Pharmacovigilance & Adverse Drug Reactions

"Medication Safety"

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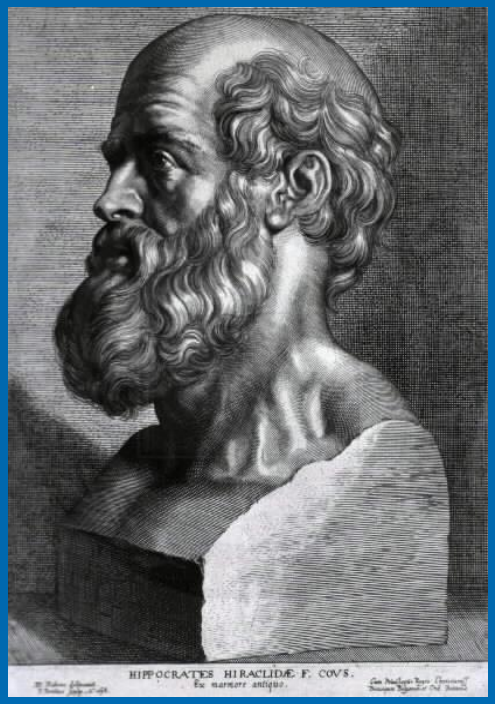
- Side effects may occur on normal doses.

'First of all be sure you do no harm'

1st rule in Medicine

Hippocrates (460-370 BC)



Pharmacovigilance (PV)

- **The root of pharmacovigilance:**

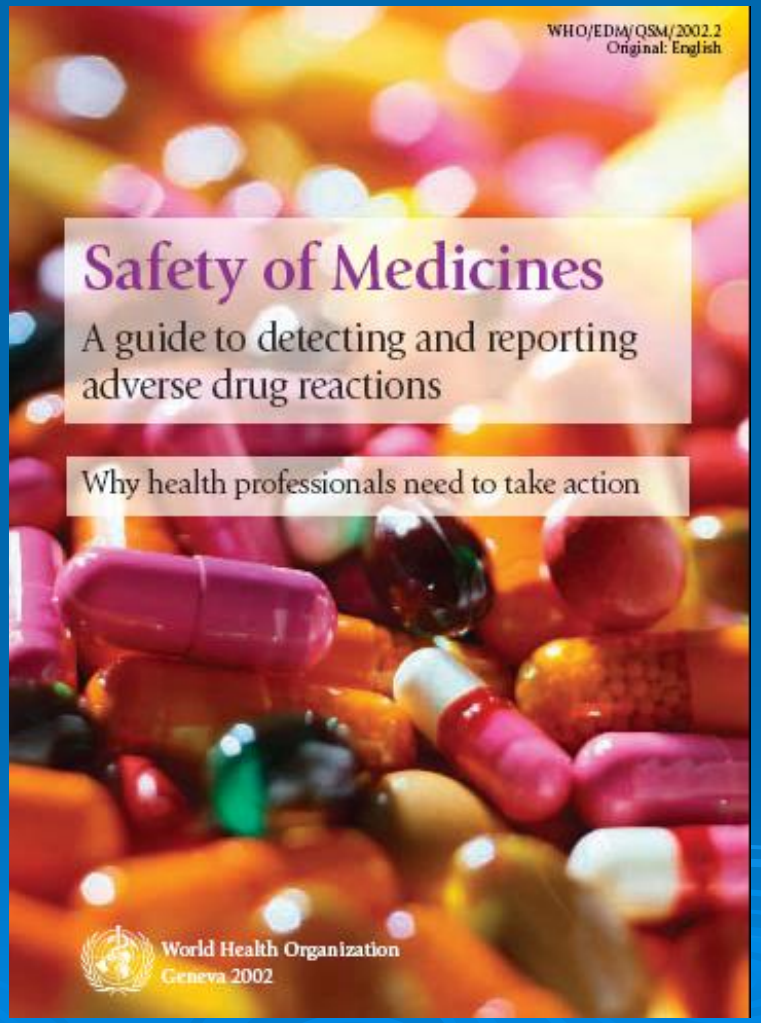
  Pharmaco (Greek)= **Drug**

  Vigilance (Latin)= to keep **awake or alert**

You have to make sure that the patient dosen't express any unwanted Adverse effects

Pharmacovigilance (PV)

- **PV is concerned with detection, assessment & prevention of adverse reactions to drugs (ADRs) or any drug-related problems**



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Drug-Related Problems

- Lack of efficacy
- Medication errors
- Drug misuse and abuse
- Overdose
- **Quality issues:**
  - Manufacturing defects
  - Contamination
  - Counterfeit products

Why Pharmacovigilance?

