram similarity, and Levenshtein distance). The relationship between orthographic similarity and the likelihood of a medication error was examined. For each measure of similarity, the frequency distribution of similarity scores for pairs of drug names

previously reported to cause confusion (error pairs) was compared with the distribution of similarity scores for control pairs randomly selected from the general index of USP DI-Volume I: Drug Information for the Health Care Professional. Then, three parallel, unmatched case-control studies were conducted to discover whether similarity was a significant risk factor for medication errors. Finally, on the basis of the three similarity measures, tests for predicting confusion were developed and evaluated. For each similarity measure, the frequency distribution of error pairs was significantly different from that for control pairs, and orthographic similarity was a significant risk factor for medication errors. Pairs of names whose measures of similarity exceeded present thresholds were between 25 and 523 times more likely to be involved in a medication error than pairs whose similarity did not exceed these thresholds. A prognostic test that correctly identified 91% of all pairs as either errors or controls was developed. This test had a sensitivity of 84% and a specificity of 99%. Automated measures of similarities between medication names can form the basis of highly accurate, sensitive, and specific tests of the potential for errors with look-alike and sound-alike medication names.

Reducing medication errors is a process of continuous quality improvement. The journey from the pen to the patient is a long one and filled with multiple areas where errors can be made. The delivery of medical care like all other systems is safe only when human error is recognized as an inevitable consequence and systems are put in place to minimize consequences [Ferner]. Current systems are not designed to capture errors and near errors because reporting is voluntary and systems for reporting do not exist [Cullen, et.al.]. What should be done is generally known as the five rights - the right drug, right dose, right route, right time and right patient [Benjamin]. Analysis of medication errors suggests that prevention strategies that target systems rather than individuals are most effective in reducing errors [Leape,et.al.]. Today, more than ever, health care has become a team activity with multiple stakeholders. While the physician still remains the driving force, inputs from clinical pharmacists, nurses, and other healthcare professionals is often helpful. Pharmacists are excellent at detecting and correcting 'clerical' errors in written prescriptions, as prospective studies show [Ferner]. However meticulously prescriptions are checked, and however carefully drugs are dispensed, there always remains the possibility of a slip in some later part of the process. An obvious example is giving vincristine intrathecally, an error that is usually lethal [Woods]. Unless there is a mechanism for making it physically impossible to attach a syringe containing vincristine to a spinal needle, the error will remain possible. The most we can hope for is that a sufficiently large number of safety checks are interposed to make the eventual failure of all of them unlikely.

(ii)To Reduce Medication Errors: When a doctor gives a prescription, patient must ask him or her to tell the name of the drug, the correct dosage, and what the drug is used for. The doctor must be sure that the patient understands the directions for any medications he may be taking including the correct dosage, storage requirements, and any special instructions. In the hospital, one must ask (or have a relative or friend ask) the name and purpose of each drug that is being given. One should be sure to tell doctor the names of all the prescription and non-prescription drugs, dietary supplements, and herbal preparations that are being taken every time the doctor writes a new prescription. This will help to prevent another type of medication problem, undesirable and potentially serious interactions among medications. Finally, never be afraid to ask questions. If the name of the drug on the prescription looks different than is expected, if the directions appear different, or if the pills or medication itself looks different, one must tell the doctor or pharmacist right away. Asking questions if at all is a free and easy way to ensure that one don't become the victim of a medication error.

