UNIT V: DRUG INFORMATION SERVICE

SECTION I: THREE TYPES OF DRUG INFORMATION LITERATURE

A. Primary Literature

Definition

Primary literature forms the foundation of the literature hierarchy. It is the source of information for the development of secondary and tertiary literature resources. Primary literature is comprised of original research that is written in the author(s) own words.

It consists of research studies, case reports, editorials, and letters to the editor. Most primary literature contains a detailed description of the study design, methodology, and scientific results. The reader is able to critique and analyze the study in order to develop a conclusion.

Examples of excellent primary literature resources include research articles and studies published in the New England Journal of Medicine, Journal of the American Medical Association, Archives of Internal Medicine, Annals of Internal Medicine, Lancet, and British Medical Journal. These publications are among about 100 others designated as Core Clinical Journals by the National Library of Medicine. They are important journals because they contain information that is significant to medical practice.

- Advantages of primary literature:

1.Information from primary literature is current, original, and "cutting-edge."Core Clinical Journals contain information about patient-oriented, evidence-based medicine that may change or affect patient care. The mnemonic POEMS (Patient Oriented Evidence that Matters) is often utilized to define this information and the journals in which it is contained.

2.Many articles undergo review by the author's peers before an article is accepted for publication, thereby incorporating unbiased views and suggestions to improve the quality of the report. This is known as the "peer-review process."

- Disadvantages of primary literature:

1.With any research report, flaws in study methodology may lead to inaccurate conclusions. For example, utilizing inappropriate statistical analysis may lead one to reach an inappropriate conclusion of the results of a study.

2.In assessing the primary literature, knowledge of scientific methods and statistics is necessary to properly interpret the information.

3.Since the information presented in the primary literature is so new, it may take time before wide acceptance occurs throughout the medical community.

- Using the primary literature:

1.Be cautious, careful, and conservative when utilizing new information from a primary literature source.

2.Is the article from a peer-reviewed journal? Articles published in peer-reviewed journals are generally better in quality and objectivity than non-peer reviewed work.

3.In utilizing data from primary sources be sure that all aspects of the primary source are understood (i.e. patient inclusion or exclusion criteria, study methods and interventions, primary outcome being assessed, statistical and clinical relevance of the reported findings), before applying that information to your patient).

4.To extrapolate primary literature data to a single patient encounter, make sure the patient population mentioned or utilized in the primary work corresponds to your practice population.

5.Remember that case reports relate only to one patient not a whole patient population. Be watchful for potential for bias and avoid relying solely on anecdotes.

B.Secondary Literature:

- Definition:

The secondary literature is compiled by indexing and abstracting services that can be used to systematically locate various types of published literature. The indexing system usually provides bibliographic information indexed by topic and will allow the user to view a brief description of the information within most citations. Examples of secondary literature databases are PubMed (Medline), Embase, National Library of Medicine Gateway, International Pharmacy Abstracts, Scopus, and Toxline. There are many secondary literature databases and each has its own scope, look, feel, and features to make it easy for the user to search the database.

- Using the secondary literature:

Here are some things to know when using and finding primary literature through the secondary literature databases.

1.Each database has its own focus, or scope, and collects primary literature in a certain field about a disease, drug-information, or literature related to patient care. Medline focuses on the biomedical sciences,Toxline focuses on toxicology, CINAHL focuses on the nursing and allied health literature.

2.The databases link you to citations that show you the author, title of thework, location and date of the publication and generally, an abstract of the manuscript. Sometimes the full text of the article will be available, but other times you need to get access to the article itself through a subscription. That's where the library comes into the picture.

The UMKC Health Sciences Library makes the article available online through its subscriptions to journals. You can always use the link to see whether the article is available electronically or in print through the library or,if the article is not available, you can order it for free from another library using the Health Sciences Library's inter-library loan service, known as "ILL."

Unfamiliar with ILL? Here's a website with more information:
http://libguides.library.umkc.edu/content.php?pid=11136.43.

The Clinical Medical Librarians (CMLs) are highly proficient in searching the secondary literature, especially if you are not well acquainted with medical subject headings(MeSH), or other terms used to index the information. The medical librarians are extremely helpful. If you have questions you can get live online help from the HSL website, or text to ask a librarian.For details on how to contact a librarian, see more information at this link:
http://library.umkc.edu/ask-a-librarian

- Advantages of secondary literature:

1.Provides quick access to the primary literature.