- Because information collected during **pre-marketing phase** are **incomplete with regard to possible ADR**
- Tests in animals are **insufficiently predictive of human safety**

Benefit - Risk ratio ⇒ increases? keep going

should be Balanced

① Any drug must be tested through clinical trials

② Clinical trials give us a feed back on a lot of people of how the drug effects and Record all the side effects.

Why Pharmacovigilance?

- **In clinical trials:** => disadvantage? They recruit low #'s of people.
- Patients are limited in number
- Conditions of use differ from those in clinical practice
- Duration of trials is limited

(Ex => like covid vaccines they had a short period of time because we had a pandemic and we wanted to end it ASAP.

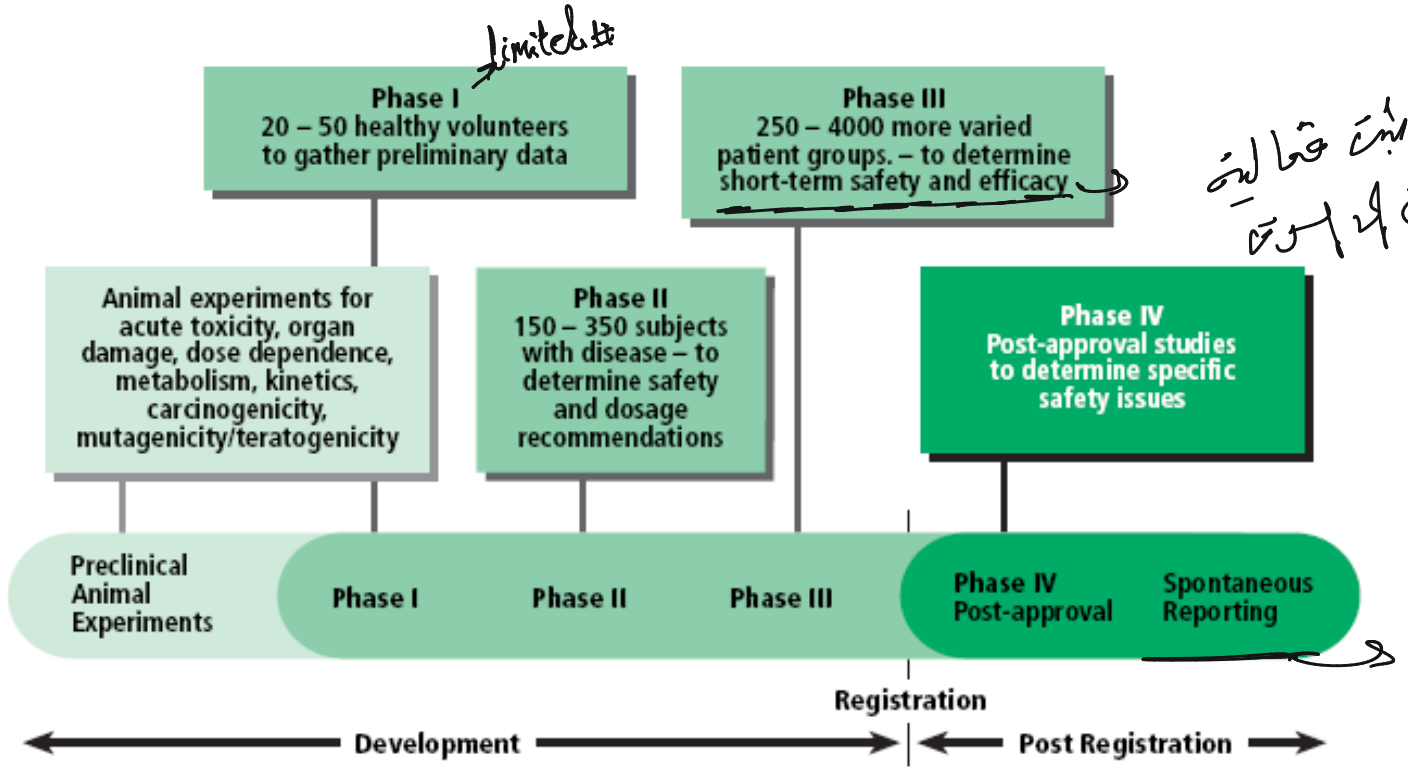
People w/ diabetes hypertensions cancers chronic diseases, etc

Why Pharmacovigilance?

