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Review Article

Review of computer applications in institutional pharmacy—1975–1981

Ken W. Burleson

A literature review of computer applications in institutional pharmacy, covering papers published from 1975 to 1981, is presented.

Articles are categorized as computer concepts, applications to administrative functions, controlled substances, drug distribution systems (including on-line and off-line services, intravenous admixture services, and ambulatory services), drug information, clinical services (including drug-use review, drug interactions and therapeutic incompatibility surveillance, and pharmacokinetics), and pharmacy-related applications developed by nonpharmacists.

Before 1975, computer applications in institutional pharmacy reported in the literature were largely single-use applications. After 1975, many reports described the integration of individual applications into sophisticated systems that supported many functions. There is still a need for good cost justification studies of computerization in pharmacy.

Index terms: Administration; Automation, data processing, computers; Controlled substances; Drug distribution systems; Drug information; Drug interactions; Incompatibilities; Pharmacy, institutional

In the past 20 years electronic data processing (EDP) in hospital pharmacy has grown from applications that improved accounting procedures to sophisticated multifunctional, integrated systems for institutional drug control and clinical pharmacy support. Early innovators were hospital pharmacists who applied computers to accounting and billing functions. However, as pharmacists became aware of the benefits of automation and as they gained expertise in the field, applications of EDP became varied. Innovative approaches to pharmacy practice have been instituted that,

without automation, would be too time-consuming, too costly, or too difficult to implement. Automated drug control systems, medication delivery systems, and support of clinical services are examples of these applications. Interest in automation for pharmacy practice has stimulated vendors of commercial systems to develop hardware and software packages designed for pharmacy.

The expanded use of electronic data processing in pharmacy practice has been due to both the development of more sophisticated hardware and software during the past 20 years and the experiences of individual practitioners in applying EDP to various segments of practice. The literature has contributed substantially to the increased awareness of the individual pharmacist of the benefits of automation. In 1975, Knight and Conrad[1] published an extensive review of pharmacy applications of electronic data processing made to that time. This article reviews those applications made from 1975 to the present.

Computer Concepts

Data processing concepts and technology are areas in which few pharmacists have had formal training. They should become familiar with fundamentals of systems analysis, design, and computer technology prior to involvement with application development. A number of articles have described the basic concepts of data processing for the pharmacist.

Nelson[2] presented an introduction to computer hardware that could be used in a pharmacy system. He described the various hardware components, including the central processing unit (CPU), input devices, and data storage devices. Advantages and disadvantages of different components were presented. Downtime, system security, and vendor systems evaluations were discussed. He also presented a dictionary of computer terminology. Mehl[3] outlined the minimum requirements for a pharmacy data processing system. He compared advantages of centralized versus decentralized systems, and examined the methods of data entry and types of drug coding for developing a data base. He also emphasized the need for order verification to prevent errors.

Computer hardware configurations range from the large mainframe computer to the minicomputer to the most recent development in the field, the microprocessor. Given the premise that the pharmacist has a choice in the selection of hardware, an understanding of the advantages and disadvantages of each can be essential to the development of a successful application. Knowles[4] explained the differences between mainframe systems and minicomputers. Lauer et al.[5] explained the apparent and subtle differences between a mainframe computer shared with other users (shared system) and a stand-alone dedicated minicomputer system for pharmacy, particularly in regard to ambulatory pharmacy practice. Advantages and disadvantages of each configuration were presented. Data storage was found to be the most serious drawback to a stand-alone system, a disadvantage that could be minimized with a properly designed system. The authors concluded that in most situations for pharmacy practice, either configuration could provide adequate support.

Another configuration is a pharmacy application developed as a part of a total hospital information system (HIS). Ball et al.[6] examined the past, present, and future developments in hospital data processing systems, from stand-alone pharmacy systems to large hospital information systems. The authors predicted that in the immediate future, many physicians would have terminals in their offices interfaced with hospital information systems. Mecklenburg[7] described the expanding applications of hospital information systems, including pharmacy and other clinical applications.

An important concept for the pharmacist to understand before developing an application is the methods used to justify the need for and cost of a computerized system. Although many articles have been written describing the varied applications of computerization, few articles have described controlled documented studies to justify the cost and evaluate the effects of a computerized system. The fact that evaluation of systems and intensive cost-benefit studies have

not been accomplished may be a major reason why there has not been a greater acceptance of pharmacy systems by hospital administrators or pharmacists. In 1975, Gouveia[8] reviewed the few studies to date that had attempted to analyse the effects of computerization on hospital costs, medication errors, and patient care. He found that the few studies published actually raised more questions than they answered. He emphasized the need for research to establish adequate cost-benefit ratios to justify computerization to hospital administrators, patients, and third party payers.

Since that time, other studies have been published describing the steps involved with analyzing and justifying the need for and cost of computerization. Freibrun[9] analyzed a traditional pharmacy system in a 360-bed hospital. He identified procedures needing improvements and examined alternate manual and automated approaches for change; areas in which automation would offer potential savings; developed a rating scale for vendors; and described steps involved in successful operations analysis in a pharmacy. Kay et al.[10] described the method used to analyse a hospital pharmacy's need for automation and identify the various areas where automation would benefit both pharmacy and the hospital. The impact of the proposed system upon other areas of the hospital were also listed. Cost justification for a dedicated mini-computer was developed. The authors were successful in justifying automation of the pharmacy department, based upon a potential cost savings and an improved medication delivery system.

Neal[11] developed an in-depth cost proposal to justify to hospital administration the computerization of a hospital pharmacy. He identified seven areas of tangible cost savings (reduction in costs, elimination of salaries paid, increased revenues) and two areas of intangible savings (reduced overhead, labor reallocation). He was able to project tangible dollar savings to each of these areas. He found that automation of the department would result in a substantial cost savings. He also described the various steps in developing and presenting the analysis to hospital administration. Gray[12] evaluated the cost of computerization of an i.v. admixture service in a hospital pharmacy. Staffing analysis and life cycle cost projection were determined. Workloads and staffing patterns both with and without the computer were calculated. The basis of the study was to determine the amount of money that could be invested in a computer system as justified by staffing reductions and other savings. The author's conclusion was that the computer was cost effective and, therefore, should be purchased.

Lauer[13] gave an overview of the need for automation in pharmacy practice and the benefits to be realized from computerization. Three areas of savings as a result of automation—time, space, and personnel costs—justified the cost of computerization.

Two authors have described the methods of dealing with vendors of computer systems. Olsen et al.[14] described the method used to select an upgraded computer system that would support an automated clinical department in the hospital. Although the article dealt specifically with an automated laboratory system, the authors presented a general

discussion of vendors, vendor selection, systems requirements, terminal requirements, and hardware and software that could be used by the pharmacist in selecting a pharmacy system. Cutely[15] presented an extensive list of questions a pharmacist should ask a hardware or software vendor of a commercial system when considering the purchase of such a system.

Before beginning development of any automated applications, the pharmacist must develop a data base, or drug file, listing all the drugs to be found in the pharmacy, along with any information pertinent to the description of each drug. The method in which a data base is developed can mean the difference between a flexible system with the ability for expanded applications and a rigid, single application system. Hanson et al.[16] have described the development of a master drug file that was developed by examining an existing computerized drug data file to determine which existing fields of information should be retained for the new data base. The new data base was developed to support increasingly sophisticated pharmacy applications. Twenty-seven data fields for the master drug file were identified. Programs were written to permit entry and maintenance of the file by using punched cards input to an offline computer. The authors envisioned using online entry of data through a cathode ray tube (CRT) in the future. Programs were written that permitted machine verification of data according to predefined specifications. Any errors detected were rejected for correction. This editing feature resulted in a high degree of accuracy of the stored data. Strand et al.[17] developed a master drug file after comparing commercially available data bases which they found to be deficient. Twenty-seven different data fields were identified and information for each drug entered to a coding form which was used for data entry. Entry was online via a cathode ray tube. The data base was used to support certain administrative and drug distribution programs for both inpatient and outpatient services. The authors also examined the cost of the development of the file. They found that more than 900 hours were involved with the development, at a total salary cost of $8451. This calculated to $7.43 per line item in the data base. Although this cost was twice that of a commercially available data base, the authors thought that the additional data fields that were available to them justified the cost.

The American Society of Hospital Pharmacists provides a computer-generated, machine-readable data base called Drug Products Information File (DPIF)[a] for use by pharmacists in computerized systems. Frankenfeld[18] examined the problems associated with the National Drug Code (NDC) system as a pharmacy data base and the potential for interfacing it to DPIF. He explained the advantages of cross-referencing the information in the two files.

Administrative Applications

Because of the computer's inherent ability to quickly tabulate numerical data, and to store, retrieve, and compile statistical information, certain administrative functions are ideally suited to automation. Among these functions are patient billing and accounting, drug use review, and inventory control. A number of articles have described applications of EDP in these areas.

Silverman[19] described the administrative functions that could be automated using a dedicated minicomputer. Among these applications were personnel management, patient billing and accounting, and inventory control.