1. A Paradigm Shift In The Patient-Provider Relationship: The first step is to allow and encourage patients to take a more active role in their own medical care. In the past the nation's health care system has generally been paternalistic and provider-centric, and patients have not been expected to be involved in the process. But one of the most effective ways to reduce medication errors, is to move toward a model of health care where there is more of a partnership between the patients and the health care providers. Patients should understand more about their medications and take more responsibility for monitoring those medications, while providers should take steps to educate, consult with, and listen to the patients. To make this new model of health care work, a number of things must be done. Doctors, nurses, pharmacists and other providers must communicate more with patients at every step of the way and make that communication a two-way street, listening to the patients as well as talking to them. They should inform their patients fully about the risks, contraindications, and possible side effects of the medications they are taking and what to do if they experience a side effect. They should also be more forthcoming when medication errors have occurred and explain what the consequences have been. Patients or their surrogates should in turn take a more active role in the process. They should learn to keep careful records of all the medications they are taking and take greater responsibility for monitoring those medications by, for example, double checking prescriptions from pharmacies and reporting any unexpected changes in how they feel after starting a new medication. Also, the healthcare system needs to do a better job of educating patients and of providing ways for patients to educate themselves. Patients should be given opportunities to consult about their medications at various stages in their care—during consultation with the providers who prescribe their medications, at discharge from the hospital, at the pharmacy, and so on. And there needs to be a concerted effort to improve the quality and the accessibility of information about medications provided to consumers. The FDA, the National Library of Medicine, and other government agencies should work together to standardize and improve the medication information leaflets provided by pharmacies, make more and better drug information available over the Internet, and develop a 24-hour national tele- ...one of the most effective ways to reduce medication errors, is to move toward a model of health care where there is more of a partnership between the patients and the health care providers and the phone helpline that offers consumers easy access to drug information.

2. To Err Is Human -- Information Technologies to the Rescue: A second important step in reducing the number of medication errors will be to make greater use of information technologies in prescribing and dispensing medications. Though technology is far from the only answer, a host of new devices have cropped up that promise to help. Leapfrog Smart Products, Inc., of Maitland, Fla., offers a "smart card" the size of a credit card that patients can keep in their wallet. Loaded with a built-in computer chip, the card stores insurance, financial, and medical information, including a patient's medication history, drug allergies, vital signs, cholesterol levels, and more. The card is inserted into a computerized reader and is updated at each medical appointment. Smart-card technology is widely used in Europe and in some Florida hospitals. Where the smart card can really help is with patients who are unconscious, confused, or who don't speak the same language as the doctor.

In 1999, a database called ePocrates was introduced by a company. This system provides information on side effects and drug interactions for more than 1,600 medications, data that can be downloaded from the Internet to a hand-held computer that a doctor can carry on rounds. The manufacturer claims that more than 80,000 doctors and nurses already use the device at teaching hospitals.

The good news is that, in response to this greater risk, a new approach to dealing with errors is emerging that sees mistakes as the result of flawed systems rather than bad doctors. To err is human, advocates of this "systems" approach say; accidents will always happen. The only answer is to fix the system itself by building in safeguards and double checks. Doctors, nurse practitioners, and physician assistants, for example, cannot possibly keep up with all the relevant information available on all the medications they might prescribe—but with today's information technologies they don't have to. By using point-of-care reference information, typically accessed over the Internet or from personal digital assistants, prescribers can obtain detailed information about the particular drugs they prescribe and get help in deciding which medications to prescribe. Even more promising is the use of electronic prescriptions, or e-prescriptions. By writing prescriptions electronically, doctors and other providers can avoid many of the mistakes that accompany handwritten prescriptions, as the software ensures that all the necessary information is filled out—and legible. Furthermore, by tying e-prescriptions in with the patient's medical history, it is possible to check automatically for such things as drug allergies, drug-drug interactions, and overly high doses. In addition, once an e-prescription is in the system, it will follow the patient from the hospital to the doctor's office or from the nursing home to the pharmacy, avoiding many of the "hand-off errors" common today. In light of all this, it is recommended that by 2010 all prescribers and pharmacies be using e-prescriptions. More generally, all health care suppliers should seek to become high-reliability organizations preoccupied with improving medication safety. To do this, they will have to take advantage of the latest information technologies and the most up-to-date organizational and management strategies. They will also need to put effective internal monitoring programs in place, which will allow them to determine the incidence rates of adverse drug events more accurately and thus provide a way of measuring their progress toward improved medication safety.

One day in the near future, computerized systems may be in place at most hospitals and clinics across the country, allowing doctors to type prescriptions directly into a pharmacy-linked computer. Double checks for dosage amounts, drug interactions, and patient allergies will be automatic, and there will be no errors due to doctors' illegible handwriting. Already in use at some of the nation's hospitals -- including Brigham and Women's Hospital in Boston -- these systems have reduced medication error by as much as 81% as reported in the July-August 1999 issue of the *Journal of the American Medical Informatics Association*.