2.Provides a broad scope and/or concise informationon specific topics. The information is usually current, but it depends on the abstracting service and the specific type of information for which one is looking.

3. Generally, the journal sources are peer reviewed and of a high standard.

4.With most resources, updated information can be sent to you periodically, i.e. weekly or monthly.

- Disadvantages of secondary literature:

1.The time period between publication and inclusion (lag time) into secondary sources can vary for each database, from days to weeks.

2.The number of journals indexed by each system depends upon the scope of the database. Hopefully, they are the journals that you consider important and regularly review.

3.Because a secondary source can encompass such a large amount of information, one must be proficient at sifting through the sources listed on a particular subject to find the exact information one is looking for.

4.To obtain useful information, one must utilize specific search terms and be proficient with a particular database's search techniques. Medical databases organize the literature using Medical Subject Headings (MeSH). The way MeSH works is this: if you search for “heart attack” in a medical database, the system will look for “Myocardial Infarction,” which is the MeSH heading. Your use of terms will influence what you find. If you search for "the use of aspirin" in a particular medical database, hundreds of articles would be reported. However, if you specify “aspirin use in myocardial infarction, secondary prophylaxis,"use of the more exact term will yieldmore focused results.

•Examples of Secondary Sources of Drug Information:¬

OVID:

The Ovid database is used by many health professionals to search large collections of scientific, medical, and technical databases (currently over 80). For the most part it is extremely easy to work with and use. The UMKC Health Sciences Library uses OVID technology which is available online. The CMLs can demonstrate how to utilize it. For a disc ussion of the company that created OVID, see the OVID website at http://www.ovid.com.¬

MEDLINE: Abstracting service produced by the National Library of Medicine; indexes articles from over 4000 journals of international biomedical literature including allied health fields; available on-line through UMKC Health Sciences Library (via the OVID Medline interface). The UMKC Health Sciences Library has excellent tutorialsavailable on-line that explain how to properly perform a search. Check them out here: http://library.umkc.edu/hsl/hslhowdoi-videoso

Access to MEDLINE is also available online from the National Library of Medicine via the Web through PubMed.

You should go to PubMed from the Library’s homepage and select it from the right-hand side of the homepage. In doing so, you will see the “Find It @ UMKC” button in the 5abstract view of articles you are searching for.

The Health Sciences library homepage is http://library.umkc.edu/hsl¬The Medical Letter : This is basically an abstracting and evaluating service that reviews recently approved medications, drug classes, and lists current treatment options for various diseases; the reviews (although brief) are excellent and non-biased and offer specific recommendations; published every two weeks.

The Medical Letter is available as an online resource from the Health Sciences Library website. It is also available in print, and can be found with the Health Sciences Library journals, filed under “M.”¬Iowa Drug Information Service: IDIS indexes English articles relevant to drugs and treatment of disease from approximately 200 journals; [http://www.uiowa.edu/~idin/]

The database is sold on a subscription basis. Full-text articles are available on the web or on CD-ROM.¬International Pharmaceutical Abstracts: Offers an extensive list of indexed information, including information pertaining to international pharmacy and pharmace utical sciences; index includes all pharmacy periodicals. IPA is available as an online database from the Health Sciences Library website in the OVIDdatabases.¬

The Cochrane Library (Collaboration): Provides an assessment of the literature on particular health care topics through a very complete and thorough literature review. Cochrane is available from the Health Sciences Library website in Evidence Based Medicine Reviews in the OVID databases.

MEDICATION ERROR

Medication Error

Experts estimate medication errors are a leading cause of death and disability.

"Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health care professional, patient or consumer."

A major medication error is one which may result in permanent harm to the patient or transfer to the ICU.

Why do medication errors happen?

Medications error may result from problems in practice, products, procedures or systems. Other factors, such as training deficiencies, undue time pressure and poor perception of risk can also contribute to medication errors.

Children are particularly vulnerable to medication errors because of their unique physiology and developmental needs. For example – Incorrect recording of patient weights leading to an incorrect medication dose and failure to note drug allergy are common causes for medication errors in the pediatric emergency department.

Characteristics of Medication Errors

An analysis of medication errors can help healthcare professionals and managers to identify error-prone medications or categories of drugs, and make improvements to prevent or reduce them.