Wuest and Schaengold[20] described an automated accounting system shared by two hospital pharmacies, using a time-shared computer system. Data were entered from dispensing records showing all transactions for each pharmacy. The system generated a monthly report of expenses for chargeable patient drugs and nonchargeable floor stock. Drug use statistics from this report were used for purchasing and inventory control. The system also printed a formulary for each hospital.

In a hospital without data processing capability, Elliott[21] contracted to use the computer services of a local drug wholesaler to develop an inventory and purchasing system. The wholesaler's programs for inventory control were modified to adapt to the special needs of the hospital. All drug issues to stock from inventory were manually recorded on an inventory master list by a clerk and this was sent to the wholesaler for keypunching into the system. A weekly computer-generated report summarized the use of each item, and this list served as a stock status report and purchase list. Each item that had reached a predetermined order point was flagged. Items supplied by the wholesaler were automatically shipped and entered into the computerized inventory. Orders to direct vendors were completed by the pharmacist, working from the report. The system also generated a hospital formulary by use of therapeutic category coding. Both an alphabetical listing and a listing by therapeutic categories were available.

Pickup et al.[22] utilized the Massachusetts General Hospital Utility Multi-Programming System (MUMPS) to develop programs to control ward stock levels and contribute to workload analysis in a quality control section of a hospital pharmacy. The system was programmed to determine each hospital ward's minimum stock levels, based upon historical demand and the ability of the pharmacy to respond to the needs of the various wards. Results showed that the system could reduce the inventory of drugs on the nursing units, thereby effecting a cost savings, without any deterioration of service or inconvenience to the nursing units. The system also handled data concerning raw materials in the quality control section. It was determined that a time savings could be realized by automating some of the reports in this area.

Automated patient billing has been a feature of hospital computer systems for many years. This is one of the earlier applications to which EDP was applied in pharmacy. Trudeau[23] modified an existing time-shared payroll and accounting system to provide drug use review and patient drug billing. The time saved from these applications was used to permit the pharmacy to complete a hospital-wide traditional unit dose system. The author did not use the computer directly to support the unit dose system. Priest[24] used com-

puter-printed gummed labels to be attached to intravenous fluids and other pharmacy patient charge items that were kept as floor stock on the nursing units. These gummed stickers functioned as a charge voucher as well as a stock replenishment mechanism. The author concluded that the system aided in the capture of more charges, while simultaneously saving personnel time.

Fish[25] described a computerized patient billing system that was based on a combination of a percentage markup of drug costs plus a dose fee. Seven different dose fees (factors) were used, depending upon the type of drug product administered to the patient; e.g., oral unit dose, injectable unit dose, and i.v. additives. Manual patient profiles were used for a unit dose medication system, and cumulative charges for each patient were maintained on these profiles. At the time of patient discharge, the profile for the patient was inactivated and all drug charges were added. A pharmacy technician also entered the patient number, computer drug code, and dose factor for all drugs. The profile was then sent to the pharmacy pricing area, where the charges were entered into the computer via a cathode ray tube. A final patient bill was produced as a result of data entry. The system offered advantages of an accurate, itemized statement; charges were equitable, based upon the type of drug administered; and the system produced useful statistical reports. The time required to enter charges manually into the system was a drawback, and the author proposed an automated unit dose system that would eliminate much of the manual data entry.

Gurtel et al.[26] projected drug use review statistics for a pharmacy and therapeutics committee to use in determining the benefit of adding a new drug to the formulary of an ambulatory patient care clinic. A computer-supported ambulatory pharmacy system was used to determine if a new drug, ticrynafen, a diuretic with uricosuric properties, would benefit patients in the clinic. The computerized patient profile was used to determine the number of patients taking a diuretic who were also taking a uricosuric agent, to determine how many patients could benefit from the new drug which offered both therapeutic actions. Computer analysis revealed that only 8% of the patients on a diuretic were simultaneously receiving a uricosuric agent. In view of the cost of the new drug and the limited application, as shown by computer analysis, the pharmacy and therapeutics committee chose to add the drug only on a restricted formulary status. The drug was eventually prescribed for four patients. Later, the drug was recalled from the market because of its adverse reactions. The computer was used to search the patient profiles for those patients receiving the drug at the time of recall, so that their physicians could contact them and make appropriate changes in therapy. The authors concluded that the use of the computerized patient information system enabled the pharmacy and therapeutics committee to prevent the potential exposure of more than 160 patients to the adverse effects of the drug.

Not all administrative applications of data processing must be developed on a computer. Word processing equipment is similar to a computer, with the exception that word processing equipment ordinarily has no built-in logic. The system is used for storage of small amounts of data and retrieval and printing of this information on a repetitive basis. Letcher[27] compared three different commercial brands of word processing equipment to various applications in hospital pharmacy. The applications studied were label production; storage of personnel information; scheduling of repetitive tasks; and composition of narrative information, such as drug bulletins and procedure manuals. The evaluation included keyboard design, disk storage capabilities, software, print format, and security of data. One of the three systems was clearly superior to the other two because of its flexibility of applications. The author summarized the results of the evaluations of each machine.

Controlled Substances Applications

Controlled substances are defined as those drugs which have the potential and liability for abuse; i.e., narcotics and barbiturates. Federal and state laws require that practitioners who dispense these medications maintain records of disposition for all drugs under this regulation. Because of the large number of drugs in this category, proper recordkeeping has been time-consuming for both the pharmacist and nursing personnel. Automation of this segment of practice can reduce time involvement for both the pharmacist and nurse, while maintaining accurate control and accountability records as required by law.

Petoletti[28] used an off-line system in an outpatient clinic to monitor for potential abuse of controlled drugs by patients. Dispensing data were entered on a source document for each prescription dispensed. These data were keypunched weekly, and reports were generated that notified the pharmacist of those patients receiving excessive supplies of controlled drugs.

McDaniel[29] modified an existing patient accounting system to develop an automated recordkeeping system. All controlled drugs were assigned specific service codes within a designated group of service numbers. A separate file was set up in the computer for this group designation. As charges were posted to the patient's account, records of controlled drugs dispensed were created. Daily and cumulative monthly reports were printed, which showed distribution of controlled drugs. Nazzaro[30] developed a program on an off-line computer to provide accurate records for controlled substances accountability, while reducing manual transcriptions involved with record maintenance. The system was used for both inpatient ward stock and outpatient prescriptions in a military hospital. All prescription transactions were recorded manually on punched cards, and included patient number or hospital ward code, physician's identification code, drug code, and quantity of drug dispensed. All data were later keypunched and entered into the computer. Various records were generated by the system, including perpetual records of each drug by patient or ward, monthly inventory of all controlled substances, and ward monitoring lists of excess stock of controlled substances. The system could also search for prescriptions by patient or prescriber.

Shaver et al.[31] described a system for an inpatient and outpatient military hospital pharmacy which used limited computer hardware. The system was run on a remote mainframe computer through a telephone hookup. A pharmacist or technician entered all transactions daily via a cathode ray tube. After data entry was complete, all transactions were verified before the update program was run, to ensure accuracy of information. The system generated a number of reports, including transactions by drug and current inventory balances. It also permitted patient drug use screening and physician prescribing screening to monitor for potential drug abuse. The system was capable of tying in terminals at other military hospitals.

Finally, Dickinson[32] reported how the Drug Enforcement Agency used computers to map entire states to show drug distribution, to pinpoint areas of potential drug abuse. Data are obtained from two sources—the Automated Reporting and Consolidated Order System (ARCOS), which shows drug distribution from manufacturers and wholesalers to pharmacies; and the Drug Abuse Warning Network (DAWN), which tracks drugs from selected hospital emergency rooms. All data were entered into the computer and analyzed. The resultant output was distributed to DEA field offices and other local and state law enforcement officials for follow-up.

Drug Distribution System Applications

Traditional manual drug distribution systems are time consuming, involve much clerical work for both pharmacist and nurse, and tend to be error-prone. Automation of the medication cycle can provide substantial benefits to the pharmacist, nurse, and patient by reducing the amount of clerical work involved with maintaining a medication system, reducing errors, improving administrative control, and freeing the pharmacist for more clinical involvement. Much work has been done in automating various segments of the medication cycle. Many pharmacists have automated one or more procedures involved in medication delivery. However, prior to 1975, only a few systems had integrated the various components of the cycle into a completely automated medication delivery system. Since that time, several articles have described the development and application of total systems for automated medication delivery. This increased development has been due, in part, to the reduced cost of hardware necessary to support an automated medication delivery system and to the entry of vendors that provide hardware and software packages. Yet, the use of EDP in the medication cycle is not extensively employed by hospitals. Stolar,[33] in a 1978 national survey of hospital pharmacies, found that of the 738 reporting hospitals, only 13% of the large hospitals and 5% of the small hospitals used computer systems in the drug dispensing process.

