Chapter 5

REPORTING, EVALUATION, MOINTORING, PREVENTING & MANAGEMENT OF ADRs.

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A comprehensive ADR-monitoring and reporting program should be an integral part of an organization's overall drug use system. An ADR-monitoring and reporting program should include the following features:

1. The program should establish

(a.) An ongoing and concurrent (during drug therapy) surveillance system based on the reporting of suspected ADRs by pharmacists, physicians, nurses, or patients.

(b.) A prospective (before drug therapy) surveillance system for high-risk drugs or patients with a high risk for ADRs.

- (c.) A concurrent surveillance system for monitoring alerting orders. Alerting orders include the use of “tracer” drugs that are used to treat common ADRs (e.g., orders for immediate doses of antihistamines, epinephrine, and corticosteroids), abrupt discontinuation or decreases in dosage of a drug, or stat orders for laboratory assessment of therapeutic drug levels.
- 2. Prescribers, caregivers, and patients should be notified regarding suspected ADRs.
- 3. Information regarding suspected ADRs should be reported to the pharmacy for complete data collection 206 Medication Misadventures–Guidelines and Analyses

- including the patient’s name, the patient’s medical and medication history, a description of the suspected ADR, the temporal sequence of the event, any remedial treatment required, and sequelae.
- 4. High-risk patients should be identified and monitored. High-risk patients include but are not limited to pediatric patients, geriatric patients, patients with organ failure (e.g., hepatic or renal failure), and patients receiving multiple drugs.

- 5. Drugs likely to cause ADRs (“high-risk” drugs) should be identified, and their use should be monitored. Examples of drugs that may be considered as high risk include aminoglycosides, amphotericin, antineoplastics, corticosteroids, digoxin, heparin, lidocaine, phenytoin, theophylline, thrombolytic agents, and warfarin.
- 6. The cause(s) of each suspected ADR should be evaluated on the basis of the patient’s medical and medication history, the circumstances of the adverse event, the results of dechallenge and rechallenge (if any), alternative etiologies, and a literature review.

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- a. Was there a temporal relationship between the onset of drug therapy and the adverse reaction
- b. Was there a dechallenge; i.e., did the signs and symptoms of the adverse reaction subside when the drug was withdrawn
- c. Can signs and symptoms of the adverse reaction be explained by the patient's disease state
- d. Were there any laboratory tests that provide evidence for the reaction being an ADR

- e. What was the patient's previous general experience with the drug
- f. Did symptoms return when the agent was readministered
- 8. A method for ranking ADRs by severity should be established.
- 9. A description of each suspected ADR and the outcomes from the event should be documented in the patient's medical record.

- 10. Serious or unexpected ADRs should be reported to the Food and Drug Administration (FDA) or the drug's manufacturer (or both).
- 11. All ADR reports should be reviewed and evaluated by a designated multidisciplinary committee (e.g., a pharmacy and therapeutics committee).
- 12. ADR-report information should be disseminated to health care professional staff members for educational purposes. Good topics for medical staff education include preventing ADRs and appropriate and effective care for patients who experience ADRs. Educational programs can be conducted as morning "report" discussions, newsletters, "grand rounds" presentations, algorithms for treatment, and multidisciplinary reviews of drug-use evaluations. Patient confidentiality should be preserved.

- 13. In settings where it is possible, a pharmacy-coorddinated ADR team or committee, consisting of a physician, nurse, quality improvement leader, an administrator, anda pharmacist is recommended.The team should be charged with adopting a definition for the organization, promoting awareness of the consequences of ADRs,establishing mechanisms for identifying and reporting ADRs, reviewing ADR patterns or trends, and developing preventive and corrective interventions.
- 14. Continuous monitoring of patient outcomes and patterns of ADRs is imperative. Findings from an ADRmonitoring and reporting program should be incorporated into the organization's ongoing quality improvement activities. The process should include the following:
- a. Feedback to all appropriate health care staff,