- Information about **rare adverse reactions**, **chronic toxicity**, use in **special groups** (children, elderly or pregnant women) or drug interactions is often incomplete or not available

Post-marketing surveillance by companies is therefore essential

Figure 1 Clinical development of medicines



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Definition of ADR

- An ADR is defined according to definition of WHO "any response to a drug which is noxious, unintended & that occurs at doses used in man for prophylaxis, diagnosis, or therapy of diseases"

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Epidemiology of ADRs

- ADRs represent a significant cause of morbidity & mortality
- Many ADRs are mild, sometimes serious & can cause death
- U.S, ADRs caused 100 000 deaths per year, 4th & 6th leading cause of death
- About 50% of ADRs are preventable

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Importance of ADRs

- Prolong length of stay in hospitals
- Increase costs of patient care (£600 million NHS in UK)
- Commonest cause of drug withdrawal from market (recall): ⇒ if the risk is higher than the Benefit!
  - ARBs (Valsartan, Losartan, Irbesartan) 2019
  - Reductil (Sibutramine) 2010 أدوية بسمنة ولكن زاد نسبة إيقافها
  - Valdecoxib (Bextra) 2005
  - Rofecoxib (Vioxx) 2004 Used in Rheumatoid Arthritis ↑ risk of CV events.

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Classification of ADRs

Type A + Type B are the most important!

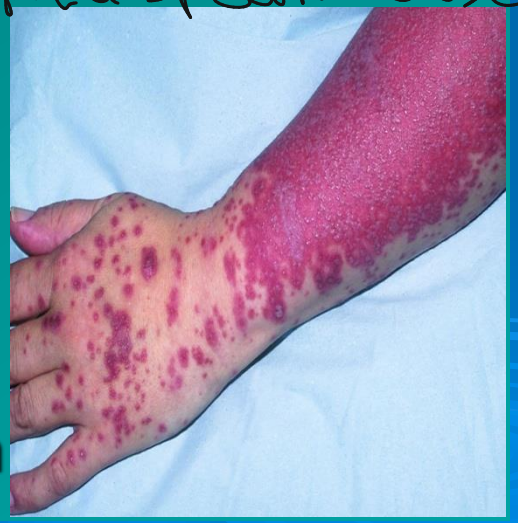
- **Classification of Rawlins & Thompson**

Type A reactions

- Augmentation of known pharmacological effect of drug
- Predictable
- Dose related
- **e.g. warfarin causing bleeding**

Type B reactions

- Bizarre (idiosyncratic)
- Not dose dependent
- Unpredictable
- **e.g. carbamazepine-induced skin rash**



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ed calf haematoma

Needs Amputation

Severe ADR's!

Carbamazepine-induced Stevens Johnson Syndrome (SJS)

Type B

skin necrolysis

- ADRs according frequency are divided into very common, common, rare, very rare
- ADRs divided according to severity into mild, moderate, severe

ADRs is considered serious if:

1. Causes death of patient
2. Life-threatening
3. Prolong inpatient hospitalisation
4. Causes significant or persist disability
5. Congenital abnormality

For the fetus if the mother took the drug.

Risk Factors Predisposing to ADRs

عوامل لازم آخذها بعين الإعتبار كطبيب لما بدي أوصف أدوية.

- Age
- Long duration of treatment
- Polypharmacy → uses too many drugs (old age) mostly
- Liver, kidney diseases

↳ you need to lower the dose then !

Causes of ADRs

1. Patient
2. Drug
3. Prescriber
4. Environmental factors plays a huge role!

Causes of ADRs

1. The patient:

- Age (over 60) ⇒ because of polypharmacy mostly!
- Genetic factors (e.g. polymorphisms in CYP450) → found in liver.
- Previous history of ADR (ex→ Asking about the Allergies! ↳ to prevent the ADR's.
- Hepatic or renal diseases

Causes of ADRs

2. The drug

- Narrow therapeutic index, e.g. **warfarin, digoxin**
- **Antimicrobials** have a tendency to cause allergy & may lead to **type B reactions**
- Ingredients of a formulation, e.g. **colouring, flavouring**

Causes of ADRs

3. The prescriber:

- A drug is used for an inappropriately long time ⇒ Ex: The body got used to the drug!.
- At a critical phase in pregnancy ⇒ Mostly 1st trimester!
- Given with other drugs **(drug-drug interactions)**