The importance of EDP in hospital drug delivery systems and the role of the pharmacist in implementing its use has been recognized by the American Society of Hospital Pharmacists (ASHP). The ASHP Statement on Hospital Drug Control Systems[34] states, "The pharmacist should utilize EDP to decrease the many traditional paper-handling chores so that his clinical role may be effectively expanded and his talents utilized properly." This position statement also outlined the many applications of EDP to pharmacy practice and the role of the pharmacist in systems development.

Off-line Medication Systems. Prior to 1975, many automated medication distribution systems were developed utilizing off-line systems, usually by modifying an existing batch process accounting system to provide pharmacy applications. In recent years, more and more pharmacists have had access to on-line computer systems, and only a few authors have described the development of systems using off-line computer hardware.

Swift[35] described a semi-automated approach to a unit dose system, in which punched cards were used to provide information for medication cart filling. Each drug order was transferred in writing by a pharmacy technician to a punched card, called the master dose card. After verification of the transcription by a pharmacist, the data were key-punched onto cards. The cards for each patient's medications were then placed in the proper medication cart drawer. These cards were color-coded by drug type and alphabetical name to simplify cart filling. The technicians filled a 24-hour supply of medication from the information on the cards. The daily charge data were then entered manually on each card for the amount of drug dispensed. After the pharmacist checked the medications in the cart, using the master dose cards, the cards were sent to the data processing center for daily charging. The cards were then returned to pharmacy for subsequent use in the medication system. The system was cumbersome, since the cards were often misplaced and daily maintenance of the patient records involved a substantial amount of paper handling. The cards were not used to generate a patient profile; therefore, monitoring of patient medication records was not possible.

Gilbert et al.[36] described a batch mode order entry procedure on an off-line computer. The pharmacist reduced all drug orders to numeric codes on punched cards. Once each eight hours, the coded orders were batch keypunched. The computer printed a drug distribution log for unit dose cart filling, a cumulative patient profile, and a daily medication charting document for nursing. Automated patient charging and census control were features of the system. The author overcame the lapse between profile printings by sending doses of medications for new orders to cover the interim until the next cart exchange.

On-line Medication Systems. On-line systems allow the operator to interact directly with the computer, allowing immediate access to data stored, thus overcoming the time lapse in information processing which occurs with off-line systems. Thus, on-line systems lend themselves to more flexible programming. For this reason, on-line medication systems have usually involved more sophisticated applications. A number of such systems have been successfully implemented, both as dedicated pharmacy modules and as subsystems of larger hospital information systems.

A series of articles has described the medication distribution system at The Johns Hopkins Hospital. Two gener-

ations of the system, the first of which was implemented in 1970, have been developed using a large computer. Derewicz and Simborg, in two separate communications,[37,38] described the second generation of this system, which used cathode ray tubes with light-pen entry capability. Each decentralized satellite pharmacy had a computer terminal. Medication orders were entered into the CRTs. Drug orders were automatically checked against patient allergies and diagnosis for incompatibility. For each hour that medications were due, the computer generated a single unit dose envelope. Pharmacy technicians placed the medications in the envelopes and these were delivered to the nursing units. The envelopes were used by the nurse to verify drug administration. The computer also generated medication profiles and medication histories. Advantages of the system included reduction of medication errors, reduction of time spent by nurses in medication administration tasks, and reduction of costs associated with drug administration. The second communication in this series was important in that it was the first description of a computerized unit dose system to appear in a publication oriented primarily toward physicians.

Later articles in this series examined comparative costs and occurrence of drug errors in the automated system versus traditional manual methods, using well-controlled studies. Arrington et al[39] compared the cost for a computer-supported unit dose system for both adult and pediatric medicine. They found that the cost per dose for pediatric medicine was less than that for adult medicine. Means et al.[40] examined medication errors occurring in a traditional multi-dose and the computer-supported unit dose system. There were significantly fewer errors in the unit dose system. In the multi-dose system, 7.35% of all doses administered were in error, while only 1.61% error occurred in the unit dose system. Only one error was attributed to the computer itself, with the remainder attributed to human error. The computer per se did not contribute to the reduced error rate in the unit dose system; rather, its benefit came from the support provided in maintaining the system.

To eliminate deficiencies found in a traditional medication delivery system, Shapin and Title[41] developed a simple on-line application for drug distribution in a multi-dose dispensing system. A pharmacist entered orders via a CRT from a copy of the physician's order. Once the order had been verified, a "piggyback" two-part label was printed and attached to the medication container, and the drug was delivered to the nursing unit. When the nurse used the last dose of the medication, she attached the top label from the container to a reorder form and sent this to the pharmacy. Reorder information was entered into the CRT and another label was printed. In an impact study, the authors found that the system reduced excessive reordering and increased credit returns. The system also featured automated billing.

Simon et al.[42] used a minicomputer to develop a drug distribution system with administrative applications. At the time the article was published, the system had been partially implemented in a large hospital. All drug orders were entered by a pharmacist via a CRT. Pharmacy technicians used a CRT display of patient profiles to fill the unit dose carts.

Intravenous fluid orders were entered via CRT and held in computer memory until needed by nursing, at which time an i.v. container label was printed. Worksheets were also generated for planning work activity. Clinical applications included drug–drug interaction screening, antibiotic use review, and patient profiles. Administrative applications included automated patient billing, inventory maintenance, statistical reports, and personnel scheduling. In a second communication describing this system, Simon and Silverman[43] envisioned other applications of automation that were planned for further development of the system into a pharmacy information system. They explained the value to the hospital pharmacist of each application. They emphasized that the usefulness of a pharmacy information system was predicated upon the creation, maintenance, and use of a patient profile.

Jackson et al.[44] used a computerized unit dose system to develop a unique way of solving problems associated with unit dose distribution from a central pharmacy. They implemented a "decentralized pharmacist" concept using a master mobile medication cart for dispensing supplies of medication to the unit dose carts. A computerized hospital information system supported the unit dose system and a comprehensive therapeutic incompatibility screening system. The decentralized pharmacist entered new medication orders into the computer via a cathode ray tube located at the nursing unit. The pharmacist was notified immediately of any potential drug interactions detected by the system, and he reported those to the physician while on the unit. Once the drug orders were entered into the system, medications needed were dispensed from the master medication cart.

Bair and Cheminant[45] also implemented mobile decentralized pharmacy services. In this institution, the computer did not support the unit dose medication system; rather, programs were developed to collect data on the impact of the medication delivery system. Data were collected regarding the number of doses handled and revenue generated for a pre-study control period and for three different post-implementation study periods of equal length. The computer was also used to record and analyze all phone calls to the central pharmacy before and after decentralization. Gathered statistics showed that fewer doses were handled for all patient care areas and fewer phone calls were made to the central pharmacy after implementation of the decentralized concept. The study showed that the decentralized pharmacist concept was more efficient than the previous centralized system by reducing the number of doses handled, reducing the number of telephone calls, and improving charge accountability.

A medication system developed within a hospital information system (HIS) may offer advantages over a dedicated computer. Although hospital information systems may assume many different configurations, all are essentially automated networks that link hospital service departments to a central on-line computer. Each department collects information concerning its component of patient care and transmits it to the computer. The stored data are available

on demand to all service departments. Although this service is costly and difficult to implement, it offers advantages over stand-alone pharmacy systems, including access to admitting and census control information, as well as laboratory and patient care data. Gousse[46] described such a system in a medical center using a commercial hospital information system. Pharmacy orders were entered into the system by a physician or his agent using a cathode ray tube with light-pen and video matrix. In the pharmacy, a copy of the order was printed and stored with the hard-copy patient profile for later use. A container label was also printed, which was placed on an envelope containing initial doses of medications to initiate the order. A medication supply list or cart fill list was printed throughout the day. When filling the carts, the technician was required to calculate the number of doses needed, based upon patient requirements, and to write this information on the fill list for later charging. The fill list and copies of new orders served as a back-up system in case of computer downtime. The author felt that the system offered a number of advantages to pharmacy, including improved receipt of new orders, patient profile maintenance, and access to all information regarding the care of the patient. However, manual calculation of doses needed daily and manual recording of this information were time-consuming tasks which could have been automated. Also, in cases where the nurse input the physician's order, the nurse's interpretation was accepted without further checks by the pharmacist.

Austin[47] described a minicomputer-based system that was developed inhouse. The system supported unit dose and intravenous admixture services. It also performed drug interaction screening, maintained inventory control, automated purchase order generation, and generated various administrative reports. The author briefly described the development of the system, including cost justification and systems requirements.

Willcox and Gibson[48] proposed a system to automate dispensing and recordkeeping in a nuclear pharmacy. The system was designed to interface with a hospital information system and would maintain patient profiles for both inpatients and outpatients. Other programs would permit radioactivity corrections, dosage calculation, inventory control, and labeling. At the time of the article's publication, the system had not been developed.

Nazzaro[49] described a mainframe computer system used in a military hospital, the Tri-Service Medical Information System (TRIMIS). The system was on-line and provided support for both inpatient and outpatient services, including order entry, label production, medication profile, duplicate medication screening, drug interaction screening, and inventory control.