Table 1: Types of Medication Errors

Types Contributing Factors Causes

1. Extra dose Distractions Performance deficit Improper dose/quantity
2. Workload increase Procedure/protocol not followed Omission error Inexperienced staff Knowledge deficit
3. Prescribing error Shift change Inaccurate or lack of documentation Unauthorized drug Agency/temporary staff Confusing communication
4. Wrong administration & technique No 24 hour pharmacy Inaccurate or omitted transcription
5. Insufficient staffing Computer entry
6. Wrong dosage form Emergency situation Drug distribution system
7. Wrong drug preparation Cross coverage Inadequate system safeguards
8. Wrong patient Code situation Illegible or unclear handwriting
9. Wrong route Untrained staff Lack of knowledge
10. Wrong time – Before or after meals viz.
11. No access to patientinformation
12. Lack of knowledge
13. Loading of drug wrongly; Wrong speed of administration
14. Errors in decimal/zero
15. Errors in units

Other reasons for medication errors

1. Dispensing errors

a) Dropper confusion – practice of prescribing dropper full preparation of injections in advance

b) Injectable solution color changes

2. Equipment errors

a) Faulty monitors

b) Faulty infusion pumps

3. History taking errors

a) Not taking history of

i. allergy to drug

ii. concurrent illness

iii. previous drug dosages

iv. drugs already taken personal history,

b) Telephonic consultant errors

c) Errors in description of disease/symptoms

d) Errors in noting down drugs

Reporting errors

There are basically four factors why medication errors are not reported: fear; disagreement on error,

1. administrative responses to medication errors, and effort required to report Medication Administration
2. Errors, as reporting is non-automated and voluntary process.
3. Reporting errors is only the first step in the process of reducing errors and continuous quality
4. improvement. An approach that is commonly used in human factor analysis is a *critical incident analysis*.
5. This analysis examines adverse events to understand where the system broke down, why the incident
6. occurred, and the circumstances surrounding the incident. Analyzing critical incidents, whether or not the
7. event actually leads to a bad outcome, provides an understanding of the conditions that produced an
8. actual error or the risk of error as well as the contributing factors.
9. Feedback and dissemination of information can create an awareness of errors that occur in the system
10. and improve system design to reduce or eliminate medication errors.

Preventing medication errors

1. It is important that five "Rights" are practiced strictly viz.,

a) Right Patient,

b) Right Drug,

c) Right Dose,

d) Right Route and

e) Right Time.

2. Drug should be administered after being cross-checked by another nurse.

3. In case prescription is not legible, confirm with doctor rather than guessing.

4. Read package insert before administering drug by intravenous or intramuscular route and follow the instructions on rate and speed of administration, diluents to be used.

5. Check the generic name of the drug in case of confusing brand names.

6. Be careful about look-alike and sound-alike drugs. They are one of the major sources of errors.

7. Never hesitate to report the Medication Error so that others do not make same error.

"A medication error is an preventable even that may cause or lead to inappropriate medication use or patient while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, producers and systems, including prescribing; order communication ; product labeling packaging and nomenclature; compounding ; dispensing; distribution;

administration; education; monitoring; and use"Most medication errors are considered latent. For example, when a pharmacist fills a prescription with the incorrect medication, patients typically realize this mistake once they have returned home and have taken the first dose. Latent errors can be described as "accidents waiting to happen " The causes of these types of errors are usually identifiable and can be corrected before the error reoccurs. Incomplete patient information (not knowing about patients' allergies, other medicines they are taking , previous diagnoses, and lab results for example)

Unavailable drug information (such as lack of up-to date warnings) Miscommunication of drugs orders, which can involve poor handwriting , confusion between drugs with similar names, misuse of zeroes and decimal points, confusion of metric and other dosing units, and inappropriate abbreviations.

Lack of appropriate labeling as a drug is prepared and repackaged into smaller units and Environmental factors, such as lighting, heat noise, and interruptions that can distract health professionals from their medical tasks.

PRESCRIPTION

COMPONENT PARTS OF THE PRESCRIPTION

The prescription consists of seven parts. Their Latin names are:

1. **INSCRIPTIO**

Here written are: the name and the surname of the doctor, the hospital, clinic or polyclinic medical center, their address, and the date. The date is important from the standpoint of ascertaining for determining the life of the prescription.

The prescription of narcotics and controlled substances are governed by special laws and regulations – it cannot be filled after more than 10 days from the date of issuance; but an order for children – 7 days after the date on which such prescription was issued.

