National University of Pharmacy
Department of pharmacology
and drug toxicilogy

SIDE EFFECTS OF DRUGS

Lecturer

prof. Shchokina C.G.

Do no harm!

The main precept of the doctor and the pharmacist is "Do no harm!". However, there is no drug completely harmless of 400-500 thousand medicines, especially in case of violation of conditions of their rational use.

If 50 years ago, the statistics showed that 5% of drugs cause side effects (SE), today statistics shows 60-70% of medicines with SE.

One of the requirements for the EU is to ensure the pharmacological supervision of drugs using and monitoring their SE according to the requirements of the WHO

Factors contributing to the growth of SE of medicines:

1. Reducing the time and volume of research of pharmacological activity and safety of future drugs.
2. Preclinical studies only provide a preliminary idea of the safety profile of the drug.
3. Shortening of the expert assessment of drug safety, speeding up the process of state registration of the new medicine.
4. Advertising of drugs, self-medication, "passion for medicine" (addiction), improper prescription (23% is dubious and 64% is inexpedient due to the route of administration, term of administration, dose, combination), technology, the shelf life

Factors contributing to the growth of SE of medicines:

5. The release of drugs with severe SE (reinforcing of carcinogenesis, etc.).
6. The lack of reliable, identical information and existence of contradictory or even distorted information about SE of medicines.
7. Widespread of dietary supplements and "pirate" generic drugs.
8. Opportunity of buying drugs using websites, which are available only through prescription.
9. Insufficient exchange of information among patients, pharmacists and physicians about the risks of drugs.

"ALPHABET" OF COMPLICATIONS IN PHARMACOTHERAPY

Safety (harmlessness) of medicines - absence of serious and unexpected side (adverse) effects or activity in clinical trials or medical use of the drug for which the corresponding value for the criterion of "benefit/risk“ is shown.

Side effects of medicines - any adverse reaction, which is caused by the pharmacological properties of the drug and observed when the drug is used in doses that are recommended for medical use.

"ALPHABET" OF COMPLICATIONS IN PHARMACOTHERAPY

Unexpected side effects of the drug **- side effects that do not match the information of the drug with its annotation.**

Serious side (adverse) effect **- any life-threatening reaction of the drug, that leads to hospitalization, disability, death of the patient, promotes fetal abnormalities.**

Non-serious side (adverse) effect **- any adverse reaction that does not meet the criteria defined as a serious adverse reaction.**

Benefit / risk ratio **- the ratio of the therapeutic effect of the drug and its known dangerous properties, which worsen the disease and cause the development of new harmful effects on the body and decrease the quality of life of the patient.**

SIDE EFFECTS OF DRUGS CLASSIFICATION

Potency of side effects :

1) weak ***3) severe***

2) moderate ***4) lethal***

Side effects depending on time:

1. ***Acute forms:*** anaphylactic shock, bronchial asthma, angioedema, vasomotor rhinitis, etc. (60 min)
2. ***Subacute forms -*** diarrhea (a day)
3. ***Prolonged forms:*** serum disease, vasculitis, etc. (over 2 days)

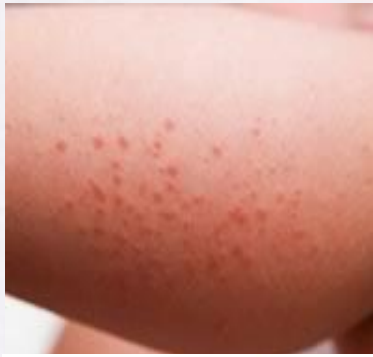
Side effects depending on severity:

1. ***Mild form:*** no need to remove the drug. Symptoms disappear within 3 days after treatment
2. ***Average severity:*** the drug should be canceled
3. ***Severe form:*** drug administration leads to disability or life-threatening

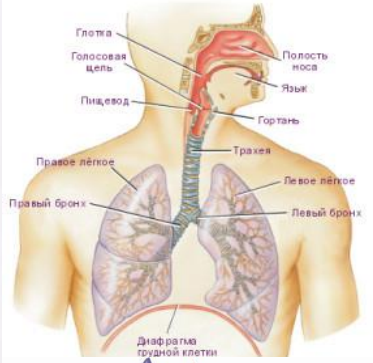
SIDE EFFECTS OF DRUGS CLASSIFICATION

Side effects that affect organs and systems:

1. ***The general reactions of the organism***
   (anaphylactic shock,
   drug allergy).

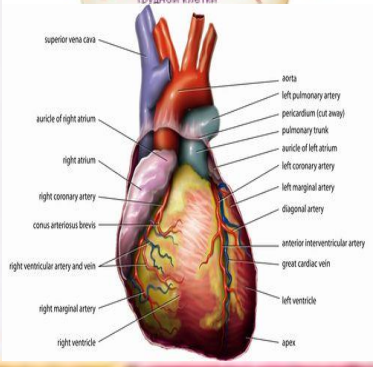


2. ***Skin and mucous membranes damage***
   (toxic epidermal necrosis,
   erosive dermatitis).



3. ***The respiratory tract damage***
   (allergic rhinitis,
   bronchial asthma, etc.).

4. ***The cardiovascular system damage***
   (heart conduction disturbance, myocarditis, etc.)



SIDE EFFECTS OF DRUGS CLASSIFICATION

Side effects depending on the cause of occurrence:

1. The undesirable effects due to pharmacological effects of drugs (atropine sulfate causes dry mouth).
2. Paradoxical effects.
3. SE associated with the cells receptors sensitivity disorder in neuroendocrine disorders.
4. True allergic reactions to medicines (antigen-antibody reaction).
5. Superinfection and dysbiosis.
6. The reactions associated with massive bacterialysis.
7. Psychogenic reactions, which develop more frequently in patients with a response to all medicines.
8. The reactions that occur due to incorrect drug administration.