- b. Continuous monitoring for trends, clusters, or significant individual ADRs,
- c. Educational efforts for prevention of ADRs, and
- d. Evaluation of prescribing patterns, patient monitoring practices, patient outcomes, and the ADR program's effect on overall and individual patient outcomes.An overall goal of the ADR process should be the achievement of positive patient outcomes.
- **Benefits**
- An ongoing ADR-monitoring and reporting program can provide benefits to the organization, pharmacists, other health care professionals, and patients. These benefits include (but are not limited to) the following:

- 1. Providing an indirect measure of the quality of pharmaceutical care through identification of preventable ADRs and anticipatory surveillance for high-risk rugs or patients.
- 2. Complementing organizational risk-management activities and efforts to minimize liability.
- 3. Assessing the safety of drug therapies, especially recently approved drugs.
- 4. Measuring ADR incidence.
- 5. Educating health care professionals and patients about drug effects and increasing their level of awareness regarding ADRs.

- 6. Providing quality-assurance screening findings for use in drug-use evaluation programs.
- 7. Measuring the economic impact of ADR prevention as manifested through reduced hospitalization, optimal and economical drug use, and minimized organizational liability
- **Management**
- Rapid action is sometimes important because of the serious nature of a suspected adverse drug reaction, forexample anaphylactic shock. Emergency treatment and
- withdrawal of all medicines is occasionally essential, in which case cautious reintroduction of essential medicines should be considered. Otherwise, using clinical benefit-risk judgment, together with help from investigations, one

- decides which medicine or medicines should be with drawn as a trial. A problem immediately arises if one or more of the medicines is essential to the patient. If the culprit is fairly clear, a benefit-risk decision needs to be taken about the need for the drug (are there equally effective substitutes that are unlikely to produce the same adversedrug reaction?), the severity of the reaction, and its potential for treatment. If several medicines could be causative, the non-essential medicines should be withdrawn first, preferably one at a time, depending on the severity of the reaction. If the reaction is likely to be dose related, dose reduction should be considered. Many prescribers unnecessarily withhold a drug when interactions are suspected, rather than adjusting the dose.
- The patient should be observed during withdrawal. The waiting period will vary, depending on the rate of elimination of the drug from the body and the type of pathology.

- For example, urticaria usually disappears quickly when the drug is eliminated, whereas fixed psoriatic skin reactions can take weeks to resolve. If the patient is clearly getting better, in keeping with the prediction, alternative
- medicines for the basic disease can be introduced if necessary. If the patient is not doing well after withdrawal of the first drug, the next most likely culprit should be considered, and the process repeated. On the other hand, the patient may be suffering through being deprived of the medicine withheld. In that case, either another suitable drug should be substituted (remembering the possibility of cross-sensitivity), or the same drug should be tried at a lower dosage (for a dose-related reaction).
- The latter approach should be tried if more than one drug was withheld, for instance if an interaction was suspected or if the seriousness of the reaction made it wise to withhold several possible drugs. Reintroduce apparently essential

- medicines one at a time, starting with the one least likely to be the culprit.
- If the patient cannot manage without a medicine that has caused an adverse reaction, provide symptomatic relief while continuing the essential treatment.
- For example:
- severe nausea and vomiting are routinely treated symptomatically in patients receiving anti-cancer drugs.
- However, when treating an adverse drug reaction, it is important not to introduce more medicines than are essential. Always have a clear therapeutic objective in mind, do not treat for longer than is necessary, and review the patient regularly and look for ways to simplify management.

- The investigation and identification of an adverse drug reaction still depands Largely on circumstantial evidence and the clinical skills of the attending physician. A knowledge of the clinical criteria and the varied manifeststions Ascribed to drug allergy,and syndromes commonly associated with certain drugs,is of great value in evaluating suspected adverse drug reactions.unfortunately, none of the clinical manifestations is unique or specific for drug reaction.