2. PRAEPOSITIO (SUPERSCRIPTION)

consists of the message to the chemist. It includes only the expression Rp./ – an abbreviation for Recipe, the Latin for Get! (Take)

3. PRESCRIPTIO

is the main part of the medical prescription, because this is the doctor's order. Here are the names of medicinal substances, the medicinal forms, and the dosages.

a) brand name (proprietary name) or generic name (INN – international nonproprietary name) may be used. The medicinal substances are required to begin with a capital letter and to be in the Genitive case.

The names of all preparations and elements end in **-um, Gen sg. –i.** The salts end in Gen. sg. **-atis (sulfate); – itis (nitrate); – idi (chloride)**

b) the medicinal form can be placed in the beginning of the prescription or after the drug's name.

c) the dose is noted after the substance or medicinal form. The strength of the medication should be written in metric units.

Example: Rp./ Tab. Paracetamoli 0,5 (or 500 mg)

Rp./ Vitamini B_{12} in ampullis 0,500 mg

4. SUBSCRIPTIO (SUBSCRIPTION)

In this part are written, if necessary, instructions to the chemist on how to make the preparation and the number of doses, or medicinal forms to be supplied to the patient.

Exampe: Rp./ Tab. Paracetamoli 0,5

Da scatulam № 2 (D. scat. №2) = Give 2 blisters

Rp./ Vitamini B_{12} 0,5 mg

Da tales doses № 10 in ampullis (D. t. d. № 10) = Dispense such doses 20 in number

5. SIGNATURA (MARK, LABEL)

Notes are written in Bulgarian. The signature is the message intended for the patient. It provides instructions as to how the medicine should be taken by the patient. This information must be sufficient to allow the patient to understand fully the amount of the drug product to be taken and the frequency and manner of administration: if the drug has to be used externally only, or to be shaken well before use, or whether it is a poison, and other such facts are included.

Example: Signa or Scribe (S.) one tablet three times a day (Ter-in-die, resp.
t.i.d. – three times daily)
Signa or Scribe (S.) One tablet when necessary (Pro re nata – p.r.n.)

6. NOMEN MEDICI

The signature of the doctor may be placed on the designated area, or after the last drug, and this is for identification data.

7. NOMEN AEGROTI

Name, address and age of the patient. This part serves to identify for whom the prescription is intended. The full name and the address are required by law on all prescriptions for controlled substances. The age of the patient is a good additional piece of information, especially with pediatric patients where dosage calculations have to be double-checked for safety. This part may be located on the designated area, or after the last drug on the back of the form.

PRESCRIPTION TYPES

Prescriptions can be classified as compounded and noncompounded.

Compounded prescription, also called *formula magistralis* (from Latin word magister – teacher) or *extemporaneous prescription* is an order that requires mixing of one or more ingredients (active medicaments) with one or more pharmaceutical necessities (vehicle, suspending agent). The physician selects the drugs, doses, and pharmaceutical form that he/she desires and the pharmacist prepares the medication accordingly. The name of each drug is placed on a separate line right under the preceding one. The order of ingredients is as follows:

Remedium cardinale (basis). The basis is the principal drug and gives the prescription its chief action.

Remedium adjuvans (adjuvant). As the name suggests, the adjuvant is a drug that aids or increases the action of the principal ingredient.

Remedium corrigens (corrective). The corrective modifies or corrects undesirable effects of the basic or adjuvant.

Remedium constituens (vehicle). The vehicle is the agent used as a solvent in the solution, to increase the size and volume, or to dilute the mixture. The most potent or principal drug is written first, the other ingredient second, and the vehicle last.

DRUG INTERACTION

A **drug interaction** is a situation in which a substance (usually another drug) affects the activity of a drug when both are administered together. This action can be synergistic (when the drug's effect is increased) or antagonistic (when the drug's effect is decreased) or a new effect can be produced that neither produces on its own. Typically, interactions between drugs come to mind (drug-drug interaction). However, interactions may also exist between drugs and foods (drug-food interactions), as well as drugs and medicinal plants or herbs (drug-plant interactions). People taking antidepressant drugs such as monoamine oxidase inhibitors should not take food containing tyramine as hypertensive crisis may occur (an example of a drug-food interaction). These interactions may occur out of accidental misuse or due to lack of knowledge about the active ingredients involved in the relevant substances.[1]

It is therefore easy to see the importance of these pharmacological interactions in the practice of medicine. If a patient is taking two drugs and one of them increases the effect of the other it is possible that an overdose may occur. The interaction of the two drugs may also increase the risk that side effects will occur. On the other hand, if the action of a drug is reduced it may cease to have any therapeutic use because of under dosage. Notwithstanding the above, on occasion these interactions may be sought in order to obtain an improved therapeutic effect.[3] Examples of this include the use of codeine with paracetamol to increase its analgesic effect. Or the combination of clavulanic acid with amoxicillin in order to overcome bacterial resistance to the antibiotic. It should also be remembered that there are interactions that, from a theoretical standpoint, may occur but in clinical practice have no important repercussions.