McGovern[50] described a system used in a 600-bed hospital that reduced the time required to fill medication carts in a unit dose system. Patient profiles were generated once daily, and these were used by pharmacy technicians to fill patient medication trays using an "assembly line" approach. Medication storage trays were set up in such a manner that each pharmacy technician filled bins with drugs stored only in a

section. The patient bin and computer-generated profile were then passed along the line to other technicians for completion. PRN medications were dispensed in a unique fashion, in that only one dose of each PRN was dispensed at a time. At the time of use, the nurse entered charting information into a CRT to document the administration of the PRN dose in the patient's automated medical record. This action generated the printing of a label in pharmacy; it was used to dispense a replacement PRN.

Some authors have studied the costs associated with a computerized unit dose system. Schnell et al.[51] performed a cost analysis of a system in a 550-bed hospital. Objectives of the study were to determine the cost per unit dose of preparing and administering a unit dose of medication and the cost per patient day. It was found that the cost per dose was inversely proportional to the number of doses administered per patient day. Beck et al.[52] implemented a computerized system in a psychiatric hospital. After almost two years in operation, the most dramatic impact of the system was the reduction in average drug cost per patient. It decreased from $23 to $14.50 per day, and the number of prescriptions per patient decreased from six to three. The authors suggested that these reductions demonstrated that the system had contributed to a more rational approach to drug therapy with less risk for drug interactions.

Finally, Walters et al.[53] studied the justification of a system to reduce medication errors. They used a computerized unit dose system and patient profiles in conjunction with primary care nursing to reduce medication errors. With the computerized unit dose system, drug errors were easier to identify and audit trails were more easily followed to determine the cause of the error. The authors found that the computerized unit dose system was an adjunct to identifying and preventing medication errors.

Intravenous Admixture Services. Automation of intravenous admixture services has ranged from systems that maintained patient profiles, generated i.v. container labels, and generated patient billing to more sophisticated systems that performed these tasks in addition to calculations of the amounts of drugs to be added to complex solutions, such as total parenteral nutrition (TPN) solutions. A number of the systems previously described under drug distribution systems had also automated intravenous admixture services.[37,38,42,46,47] Other authors have described dedicated systems for intravenous admixture services.

Hauss et al.[54] described the use of a commercial intravenous admixture system which used a microprocessor computer. This system was dedicated to support of the i.v. admixture service, and featured on-line data storage. All orders were entered into a cathode ray tube using a system of mneumonic codes. The patient data base contained the patient's height and weight as well as drug allergies. The system maintained patient profiles and generated i.v. container labels. Labels for i.v. fluids having a scheduled hour of administration were printed for a preselected time interval, the time limits being selected by the operator. It allowed printing of labels by either drug group or by nursing station. The system also generated a "shopping list" which

summarized all fluids and drugs required for compounding the admixtures for which labels had been printed. A nursing station profile of all admixtures for patients on a unit was printed. One copy of this profile was used by nursing personnel to update information needed by pharmacy concerning changes in fluid flow rates, discontinued orders, etc. This profile served as a communications document between nursing and pharmacy. Automated patient billing records and statistical data were also generated by the system, which also monitored drug incompatibilities and allergies.

Lausier[55] described an intravenous admixture service that was a component of a hospital information system. All orders for intravenous fluids and additives were input via a CRT by the physician or his agent; e.g., a nurse. The order was printed in pharmacy and a copy of the order was affixed to a manually maintained patient profile. The system also printed a container label for the fluid. The author felt that the system had improved the quality of intravenous admixture services in the hospital, although the system did not perform totally automated label generation, did not eliminate the need for a manually maintained patient profile, and did not perform screening for drug interactions or drug incompatibilities. Gousse[46] described the automated medication delivery component of this system in the same hospital. The same shortcomings that have been mentioned previously in regard to the medication system also existed with the intravenous admixture service.

A number of articles have described the use of the computer in calculating complex formulas for TPNs. Bellis et al.[56] developed a system that predicted the patient's need for TPN based upon analysis of the patient's fluid losses and serum biochemistry. The data base included the types of TPN fluids available. Based upon the patient's needs, the computer selected the preparations and additives that would meet those needs. The pharmacist reviewed the computer recommendations, particularly when additives were to be included. He then determined the method of admixture of additives and the computer-generated information was presented to the physician in a format that was easily transcribed to a written order. Moan and Buth[57] described the use of a microprocessor to calculate formulations of total parenteral nutrition in a military hospital. The physician indicated the grams of protein, calories, electrolytes, and intravenous fat desired per day. The pharmacist entered these specifications into the computer and the proper quantities of each ingredient needed to prepare daily therapy were calculated. The computer eliminated many time-consuming calculations, while insuring accuracy. Schallock[58] described a TPN program that performed a nutritional assessment of the patient, then calculated the quantities of additives needed to supply the patient's requirements. The system also generated container labels and made automated charges. Warden[59] modified a financial system to handle calculations for preparing TPN formulas for newborns. The physician specified the protein equivalent, dextrose, electrolytes, fluid volume, and other additives desired. Pharmacists input these data, plus the patient's weight, via a cathode ray tube. The system calculated the amounts of each component for the fluid, and printed a flow chart for the preparation of the fluid. A container label was also printed. The author stated that the system saved approximately 900 man-hours per year over the prior manual system of calculation.

Jackson et al.[60] described the experimental use of a microprocessor programmed to monitor the blood pressure of a patient with malignant hypertension, to achieve a constant therapeutic flow rate of sodium nitroprusside. The microprocessor was preprogrammed to a desirable systolic blood pressure and it regulated intravenous administration of the drug to maintain this pressure. The desired pressure was maintained for six days by the micropressor until the patient was converted to oral medication.

Ambulatory Services. Before 1975, only a few authors had described automated systems for ambulatory pharmacy practice. Since that time, a number of authors have described such systems, and the future should see more applications in this area as interest in ambulatory care and preventive medicine increases.

Automation can improve ambulatory health care in the hospital outpatient clinic. In the traditional dispensing system, the patient presents a prescription to the pharmacist, who dispenses medication to the patient with directions for administration. Usually the pharmacist has no knowledge of the patient's diagnosis, allergies, or other drugs being taken concurrently. This situation can create a treatment dilemma, since the patient may be allergic to the drug, may already be taking a similar drug ordered by another physician, or may experience a drug interaction. Automation of patient records, profiles, and prescription data is the most expedient manner to improve this situation.

EDP has not been fully used in ambulatory patient care. A survey of university hospitals done in 1978[61] revealed that in hospitals with outpatient departments, only 28% used computerization of any type. These applications were primarily restricted to accounting and inventory control.

Braunstein and James[62] developed an on-line system for an outpatient clinic that was also in use on an experimental basis in several community pharmacies in the area. CRT input of prescription data provided the pharmacist with a dispensing label, automated patient billing, and drug interaction alerts. The computer was also programmed to check for patient noncompliance by determining the date for which a given supply of medication would be exhausted if taken properly. A weekly printout of all such prescriptions that had not been refilled was generated.

Weissman et al.[63] developed a similar system that included more therapeutic checks. The system was designed to support a number of remote clinics on-line by linking them to a central computer via dedicated phone lines. The computer stored patient profile data on all active patients. Technicians entered prescription data via a CRT. The computer performed various programmed checks on a prescription, and alerted the pharmacist of potential drug interactions, drug-laboratory test interferences, drug allergies, or drug-disease state contraindications. The system also provided drug use statistics.

Wilkerson and Libby[64] implemented an ambulatory pharmacy system, based upon a minicomputer, in a military hospital. The pharmacist entered prescription orders into a cathode ray tube and the system updated the patient's profile, printed a prescription label, and maintained inventory records. It also screened for potential drug interactions. Three separate search files were also created, as to patient, prescriber, and drug. Irgens et al.[65] developed a similar system in a university hospital outpatient pharmacy, using two minicomputers connected in series. The system maintained patient profiles, printed prescription labels, checked for drug interactions, and maintained updated inventory control information. It also printed a clinic formulary. The authors discussed the design of the system and the logic used in developing the various files for the data base.

The inpatient support offered to a military hospital by the Tri-Service Medical Information System (TRIMIS) has been described.[49] In the same article, Nazzaro detailed the support offered by the system to the ambulatory pharmacy in the same hospital. The system provided order entry, label production, medication profiles, duplicate medication screening, drug interaction screening, and inventory control. A unique feature of the system was an interface to automated drug storage cells. As a result of order entry for one of the drugs stored in these cells, the system automatically counted the proper quantity of medication to be dispensed. This resulted in a time savings in the dispensing process. In a second communication,[66] the author described how the system enabled four pharmacists to supervise dispensing for 200 inpatient beds plus approximately 1100 outpatient prescriptions daily.