- **REPORTING TO THE FDA**:
- Three of the five major centers at the FDA are involved with evaluating the safety and efficacy of drug and efficacy of drugs.
- The largest center is the center for drug evaluation and research (CDER) which overseas both prescription and non prescription over the counter (OTC) drugs.
- In 2002, CDER established the adverse events reporting system (AERS), a computerized data base designed to support FDA'S post marketing safety program for drugs and therapeutics biological products.
- The center for biological evaluation and research (CBER), ensures the safety and efficacy of blood products, Vaccines, biological therapeutics, Gene therapy, medical devices and tests, xenotransplantation products, banked human tissue and cellular products.

- The center for food safety and applied nutrition(CFSAN) established the CFSAN adverse events reporting system (CAERS) in 2002
- The CAERS provides a monitoring system to identify potentially serious problem secondary to non -FDA-approved herbs, minerals, vitamins, dietary supplements, and other substances.
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- The National vaccine adverse event reporting system (VAERS) is co administered by the FDA and the centers for disease control and prevention (CDC).Although vaccines protect many people from dangerous diseases they do have the potential to cause adverse effects
- 1.The national childhood vaccine injury act(NCVIA) requires health professionals to report
- a. adverse events after the administration of vaccines specified in the act, as described in the “Reporting events tables”with in the specified time period (available at www.vaers.hhs.gov)
- b.any event listed in the manufacter package insert as an contraindication to subsequent doses of the vaccine
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- 2. in 1990 VAERS was set up to receive all reports of suspected adverse events caused by any U.S.licensed vaccine
- 3. the VAERS depends on voluntary reporting by health professionals to :
- a.identify rare adverse reaction not detected in pre-licensing studies
- b.monitor for Increased in already known reactions
- c.identify risk factors or pre existing conditions that promote reactions
- d. identify particular vaccines lots with unusually high rates or unusual type of events.
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- B.MEDWATCH ,the FDA’S medical products reporting program established in 1993,is a voluntary system for healthcare products.The goals of the program are to increase awareness of reporting of medical product induced diseases and the importance,to clarify what should be reported, to make reporting as easy as possible,and to provide feedback to health professionals

- A.preventing of ADR’S is an important startegy in health care.It has been further noted that preventable ADR’S tend to be treat and cause the greatest degree of patient morbidity.
- B.recognition of previously undiscovered ADR’S attributable to a drug is particulary true in the case of newly marketed products
- C.prompt recall in cases of product problems are accomplished when the Medwatch programm is used to report product problems or device defects

- **Role of the Pharmacist**

- Pharmacists should exert leadership in the development, maintenance, and ongoing evaluation of ADR programs. They should obtain formal endorsement or approval of such programs through appropriate committees (e.g., a pharmacy and therapeutics committee and the executive committee of the medical staff) and the organization's administration. In settings where applicable, input into the design of the pro-gram should be obtained from the medical staff, nursing staff,quality improvement staff, medical records department, and risk managers.
- The pharmacist should facilitate
- 1. Analysis of each reported ADR,
- 2. Identification of drugs and patients at high risk for being involved in ADRs,
- 3. The development of policies and procedures for the ADR-monitoring and reporting program,

- 4. A description of the responsibilities and interactions of pharmacists, physicians, nurses, risk managers, and other health professionals in the ADR program,
- 5. Use of the ADR program for educational purposes,
- 6. Development, maintenance, and evaluation of ADR records within the organization,
- 7. The organizational dissemination and use of information obtained through the ADR program,
- 8. Reporting of serious ADRs to the FDA or the manufacturer (or both), and

- 9. Publication and presentation of important ADRs to the medical community.
- Direct patient care roles for pharmacists should include patient counseling on ADRs, identification and documentation in the patient's medical record of high-risk patients, monitoring to ensure that serum drug concentrations remain within acceptable therapeutic ranges, and adjusting doses in appropriate patients (e.g., patients with impaired renal or hepatic function)