The pharmaceutical interactions that are of special interest to the practice of medicine are primarily those that have negative effects for an organism. The risk that a pharmacological interaction will appear increases as a function of the number of drugs administered to a patient at the same time.

It is possible that an interaction will occur between a drug and another substance present in the organism (i.e. foods or alcohol). Or in certain specific situations a drug may even react with itself, such as occurs with dehydration. In other situations, the interaction does not involve any effect on the drug. In certain cases, the presence of a drug in an individual's blood may affect certain types of laboratory analysis (**analytical interference**).

It is also possible for interactions to occur outside an organism before administration of the drugs has taken place. This can occur when two drugs are mixed, for example, in a saline solution prior to intravenous injection. Some classic examples of this type of interaction include that Thiopentone and Suxamethonium should not be placed in the same syringe and same is true for Benzylpenicillin and Heparin. These situations will all be discussed under the same heading due to their conceptual similarity.

Drug interactions may be the result of various processes. These processes may include alterations in the pharmacokinetics of the drug, such as alterations in the absorption, distribution, metabolism, and excretion (ADME) of a drug. Alternatively, drug interactions may be the result of the pharmacodynamic properties of the drug, e.g. the co-administration of a receptor antagonist and an agonist for the same receptor.

ADVERSE DRUG REACTION:

An **adverse drug reaction** (**ADR**) is an injury caused by taking a medication.[1] ADRs may occur following a single dose or prolonged administration of a drug or result from the combination of two or more drugs. The meaning of this expression differs from the meaning of "side effect", as this last expression might also imply that the effects can be beneficial.[2] The study of ADRs is the concern of the field known as *pharmacovigilance*. An **adverse drug event** (**ADE**) refers to any injury occurring at the time a drug is used, whether or not it is identified as a cause of the injury.[1] An ADR is a special type of ADE in which a causative relationship can be shown.

Classification

ADRs may be classified by e.g. cause and severity.

Cause

- Type A: Augmented pharmacologic effects - dose dependent and predictable

  Type A reactions, which constitute approximately 80% of adverse drug reactions, are usually a consequence of the drug's primary pharmacological effect (e.g. bleeding when using the anticoagulant warfarin) or a low therapeutic index of the drug (e.g. nausea from digoxin), and they are therefore predictable. They are dose-related and usually mild, although they may be serious or even fatal (e.g. intracranial bleeding from warfarin). Such reactions are usually due to inappropriate dosage, especially when drug elimination is impaired. The term 'side effects' is often applied to minor type A reactions.[3]

- Type B: Idiosyncratic

Types A and B were proposed in the 1970s,[4] and the other types were proposed subsequently when the first two proved insufficient to classify ADRs.[5]

Seriousness and severity

The American Food and Drug Administration defines a serious adverse event as one when the patient outcome is one of the following:[6]

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability - significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life.
- Congenital anomaly
- Requires intervention to prevent permanent impairment or damage

Severity is a point on an arbitrary scale of intensity of the adverse event in question. The terms "severe" and "serious" when applied to adverse events are technically very different. They are easily confused but can not be used interchangeably, requiring care in usage.

A headache is severe, if it causes intense pain. There are scales like "visual analog scale" that help clinicians assess the severity. On the other hand, a headache is not usually serious (but may be in case of subarachnoid haemorrhage, subdural bleed, even a migraine may temporally fit criteria), unless it also satisfies the criteria for seriousness listed above.

Location

Adverse effects may be local, i.e. limited to a certain location, or systemic, where a medication has caused adverse effects throughout the systemic circulation.

For instance, some ocular antihypertensives cause systemic effects,[7] although they are administered locally as eye drops, since a fraction escapes to the systemic circulation.

Adverse drug reaction leading to hepatitis (drug-induced hepatitis) with granulomata. Other causes were excluded with extensive investigations. Liver biopsy. H&E stain.