Johnson[67] used a computer-supported ambulatory pharmacy system to determine the impact of a drug profile upon the prescription writing habits of physicians in a health maintenance organization (HMO). A monthly computer-generated profile for each patient was presented to the prescribing physician. Drug order notations made by the physician in each outpatient chart were reviewed to determine if the computer profile influenced physicians to record more complete and accurate data. The author determined that the profile had no influence on the thoroughness of recorded chart information.

Drug Information

Because of the vast amount of information available on drugs and disease states, and the need to readily retrieve this information, computerization of this area of pharmacy practice seems logical. The ASHP Statement on the Hospital Pharmacist and Drug Information Services[68] states that the hospital pharmacist be ". . . familiar with electronic data processing methodology to the extent necessary for him to utilize its services for information storage, processing, and retrieval." A number of practitioners have developed various approaches to automated information services. However, development of this segment of computerized pharmacy systems has lagged behind other areas. Perhaps this has been due to the overwhelming task of assembling data, main-

taining data, and the high cost of sophisticated hardware to store vast amounts of information for ready retrieval.

An early application of EDP to drug information, and one that perhaps many pharmacists use, is the preparation of a hospital formulary. A hospital formulary may be defined as a continually revised compilation of pharmaceuticals which reflects the current clinical judgment of the medical staff. Manual production of a formulary has been a time-consuming task of selecting, arranging, printing, and reviewing a long list of drugs. After the initial printing, there remains the task of revising these lists to keep the formulary up-to-date. The maintenance of the formulary can be greatly simplified by using electronic data processing techniques. Although the preparation of an initial format is still time-consuming, revision is greatly simplified using EDP. Before 1975, numerous articles explained the methods used to generate an automated formulary. Since that time, little work has been done in this area. Hooper[69] described a system for producing formularies for a nationwide network of government hospitals, in which a central data processing unit printed all the formularies. Each hospital used a standardized form to send data to the central unit for initial preparation and revision. This was keypunched, printed, and an individualized formulary returned to each hospital. Kittel et al.[70] developed a computerized formulary for use in a number of Veterans Administration hospitals. The data base was designed to be flexible, to allow it to be used for future, unrelated applications. Each drug record consisted of 15 fields of data to describe the drug. All records were input and stored on magnetic tape. The formulary was printed by both alphabetical listings and therapeutic categories. The programs for printing and maintenance were designed to allow flexibility in the maintenance of the data base and the printed copy of the formulary. Additions and deletions to the printed copy could be done without the need to print the entire document. Other hospitals in the region accessed the data base via telephone connection to the computer.

The application of EDP to drug information services usually involves searching for and retrieving bibliographical citations regarding specific topics. These searches can be based on existing data bases, of which there are a number in existence. Some authors have described the development of such data bases for bibliographical search and retrieval. Caldwell[71] examined the development of MEDLARS, the off-line literature storage system of the National Library of Medicine. Ball and Wolfe[72] described the development and maintenance of a commercially available drug information data base, Excerpta Medica.[b] They described the guidelines used to determine the inclusion of an article in the data base, the storage of data, and methods of indexing for retrieval. Schneider[73] reported on the International Cancer Research Data Bank (ICRDB) and its use to dessiminate selected information to cancer researchers. The system was used to develop files for a bibliographical citation system, CANCERLINE. Simon and Kovacs[74] described the development and use of HISTOX, a historical toxicology information data system developed for the National Cancer Institute. O'Brien[75] examined the growth of on-line bibliographic

systems inservices, the current impact of the various data bases on medical library services, and the future of on-line search systems.

The Iowa Drug Information Service (IDIS)[c] is a computer-generated microfiche retrieval system of published articles. Milne[76] compared searching IDIS manually with the use of a computerized bibliographic search system (MEDLINE), to provide information and response to specific information requests received by a drug information center. Ease of use, availability of references retrieved, cost, and time involved were evaluated for both systems. Both methods had strong and weak ponts. MEDLINE was more rapid in recall of data. However, only a citation to an article was given; IDIS provided the complete article to the user. MEDLINE had other drawbacks, such as availability of references and initial access to the system. Seaba[77] reported, in 1975, that IDIS indexes were at that time available on magnetic tape for computer searching. Cornell et al.[78] used the magnetic tape to compare searching the IDIS index both manually and by computer. Identical headings were searched in the IDIS index both manually and by computer. The searches were timed and the costs were analyzed. Both methods yielded a similar number of relevant references. The computer system was more expensive for start-up and maintenance costs, but less expensive for operational costs. The authors calculated the break-even point at 980 uses per year, at which level the computer system was projected to be less expensive than manual searches.

Sloggem[79] compared the commercially available manual and automated reference sources and bibliographical indexing systems. Madden and McDonald[80] compared a number of these manual and computerized drug information retrieval services for accuracy, ease of use, and thoroughness of search.

In a survey of 42 drug information centers, Ruger[81] examined the use of automated retrieval systems in providing drug information. Twenty-six of the centers reporting had access to automated data retrieval through computerized bibliographical data bases. MEDLINE was the most frequently mentioned source available, with TOXLINE and CANCERLINE second and third, respectively.

Schneiweiss[82] subscribed to a commercial bibliographical service that offered access to various computerized bibliographical data bases. The system was used in a university-based drug information center and was connected to the central computer through a remote terminal. Although 20 data bases were available, 99% of all requests were answered by searching MEDLINE only. To facilitate input of the search variables by pharmacists using the terminals, the author developed a comprehensive request form to be used by requesters to define the question and to establish indexing terms. A copy of the form was presented. Sasich and Morris[83] described a computerized drug information retrieval system developed inhouse to solve problems associated with manual retrieval of drug information sources from five separate files. The system, the Drug Information Retrieval Terminal System (DIRTS), was a key-word indexing system that permitted indexing of information by one or

more of four general source categories. Data base input included one of the four general categories to describe the type of literature, then one or more key words to describe the information. The user entered drug name, disease state or other key word, or a combination of these. Printed output listed the location of the hard-copy information in the files, and other information to facilitate retrieval. Key word selection was not rigidly structured according to a standard index, thus the system was considered self-indexing. Key words were edited to maintain uniformity. Fischer[84] developed a computerized system to index questions received by a drug information center. The system used a data base management system and a computer language to interface input and output information about each question. A monthly summary of questions received was generated.

Two reports have described prototypes for automated drug information systems that would provide both the literature citation and a copy of the article. Berkowitz and Chang[85] described a preliminary plan for developing a centralized integrated data storage system in Canada, which would be funded by the government, pharmaceutical manufacturers, and users. This system was not developed at that time. Padfield et al.[86] developed a prototype drug information storage and retrieval system. The system was designed to economically store an essentially unlimited amount of information. The data base consisted of evaluated reports, rather than citations; thus, the user had access to complete abstracts. The system stored data at different levels of retrievability, allowing the user to access brief summaries as well as the complete abstract. The system was not operational, but was planned to be accessible from remote terminals when implemented.

Another aspect of drug information is the provision of poison control information. A number of data bases exist that may be used for searching specific information regarding toxicological data. Lorent[87] evaluated a number of automated biblioigraphic data bases as to ability to provide rapid access, up-to-date toxicology information on drugs and chemicals. Vasta[88] described the use of the National Library of Medicine's TOXLINE and CHEMLINE for retrieval of toxicological data. Lawrence et al.[89] described the integrated data base used by the National Center for Toxicology Research for storage and retrieval of research data.

A number of authors have described the use of automated drug information retrieval in the provision of toxicological information and treatment. Schaap[90] evaluated six different automated literature retrieval systems for a poison control center, to determine the one system to be used to provide updated toxicology data. The advantages and disadvantages of each system were described. The National Clearinghouse for Poison Control Centers has placed computerized, remote terminals at its regional centers to supplement its manual reference system. Armstrong[91] described the advantages of using the on-line search capability in the provision of poison control information through these remote terminals. A number of features were available to the on-line user that were not available to the user of the manual reference system. POISINDEX[d] is a commercially available microfiche

poison information system. Rumack[92] described the use of an off-line computer and computerized file to generate the microfiche for POISINDEX. The automated system maintained updated files and the microfiche service. To simplify the retrieval of toxicological data, Johnson et al.[93] developed a generalized retrieval programming language, called the Query Language Processor (QLP). The program eliminated the need to write specialized programs for specific information requests.

As described by Knight and Conrad,[1] perhaps the ultimate development of computerized drug information would be a machine readable data base containing all diagnostic, pathologic, pharmacologic, and pharmaceutical information so that the information would be available to anyone at any time. Thus far, this has not been accomplished because of the overwhelming costs and task of data base development. Rucker[94] proposed such a national system of health care information, including patient medical profiles and histories. The system was conceptualized to aid physicians and pharmacists in prescribing and dispensing medications, and also ensure patient compliance, monitor for therapeutic incompatibilities, accumulate drug use data, and reduce the overall costs of drug therapy by increasing appropriate use. He estimated the annual costs of such a system to be $600 million, much of which would be offset by the projected savings in drug therapy. However, Lee[95] challenged Rucker's cost estimates in both the projected cost of the system and the savings to be realized. He felt that such a system would not pay for itself. Neither author examined the potential inpact of such a system on privacy of information.