3. Improved Labeling and Packaging of Medications: Another way to reduce medication errors is to ensure that drug information is communicated clearly and effectively to providers and patients. Some errors occur simply because two different drugs have names that look or sound very similar. It is recommended that the drug industry and the appropriate federal agencies work together to improve drug nomenclature, including not just drug names but also abbreviations and acronyms. At the same time, the information sheets that accompany drugs should be redesigned, taking into account research that identifies the best methods for communicating information about medications.

4. Policy Recommendations: Reducing preventable adverse drug events will demand the attention and active involvement of everyone involved. The federal government should, for example, pay for and coordinate a broad research effort aimed at learning more about preventing medication errors. Various regulatory agencies should encourage the adoption of practices and technologies that will reduce medication errors. Accreditation agencies should require more training in medication-management practices. These efforts will pay off in far fewer medication errors and preventable adverse drug events, far less harm done to patients

by medications, and far less cost to the nation's economy. The drug industry and the appropriate federal agencies work together to improve drug nomenclature, including not just drug names but also abbreviations and acronyms.

Today, reducing medication errors and improving patient safety have become common topics of discussion for the president of the United States, federal and state legislators, the insurance industry, pharmaceutical companies, health care professionals, and patients. But this is not news to clinical pharmacologists. Improving the judicious use of medications and minimizing adverse drug reactions have always been key areas of research and study for those working in clinical pharmacology. However, added to the older terms of adverse drug reactions and rational therapeutics, the now politically correct expression of medication error has emerged. Focusing on the word error has drawn attention to "prevention" and what can be done to minimize mistakes and improve patient safety. Webster's New Collegiate Dictionary has several definitions of error, but the one that seems to be most appropriate in the context of medication errors is "an act that through ignorance, deficiency, or accident departs from or fails to achieve what should be done." What should be done is generally known as "the five rights": the right drug, right dose, right route, right time, and right patient. One can make an error of omission (failure to act correctly) or an error of commission (acted incorrectly). An error can be prevented. However, the practice of medicine, pharmacy, and nursing in the hospital setting is very complicated, and so many steps occur from "pen to patient" that there is a lot to analyze. Implementing safer practices requires developing safer systems. Many errors occur as a result of poor oral or written communications. Enhanced communication skills and better interactions among members of the health care team and the patient are essential. The informed consent process should be used as a patient safety tool, and the patient should be warned about material and foreseeable serious side effects and be told what signs and symptoms should be immediately reported to the physician before the patient is forced to go to the emergency department for urgent or emergency care. Last, reducing medication errors is an ongoing process of quality improvement. Faulty systems must be redesigned, and seamless, computerized integrated medication delivery must be instituted by health care professionals adequately trained to use such technological advances. Sloppy handwritten prescriptions should be replaced by computerized physician order entry, a very effective technique for reducing prescribing/ordering errors, but another far less expensive yet effective change would involve writing all drug orders in plain English, rather than continuing to use the elitists' arcane Latin words and shorthand abbreviations that are subject to misinterpretation. After all, effective communication is best accomplished when it is clear and simple.

Computerised Physician Order Entry (COPE) and Clinical Decision Support Systems (CDSS) are promising systems, but need to be balanced against an initial expenditure that must be borne for long term benefits, which in turn need to be monitored and measured [Kaushal et.al]. Use of standard protocols and guidelines coupled with academic education promote a more consistent approach to patient care and these should be put in place. Breakdown in communication is a common cause of harm to patients [Wilson, et.al] and this needs to be addressed at several levels. It is vital to evaluate the prescription writing skills acquired by students [Ferner]. The issue of medication errors in India is extremely complex and goes much beyond brand names and phonetics since generic brands offer the considerable advantage of quality combined with cost effectiveness in the treatment of a variety of diseases [Dyer]. Much has been done to date and much more is being done. Finally, it is important to work in conjunction with the most important stakeholder- the patients and help them understand the risks involved in healthcare and work with them to reduce harm.

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