As research better explains the biochemistry of drug use, fewer ADRs are Type B and more are Type A. Common mechanisms are:

- Abnormal pharmacokinetics due to
  - genetic factors
  - comorbid disease states
- Synergistic effects between either
  - a drug and a disease
  - two drugs

Abnormal pharmacokinetics

Comorbid disease states

Various diseases, especially those that cause renal or hepatic insufficiency, may alter drug metabolism. Resources are available that report changes in a drug's metabolism due to disease states.[8]

Genetic factors

Abnormal drug metabolism may be due to inherited factors of either Phase I oxidation or Phase II conjugation.[9][10] Pharmacogenomics is the study of the inherited basis for abnormal drug reactions.

Phase I reactions

Inheriting abnormal alleles of cytochrome P450 can alter drug metabolism. Tables are available to check for drug interactions due to P450 interactions.[11][12]

Inheriting abnormal butyrylcholinesterase (pseudocholinesterase) may affect metabolism of drugs such as succinylcholine[13]

Phase II reactions

Inheriting abnormal N-acetyltransferase which conjugated some drugs to facilitate excretion may affect the metabolism of drugs such as isoniazid, hydralazine, and procainamide.[12][13]

Inheriting abnormal thiopurine S-methyltransferase may affect the metabolism of the thiopurine drugs mercaptopurine and azathioprine.[12]

Interactions with other drugs

The risk of drug interactions is increased with polypharmacy.

Protein binding

These interactions are usually transient and mild until a new steady state is achieved.[14][15] These are mainly for drugs without much first-pass liver metabolism. The principal plasma proteins for drug binding are:[16]

1. albumin
2. α1-acid glycoprotein
3. lipoproteins

Some drug interactions with warfarin are due to changes in protein binding.[16]

Cytochrome P450

Patients have abnormal metabolism by cytochrome P450 due to either inheriting abnormal alleles or due to drug interactions. Tables are available to check for drug interactions due to P450 interactions.[11]

Synergistic effects

An example of synergism is two drugs that both prolong the QT interval.

Assessing causality

Causality assessment is used to determine the likelihood that a drug caused a suspected ADR. There are a number of different methods used to judge causation, including the Naranjo algorithm, the Venulet algorithm and the WHO causality term assessment criteria. Each have pros and cons associated with their use and most require some level of expert judgement to apply.[17] An ADR should not be labeled as 'certain' unless the ADR abates with a challenge-dechallenge-rechallenge protocol (stopping and starting the agent in question). The chronology of the onset of the suspected ADR is important, as another substance or factor may be implicated as a cause; co-prescribed medications and underlying psychiatric conditions may be factors in the ADR.[2]

Assigning causality to a specific agent often proves difficult, unless the event is found during a clinical study or large databases are used. Both methods have difficulties and can be fraught with error. Even in clinical studies some ADRs may be missed as large numbers of test individuals are required to find that adverse drug reaction. Psychiatric ADRs are often missed as they are grouped together in the questionnaires used to assess the population.[18][19]

IDIOSYNCRATIC CASES:

Idiosyncratic drug reactions, also known as **type B reactions**, are drug reactions that occur rarely and unpredictably amongst the population. This is not to be mistaken with idiopathic, which implies that the cause is not known. They frequently occur with exposure to new drugs, as they have not been fully tested and the full range of possible side-effects have not been discovered; they may also be listed as an adverse drug reaction with a drug, but are extremely rare.

Some patients have multiple-drug intolerance. Patients who have multiple idiopathic effects that are nonspecific are more likely to have anxiety and depression.[1]

Idiosyncratic drug reactions appear to not be concentration dependent. A minimal amount of drug will cause an immune response, but it is suspected that at a low enough concentration, a drug will be less likely to initiate an immune response.

Mechanism

In adverse drug reactions involving overdoses, the toxic effect is simply an extension of the pharmacological effect (Type A adverse drug reactions). On the other hand, clinical symptoms of idiosyncratic drug reactions (Type B adverse drug reactions) are different from the pharmacological effect of the drug.

The proposed mechanism of most idiosyncratic drug reactions is immune-mediated toxicity. To create an immune response, a foreign molecule must be present that antibodies can bind to (i.e. the antigen) and cellular damage must exist. Very often, drugs will not be immunogenic because they are too small to induce immune response. However, a drug can cause an immune response if the drug binds a larger molecule. Some unaltered drugs, such as penicillin, will bind avidly to proteins. Others must be bioactivated into a toxic compound that will in turn bind to proteins. The second criterion of cellular damage can come either from a toxic drug/drug metabolite, or from an injury or infection. These will sensitize the immune system to the drug and cause a response. Idiosyncratic reactions fall conventionally under toxicology.