Clinical Services Applications

The provision of clinical pharmaceutical services can be facilitated by the use of the computer, due in part to the vast amount of information to be stored, correlated, and retrieved when providing clinical services. A number of these areas have been developed and described in the literature. They include drug use review statistics, therapeutic incompatibility screening, and pharmacokinetic dosing.

Drug Use Review. The use of the computer in drug use review aids in collection of data, correlation of statistics, and retrieval of information. Crootof et al.[96] developed a drug use review program for a health maintenance organization. Data entry consisted of the drug prescribed and prescription directions. The pharmacist coded the drug dispensed and prescription directions on a special form. At the end of each day, the forms were batched, keypunched, and fed into an off-line computer. The computer produced reports that were used for drug use review, adverse drug reaction detection, and analysis of physician prescribing practices.

Antibiotic prescribing is one major area of drug use review, because of the high cost of these drugs and the potential for inappropriate use. Pelissier[97] modified an existing off-line patient billing and accounting system to summarize drug use of 18 major antibiotics. As a byproduct of patient charges, the computer accumulated statistical data of monthly use of enteral and parenteral forms of each antibiotic. A monthly printout presented the use of each class of drugs by number of patients, days of therapy, and total patient charges. Another monthly report presented the same information for a specific class of antibiotic, the penicillins. At the end of each year the data were summarized by the computer and a bar graph summary of the use of each drug was prepared. The use of the two previous years was also shown by comparison on the bar graph. This information was used by the various committees in the hospital to control antibiotic prescribing. Klapp[98] described the approach used by a teaching hospital to develop an automated antibiotic use review system. The hospital did not have an automated pharmacy system; therefore, an off-line system was programmed for the purpose. To permit the development of a flexible system, a commercial data base and programming language was selected. Information regarding the use of antibiotics was manually compiled from patient profiles and entered into the system. Additionally, microbiology sensitivity data were also entered. System output was presented in numerous formats. The pharmacist could select one or more of 22 variables to analyze antibiotic use in the institution. Standard reports were distributed to the various hospital committees periodically. The system's flexibility enabled the pharmacists and programmers to write special programs to collect data for specific problems.

Helling et al.[99] examined the accuracy and efficiency of four different methods for drug use review. Two of the methods were totally manual and two used computer assistance. A random sample of 40 medical records was selected from the records of 470 patients treated for hypertension in two ambulatory clinics. Prescription information regarding treatment of hypertension was collected and transferred to the computer storage. Explicit drug therapy audit criteria defining appropriate use of drugs and treatment of hypertension were developed. Four audit methods were used and evaluated on the basis of accuracy and time-cost efficiency: (1) a complete manual audit using explicit criteria; (2) a computerized prescription screening using explicit criteria; (3) a computer-assisted medical record audit combining Method 2 and modified Method 2 criteria; and (4) a quantitative study of the prescriptions written. The computer-assisted review was the most efficient in terms of time involved but was least accurate in evaluating appropriateness of therapy. The modified manual and automated review was intermediate in both time involved and level of accuracy. The authors concluded that this approach to drug use review was acceptable.

Although drug use review is becoming an accepted practice in providing quality medical care, collection of meaningful data concerning inpatient drug use on a national basis is deficient. Recently, Forbes et al.[100] proposed a national data collection system based on statistical sampling methods and automated storage, correlation, and retrieval of data. The authors developed a set of minimum uniform data elements to provide useful drug use review information. Benefits of such a national system and the role of the hospital pharmacist in the collection of data were enumerated.

Drug Interaction and Therapeutic Incompatibility

Surveillance. Computerization of drug interaction data can assist the pharmacist in screening for drug interactions by monitoring the multiple drug entries to a patient's profile and alerting the pharmacist to a potential drug interaction. This system can also be expanded to screen for potential drug-laboratory test interferences, therapeutic incompatibilities, and drug-disease state contraindications.

Hulse et al.[101] developed a system using the patient's complete medical record to monitor for drug-drug, -laboratory test, -allergy, and -disease state interactions and contraindications. The Health Evaluation through Logical Processing (HELP) system used Boolean logic to enable the computer to make decisions as to whether an interaction message was to be displayed to the pharmacist. For example, if a patient were receiving digitalis therapy and had a low serum potassium level, a warning message would be displayed. If the serum potassium level were normal, no message would be displayed. Warning messages were used by the pharmacist to report potential therapeutic problems to the physician. The authors found that the majority of potential interactions occurred with drug-laboratory test interactions (44.9%), while drug-drug interactions accounted for only 28.9%. They concluded that monitoring for only drug-drug interactions failed to detect many therapeutic problems, and that the incorporation of drug-laboratory test interference monitoring should be a necessary part of any monitoring system.

An on-line system for prospective monitoring of drug interactions was described by Tatro et al.[102,103] The Monitoring and Evaluation of Drug Interactions by a Pharmacy Oriented Reporting (MEDIPHOR) system was a subroutine of a pharmacy dispensing system. The data base was developed from primary references in the medical literature that were evaluated by the authors before inclusion. The data base was updated routinely. Medication orders were entered via a CRT and a computer search for potential interactions was performed. If a potential interaction were detected, an interaction report document was generated. This comprehensive report described the interaction and mechanism, expected results of the interaction, severity, and management recommendations. The reports were used by the pharmacist to notify the physician or were placed on the patient's chart for physician perusal. The system was also designed to retain a discontinued drug in the interactive file until it could no longer participate in an interaction. Production of patient profiles and prescription labels was another feature of this system. In a second communication describing MEDIPHOR,[104] the authors modified the drug interaction program to detect adverse drug reactions. The patient's adverse drug reaction history was obtained by nursing personnel and input by pharmacy personnel. The system screened for adverse drug reactions as a byproduct of physician order entry for drug therapy. Printed reports were generated for any potential adverse drug reactions detected, and the reports were placed on the patient's chart for physician reference. Hood and Miller[105] also developed a screening system for adverse drug reactions by modifying the data base of an existing computer drug interaction

screening system. Cross-referencing of drugs used to treat complications of adverse reactions (e.g., certain antibiotics interacted with antihistamines that might be used to treat the consequences of drug allergy) extended the capability of the system to screen for such therapeutic complications. The author found that 15% of all interactions detected during a three-year study period involved drug-disease state interactions and adverse drug reactions.

A series of papers have described the Pharmacy Automated Drug Interaction Screening (PADIS) system. Greenlaw and Zellers[106] developed a drug interaction screening system which was designed to interface with an existing medication dispensing system. PADIS contained secondary references to over 24,000 drug interactions and was updated monthly. Although the medication system was on-line, the drug interaction screening system was designed to run as a batch program, to which data were entered once daily to screen all patent profiles for interactions. Printouts were generated for any potential interaction detected, and these were used by the pharmacist or physician. The authors enumerated the reasons they chose to run the interaction system in a batch mode, rather than on-line. In an evaluation of the system, a number of physicians participated in a study of the impact of the drug interaction's screening system[107]; 1219 drug interactions were detected. On evaluation of these, only 116 (9.5%) were deemed clinically significant. Of these, 59 (51%) were resolved by pharmacists rescheduling the administration of the drugs. Of the remaining interactions, reports were placed on the chart for review by the physician. Physicians responded positively to 82% of the recommendations by altering drug therapy. A subsequent article[108] evaluated the cost of the PADIS screening system. Data were collected during the development of the screening system and later during a one-year study period of operation. Costs were analyzed by various methods, including potentially significant drug interactions detected and monitored, and clinically significant drug interactions prevented. Total annual cost of the program was $5603. Salaries accounted for 63% of the total, computer time costs for 17%, annual leasing of the data base 16%, and paper supplies 4%. The cost for each drug interaction detected was 51¢. The cost of the system per patient day was 42¢. During the study, 341 clinically significant interactions were prevented at a cost of $16.43 each. The author felt that the system was an inexpensive means of detecting and preventing drug interactions.

Kong[109] has described a commercially available dedicated microprocessor program for screening drug interactions. In a brief communication he described the use of the system, which automated patient profiles specifically for the purpose of drug interaction monitoring. A listing of potential interactions was printed for each patient, along with a reference number to a drug interactions manual which accompanied the system. Interaction information was provided to the physician by the pharmacist either orally or in writing. The system limitation was that it required the pharmacist to enter all drug orders into the computer solely for the interaction screening. The system did not support other phar-

macy applications. The reports produced did not contain clinical information.

A number of authors have studied the occurrence of drug interactions to determine the significance of a screening system. Ford et al.[110] used a screening system for a trial period, during which all inpatients were screened for potential interactions, of which 140 were found in 77 patients during the study. Seven of these were considered clinically significant. The authors found that either warfarin or digitalis was one of the offending drugs in six of the seven clinically significant interactions. Armstrong et al.[111] performed a similar study in a nursing home. During the study period the authors found that the majority of the interactions could be handled with close patient monitoring, although in 9.1% of the cases, discontinuation of one of the drugs would have been appropriate, and in 4.7%, reduction in dosage would have been appropriate.