World Health Organization

Side effect of drugs according to WHO classification

The type of SE	The frequency of occurrence	SE predictability	SE examples
Dose-dependent SE (type A)	Occur often (more than 1 in 100)	Due to the pharmacological effect of the drug or its time of administration	Excessive therapeutic effect
Dose-nondependent SE (type B)	Occur rarely (less than 1 in 1000)	There are predisposing factors	Allergy
SE in case of prolonged therapy (type C)	Occur rarely after prolonged administration	The nature of the drug is difficult to trace	Tolerance Dependence Withdrawal syndrome
Delayed SE (type D)	Delayed effects of the drug (in months and years)	They are extremely difficult to diagnose	Carcinogenicity Mutagenicity Teratogenicity

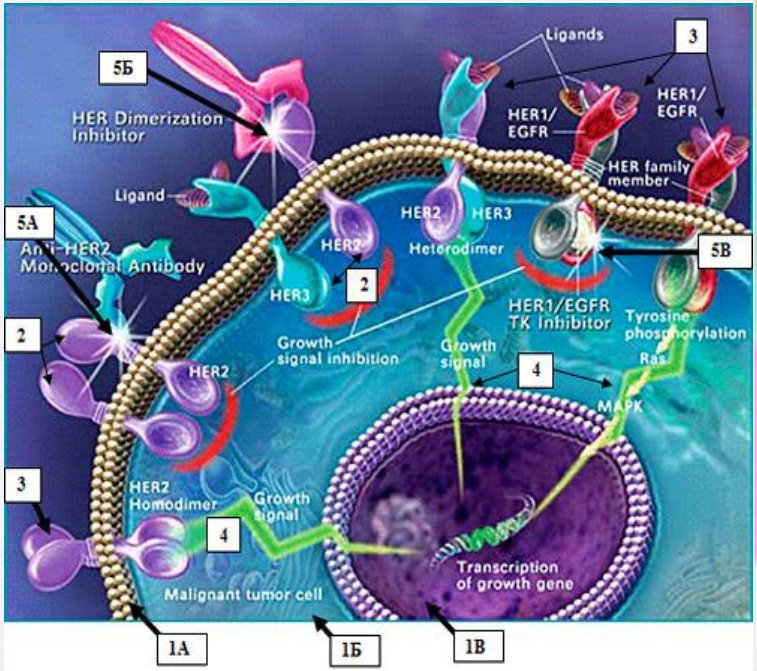
Mechanisms of side effects development

- Direct toxic damage to cells and tissues. SE with direct toxicity tend to have dose-dependent effect and are predictable;

- Mechanisms of pharmacokinetics;

- Mechanism of pharmacodynamics;

- Drug interactions, developing due to pharmacodynamic and pharmacokinetic mechanisms.



The principles of SE prevention

A doctor, a pharmacist and a patient must remember!

1. Drug therapy should not be more dangerous than the disease itself
2. Avoiding the use of new drugs that "give 100% success"
3. Avoiding polypharmacy: focus on the main effects
4. The treatment begins with small dose, gradually increasing it until the effective
5. The more therapeutic window is, the less likely SE
6. The higher selectivity of the drug, the less SE is
7. Prefer single component drugs to combined
8. To reduce SE of medicines is recommended to administrate them with cover (antibiotics and antifungals)
9. With increased drug sensitivity it is necessary to avoid using obligate allergens, histamine releasing drugs, etc.
10. Take into account the period of pregnancy, lactation, elder age and children

During pregnancy and lactation one must remember:

1. Do not prescribe a new and poorly-studied drugs
2. Medicines should be prescribed in minimal dose
3. Using specific drug labeling in drugs with absolute contraindications in pregnancy (teratogenicity)
4. Take into account the fact that many of drugs are released with milk
5. The child should be fed before the next drug intake

The state must be responsible for the quality of medicines, information and their realization

1. Presence of public authority coordinating the correct drug prescriptions and SE monitoring

2. Independent information about SE of medicines (from companies, pharmacies and others).

3. Preventing selfish financial interests in drugs realization.

4. Adequate state funding, ensuring the availability of medicines.

Changing stereotypes in the work of doctors and pharmacists in irrational prescribing and patients attitude to their use

1. Training doctors and pharmacists in the assessment of benefit / risk ratio and the rational use of drugs.

2. Involve doctors, pharmacists and pharmaceutical companies to participate in the conferences on the problems of drugs SE.

3. Doctors who earn money from drugs sale, prescribe a lot of most expensive drugs. Therefore, doctors should not be able to sell drugs.

4. Change people's attitude to self-treatment.

PHARMACOLOGICAL SUPERVISION is a state system of data collection, scientific assessment and monitoring of information about SE (adverse reaction) for the purpose of making appropriate decisions on the stage of clinical trials and medical use of a medicine.

Services of **pharmacological supervision** are created in more than 80 countries, including Ukraine (since 2002), the WHO administers the International Monitoring Program.

Years of pharmacological supervision creation in some countries

1968 – Australia, Great Britain, Germany, Denmark, New Zealand, Sweden

1972-1975 – Japan, Italy

1986 – France

1991 – Switzerland, Austria, Hungary, USA

1997 – Belgium, Russia, China

2002 – Ukraine

The economic and organization WHO Centre is located in Uppsala (Sweden), the formal guidance and coordination is done by the central office of WHO in Geneva (Switzerland)

Thank you for attention!