Kwan et al.[112] performed a retrospective study to determine the incidence of potential drug interactions, their clinical significance, and the influence of these upon length of stay in the hospital. Data were collected on 5200 patients as a byproduct of computerized medication profiles. Most interactions detected were not clinically significant. Many were anticipated and adjustments in dosage or administration times were made to minimize the effect. However, 10% of those detected, affecting 1% of the hospital population, were clinically significant. The authors projected a yearly cost of $29,250 to result from these interactions due to increased patient stay and subsequent therapy. They concluded that a clinical pharmacy service supported by computer could be justified on the basis of cost savings to conduct drug interaction screening.

Clinical Pharmacokinetic Services. The use of computers to calculate and project drug dosages has increased since 1975. Slattery and Levy[113] used a previously reported computer model for predicting acetaminophen elimination. The program compared the plasma concentrations over time with actual concentrations reported in a patient who ingested between 24 and 30 g of acetaminophen, along with large amounts of other central nervous system depressants. The computer prediction compared favorably with actual plasma levels in the time period of 18 to 34 hours, during which plasma concentrations declined by about 85%. Afterward the plasma concentrations declined more slowly than those predicted by the computer, consistent with evidence of hepatic damage in the patient. Hepler and Prince[114] developed a prototype computer program to calculate doses and dosage intervals for drugs exhibiting nonlinear elimination kinetics; i.e., drugs that do not follow first-order elimination patterns due to tissue saturation or slow absorption and elimination. The authors developed a mathematical model and resulting computer program using an iterative digital-analog simulator (IDAS) program. The program consisted of two sections—a simulation model that calculated minimum and maximum serum levels based on a dose and dosage frequency, and an iteration control module, that used these values to project a new dose and dosing interval. The model was tested by comparing simulation results with actual patient data for two drugs that exhibit nonlinear elimination kinetics, phenytoin and theophylline. The predicted doses and intervals were not statistically different from the actual patient values. The authors concluded that the programs were valid and encouraged other investigators to examine this method for pharmacokinetic dosing of drugs showing nonlinear elimination kinetics.

Rich et al.[115] evaluated the effect of a computerized digoxin pharmacokinetic consultation service on patient response. A pharmacy-based digoxin pharmacokinetic service was implemented to determine the influence on patient digoxin dosing. Changes in dosages and serum levels were evaluated during a three-week control period and a three-week study period. Patients receiving the consultation service had significantly greater numbers of dosage changes resulting in therapeutic serum levels as compared with the control group whose physicians relied only on serum levels for dosage adjustment. The number of patients with steady state levels in the therapeutic range of 1–2 ng/ml increased from 45.5% to 80% as a result of the service.

Bootman et al.[116] analyzed the cost per analysis for a computer-assisted aminoglycoside pharmacokinetic dosing service in a 450-bed hospital. The system predicted dosage regimens, based upon patient data input. Pharmacists recommended dosage schedules and regimens to physicians based upon the computer output. The fixed and operating costs of the system were calculated. It was found that the estimated cost of each analysis, based upon 4305 samples per year, was $17.35 per sample.

Other Clinical Applications. Gilroy et al.[117] integrated pharmacy data input and retrieval into a computerized problem-oriented medical information system (PROMIS). The system was implemented on a 20-bed nursing unit as a demonstration project. Entry of all information to the patient's chart was done by the originator of the data; e.g., physician, nurse, laboratory technician. The system was on-line, using touch-screen cathode ray tubes to display information and permit data input. All information in the patient's medical record was stored by the computer and was readily retrieved by any member of the health care team. In addition, medical information concerning drug therapy and medical treatment of diseases was stored as "frames" (CRT screen displays) of data and were readily retrieved for display as reference. The availability of information contained in a patient's record was used to improve pharmacy practice. With the physician directly inputting the drug order, transcription of the order was eliminated. Upon entry of an order by the physician, the computer generated a drug container label, added the order to a nursing medication charting document, and placed the order on a pharmacy drug audit list. The pharmacy drug audit list was used by the pharmacist to perform drug use review and therapeutic contraindication screening. Audits were done on a priority basis by use of an algorithm that predetermined potential problems based upon the drug prescribed for the patient's medical history or diagnosis. To perform an audit, the pharmacist accessed the patient's medical record via the CRT, and visually determined any actual or potential therapeutic prob-

lems, contraindications, allergies, or drug interactions. If problems were detected, the pharmacist corrected the problem by contacting the physician or rescheduling administration of the drug. After the audit was performed, the pharmacist documented his evaluations in the system by either acknowledging that the audit was acceptable or, if unacceptable, noted the actions that were taken to correct the problem. The PROMIS system did not make full use of the computer's ability to automatically check for therapeutic problems and contraindications, although the authors acknowledged that the potential to automate these checks did exist in the system.

In addition to antibiotic review, as previously described, other programs have been developed for antibiotic prescribing to aid the physician in selecting the appropriate drug or to aid the hospital in monitoring the use of antibiotics. The Bac-Data Medical Information System[e] is a commercial subscriber service that collects data from hospital subscribers on bacterial incidence within each institution. In one hospital user of the system,[118] laboratory bacteriology culture information was keypunched daily. The pharmacy received a monthly printout detailing incidence patterns and antibiotic sensitivities in the hospital. The report also compared the hospital's statistics with other hospitals using the system on a national basis. Goode and Greenhalgh[119] described a system for gathering data concerning the incidence of infection in a 650-bed community hospital. The system reported antibiotic sensitivities, incidence of infection, types of organisms, and also performed special investigation reports.

Wraith et al.[120] developed a prototype computer-based consultation system, called MYCIN, to assist physicians in selecting antimicrobial therapy. The data base was developed from information provided by experts in infectious diseases. Patient data were input by physicians using a CRT through a series of questions and answers. Based upon the patient data and information in the data base, the computer made diagnostic decisions as to the probable causative organism(s). The diagnostic decision included a probability factor that clarified the conclusion. At any point in the program the physician could question the computer's logic for arriving at a conclusion and the computer displayed data base information used in its reasoning, thus making the program a teaching tool. The computer also suggested appropriate antimicrobial therapy and dosage for those patients with normal renal function. At the time of publication, programs were being added to permit calculation of dosage in those patients with compromised renal function. Yu[121] later compared the decisions made by MYCIN with those of physicians in selecting therapy to treat meningitis before the causative organism had been identified. In selecting the appropriate therapy, MYCIN considered organism sensitivity, synergistic drug combinations, and patient drug allergies. Eight evaluators with expertise and management of meningitis compared MYCIN's selection with choices of nine physicians for 10 test cases of meningitis. MYCIN received an acceptable rating of 65%, compared with a 62.5% acceptability rating for the prescribing physicians' selections.

The system prescribed treatment for all treatable organisms, while selecting the minimum number of antimicrobial agents to be prescribed.

Bennett and Scott[122] developed a computer-based consultation program designed to individualize antimicrobial therapy for patients with meningitis or bacteremia. The user input information regarding infection site, antibiotic sensitivity of the organism, and the patient's clinical status and drug history. The program selected appropriate regimens and dosages. It also printed a graph depicting expected blood levels of each drug over time. Both the minimum inhibitory concentration (MIC) and the toxic level of the drug selected were shown. Dosage adjustments for drugs excreted by the kidneys were made by the program in presence of renal impairment.

Pharmacy-Related Applications

Several clinical applications that have a direct impact on pharmacy practice have been developed by individuals other than pharmacists. These systems, usually developed by physicians or other health professionals, have included drug use studies, poison control information, and dosage regimen calculations.

Drug Dosage Calculations. Mawer[123] presented the principles of developing computer programs for drug dosage adjustments. He described three different types of programs—fixed, adaptive, and empirical. The fixed program was based upon a fixed kinetic model, usually a simple one-compartment model. The adaptive method was similar to the fixed except it modified the model based on individual patient drug serum concentrations. The empirical model used variables derived from observed requirements of individual patients to predict dosage requirements.

The aminoglycoside antibiotics have been studied extensively in regard to dosage adjustments and presence of kidney impairment. Hull and Sarubbi[124] developed a computer program for prediction of serum levels of gentamicin, given either intravenously or intramuscularly to patients with unstable renal function. Predicted serum levels were calculated using lean body weight. Serum levels of gentamicin were compared with predicted levels, and a statistically significant relationship was shown. The authors determined from their study that lean body weight, rather than total body weight, was a more accurate reflection of volume of distribution. The authors developed a dosing nomogram for gentamicin, based on lean body weight. These authors also studied amikacin pharmacokinetics using computer programs.[125] A group of 26 patients received intramuscular or intravenous amikacin in a fixed dosage and frequency of administration to determine if a digital computer program could accurately predict serum concentrations. The program accurately predicted serum levels. From their research, the authors presented a new dosing chart for amikacin, based upon the pharmacokinetics generated by the computer. Ritschel et al.[126] also tested the accuracy of a computer program to predict serum levels of kanamycin in patients with renal impairment. Kanamycin was given intramuscu-

larly to eight patients with varying degrees of renal impairment in a series of doses at a standard frequency. The computer calculated the dosage for each patient. The expected multiple dose serum levels were simulated using an analog computer. Blood samples were drawn and serum levels were determined. There were no significant differences between the actual serum levels at steady state and those predicted by computer. Colburn et al.[127] developed a computerized program using a one-compartment pharmacokinetic model to monitor serum levels in six patients requiring gentamicin therapy. Three of the six developed nephrotoxicity during therapy, while the other three had no evidence of toxicity. The computer accurately predicted the prenephrotic state on the basis of decreasing elimination rate of gentamicin.

Greenblatt et al.[128] used an analog computer to plot the time course of lidocaine plasma concentrations. The study was designed to determine the ideal initial dose of lidocaine to be given intravenously to initiate therapy. Programs were written using pharmacokinetic formulas for lidocaine absorption and elimination. The authors determined an ideal dose for most patients, but they emphasized that the use of clinical judgment must also be used along with computer predictions.

Scheiner et al.[129] compared the accuracy of a computer dosage program against physician predicted serum levels in a prospective, randomized study of 51 patients receiving digoxin therapy. The results of the study showed that the computer predicted serum levels as accurately as the physicians, and was more accurate when two or more digoxin serum levels values were available for evaluation. Gorry et al.[130] developed a prototype computer program for digoxin that first constructed a patient-specific model to determine initial dosage calculations and recommendations. Patient response and variables were then entered into the system as available, and the computer used pharmacokinetic calculations to adjust dosage recommendations based upon these data. A clinical trial proved the utility of the system in predicting digoxin dosage for acutely ill patients.

Ambulatory Clinic Prescribing. Two articles have described the use of computerized systems developed by physicians to aid in prescribing for ambulatory patients. Bradshaw-Smith[131] described a computerized on-line patient record system for an ambulatory care setting. Each physician had access to a cathode ray tube connected to a central computer. Display of a patient's record showed allergies, summary history, current medications, and current symptoms or complaint. The system was designed to function both as a traditional diagnostic model or as a problem-oriented model. The physician entered all orders and comments into the computerized record. The system printed out summary records and refill prescription orders. It also provided the physician with a microfiche copy of the record.

McDonald[132] described a pilot study in which a computer generated suggestions to physicians concerning management of clinical events occurring in patients. The system was developed for an ambulatory clinic, and a computerized medical record was used to collect, store, and retrieve medical data. A set of clinical management protocols for various clinical events was established. Most of the protocols dealt with the management of drug-induced problems. Other protocols dealt with the management of laboratory test results or patient symptomatology. Based on information from the patient's medical record and the protocols, the computer generated treatment suggestions to the physicians. In a cross-over pilot study of the system involving nine physicians, the author found that the physicians responded favorably to twice as many clinical events when the computer reminded them, as occurred in a control study where computer reminders were not available. The author concluded that the positive response to computer-assisted treatment indicated a deficit on the part of the physician to mentally process all the information available to him, rather than a lack of medical knowledge on his part. He concluded that computer-assisted management suggestions could augment quality of care provided by the physician.

Other Applications

Other applications that have an indirect impact on pharmacy practice have been described. A computerized drug information retrieval system for articles describing the use of lithium in the treatment of psychiatric disorders has been described.[133] This system, called the Lithium Librarian, contained over 4000 articles from the world literature describing the use of lithium. Before development of this system, searches of various data bases were required to obtain a complete bibliography. The system consolidated all references to one file. The system was designed to permit ease of use and access to information, and could be searched by remote connection through terminals and telephone connection. Searches were available according to author, title, journal, or subject. Boolean logic in the system permitted simultaneous searches by any one of a number of descriptors. The system was also designed to incorporate other similar indexes.

Horwitz et al.[134] presented a pilot study undertaken to determine the applicability of a computerized gas chromatograph/mass spectrometer to analyze body fluids of poisoned patients for chemical identification of possible ingested drugs. During a nine-month trial period, fluid samples from approximately 1000 victims from area emergency rooms were analyzed. At least one toxic substance was identified by the system in 57% of the patients, and 19% had two or more chemicals present. The authors concluded that the availability of such a system could provide hospital emergency rooms and physicians with rapid information to be used in the treatment of poisoned patients.

Two articles have described the development of a data base for monitoring modifications of clinical laboratory tests caused by drugs.[135,136] The system, Computerized Listing of Abnormal and Unusual Drug Effects (CLAUDE), contained 17,500 abnormal effects on laboratory tests, both in vivo and in vitro, caused by 1500 different drugs. The system was designed to aid physicians and clinical laboratories in correctly interpreting laboratory tests in the presence of certain drugs that might cause aberrations. The files were

used to publish a hard-copy manual of these interactions.

Rickels[137] used computer-analyzed data to evaluate four double-blind clinical trials of amitriptyline/perphenazine and doxepin in the treatment of depressed and mixed depressed patients. Clinical improvement and side effects were input to the computer system. Data showed that a fixed dose of amitriptyline/perphenazine was slightly more effective than doxepin, but this combination also produced more side effects.

To solve the problem of identifying unknown drugs in a hospital setting, Ritchie et al.[138] developed a system of using punched cards to catalog the physical characteristics of drugs to permit identification of an unknown oral solid. Each card in the system represented a physical feature of the tablet, pill, or capsule. Numbered portions on the card featured the items to be indexed, such as size, shape, and color. Each drug had a unique identification number and was represented by the same one of 2500 different portions on the card. To identify a drug, cards representing all physical characteristics of it were selected and stacked together. A light source shown through the cards passed through the holes of all cards corresponding to the drug in question. The drug was identified from the coded card.

Finally, the use of the computer in collecting data from large-scale, clinical drug trials has been described.[139] A computerized system was used to collect and analyze laboratory data in patients in clinical drug studies at different institutions. The data were entered into the system and a screening was done by the system to identify potentially clinically significant laboratory abnormalities. A physician then examined a patient record to determine if the abnormal result was probable drug-induced. The system collected cumulative data on these abnormal results to provide statistical analysis of the potential laboratory abnormalities in various clinical trials.

Conclusion

From the many articles that have been published describing varied applications of automation of pharmacy practice, it can be seen that electronic data processing has become a valuable tool for the pharmacist. The past 20 years have seen a myriad of programs and systems described in the literature. Before 1975, applications were somewhat more fundamental, reflecting the fact that pharmacists were experimenting with and developing single-use applications. However, by 1975, pharmacists were integrating many single applications into one system to support a number of functions. Systems have been described that perform both medication distribution system support, as well as administrative tasks and clinical functions.

System configuration has also changed, from the large mainframe computer into which data were fed on punched cards, to the on-line dedicated minicomputer, and most recently, to the microprocessor. Improved program designs and programming techniques have meant more sophisticated approaches to applications.

What of the future of EDP in pharmacy practice? In the near future, the development and implementation of a national drug information network may become a reality. McEvilla and Lewis,[140] in describing their vision of pharmacy practice in the year 2000, forecast that a central data bank of drug information would be a reality. They envisioned that the physician would enter all patient information into the central data bank and prescription and other medical information would be transmitted to a selected pharmacy for dispensing of the drug. They predicted that automation in pharmacy practice would become an absolute necessity, to free the pharmacist for more direct patient care.

Yet, for all the work done in the field, the use of data processing techniques in support of pharmacy activities on a nationwide basis is still not widely accepted. If automation of pharmacy practice is to become the norm, there is an obvious need for justification of systems. As Gouveia commented in 1975,[8] the lack of well-controlled documented studies analyzing the cost benefits of computerization still hampers acceptance of the concept in hospital pharmacy. More research is needed in this area, and more literature must deal with this aspect, before the role of EDP in pharmacy practice will be universally accepted.

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[a] American Druggist Blue Book Data Center, Burlingame, CA 94010.
[b] Elsevier-North Holland Publishing Company, New York, NY
[c] Iowa Drug Information Service, Iowa City, IA 57242
[d] Micromedex, Inc., Ridgefield, CT 06877.
[e] Bac-Data Medical Information Systems, Inc., Clifton, NJ

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Improving Drug Prescribing

...Pharmacists are recognizing that a complete set of pharmaceutical services to inpatients must include (1) impersonal, production-oriented goods and services (e.g., the materials distribution system) and (2) personal, patient-specific services (e.g., discharge counseling, therapeutic monitoring). In an analogous manner, a complete set of influences to encourage better drug prescribing must include (1) distribution of reliable information through a stable influence network (perhaps involving the P & T committee and its appendages) and (2) personal, patient-specific advice from a therapeutic advisor (e.g., a clinical pharmacist). A complete drug-use control system should weld these activities into a unified whole.

—Hepler CD, Segal R, Freeman RA. How physicians choose the drugs they prescribe. *Topics Hosp Pharm Manage.* 1981; 1(Nov):23–42.