4. Environmental factors:

- Diet, smoking, alcohol

Drugs Most Commonly Causing ADRs

- Warfarin
- Diuretics
- Digoxin => Heart failure
- Antibacterials
- Steroids => Eg, Corticosteroids is good but has too many ADRs.
- Antihypertensives
- Anticancer drugs
- Immunomodulators
- Analgesics
- Biological & biosimilars

Burden of Adverse Drug Reactions

Admission

Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients

Munir Pirmohamed, Sally James, Shaun Meakin, Chris Green, Andrew K Scott, Thomas J Walley, Keith Farrar, B Kevin Park, Alasdair M Breckenridge

In patients

Adverse Drug Reactions in Hospital In-Patients: A Prospective Analysis of 3695 Patient-Episodes

Emma C. Davies[1,2], Christopher F. Green[3], Stephen Taylor[4], Paula R. Williamson[4], David R. Mottram[2], Munir Pirmohamed[5]*

A & E

National Surveillance of Emergency Department Visits for Outpatient Adverse Drug Events

Daniel S. Budnitz; Daniel A. Pollock; Kelly N. Weidenbach; et al.

Primary care

PATIENT SAFETY

Adverse Drug Events in Ambulatory Care

Tejal K. Gandhi, M.D., M.P.H., Saul N. Weingart, M.D., Ph.D., Joshua Borus, B.A., Andrew C. Seger, R.Ph., Josh Peterson, M.D., Elisabeth Burdick, M.S., Diane L. Seger, R.Ph., Kirstin Shu, B.A., Frank Federico, R.Ph., Lucian L. Leape, M.D., and David W. Bates, M.D.

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verse Drug Reactions

Adverse drug reactions experience in a teaching hospital in Jordan

Mohammed Alsbou[1] · Sameh Alzubiedi[2] · Hamed Alzobi[3] · Nawal Abu Samhadanah[4] · Yousef Alsaraireh[1] · Omar Alrawashdeh[5] · Amin Aqel[3] · Khalil Al-Salem[6]

Drug-induced admissions to medical wards at Jordan University Hospital

M. Gharaibeh[1], S. Zmeili[1], A. Abu-Rajab[2] and Z. Daoud[2]

[1]Department Pharmacology and
[2]Internal Medicine, Faculty of Medicine, University of Jordan, Amman, Jordan

(Inter J of Cl Phar & Ther,1998, 36(9):478-482)

Admission

In patients

Incidence of Adverse Drug Reactions in Alkarak Hospital: A Pilot Study

Mohammed Alsbou[*1]

(J Med J, 2010; 44(4):442-446)

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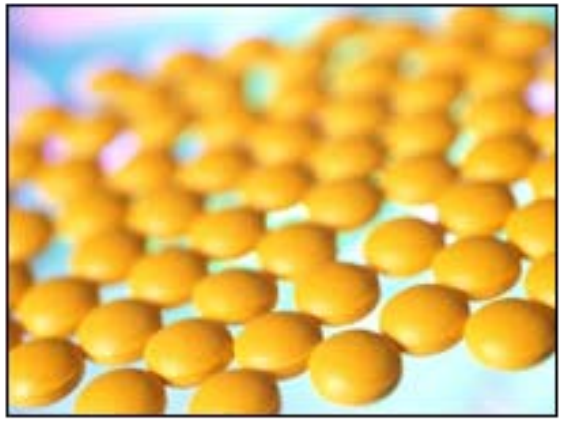
Medicines 'killing 10,000 people'

More than 10,000 Britons may be dying each year because of bad reactions to medication, a study suggests.

Researchers at the University of Liverpool assessed 18,820 people admitted to two hospitals in Merseyside between November 2001 and April 2002.



Some drugs can have serious side-effects

Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients

Munir Pirmohamed, Sally James, Shaun Meakin, Chris Green, Andrew K Scott, Thomas J Walley, Keith Farrar, B Kevin Park, Alasdair M Breckenridge

BMJ 2004;329:15–19

- **6.5%** (n=1224) of admissions are due to ADRs
- **Seven 800-bed** hospitals are occupied by ADR patients
- **Death** in **0.15%** - equivalent to **5700** deaths per year
- **Cost NHS £600 million per annum**

Incidence of Adverse Drug Reactions in Alkarak Hospital: A Pilot Study

Mohammed Alsbou[*1]

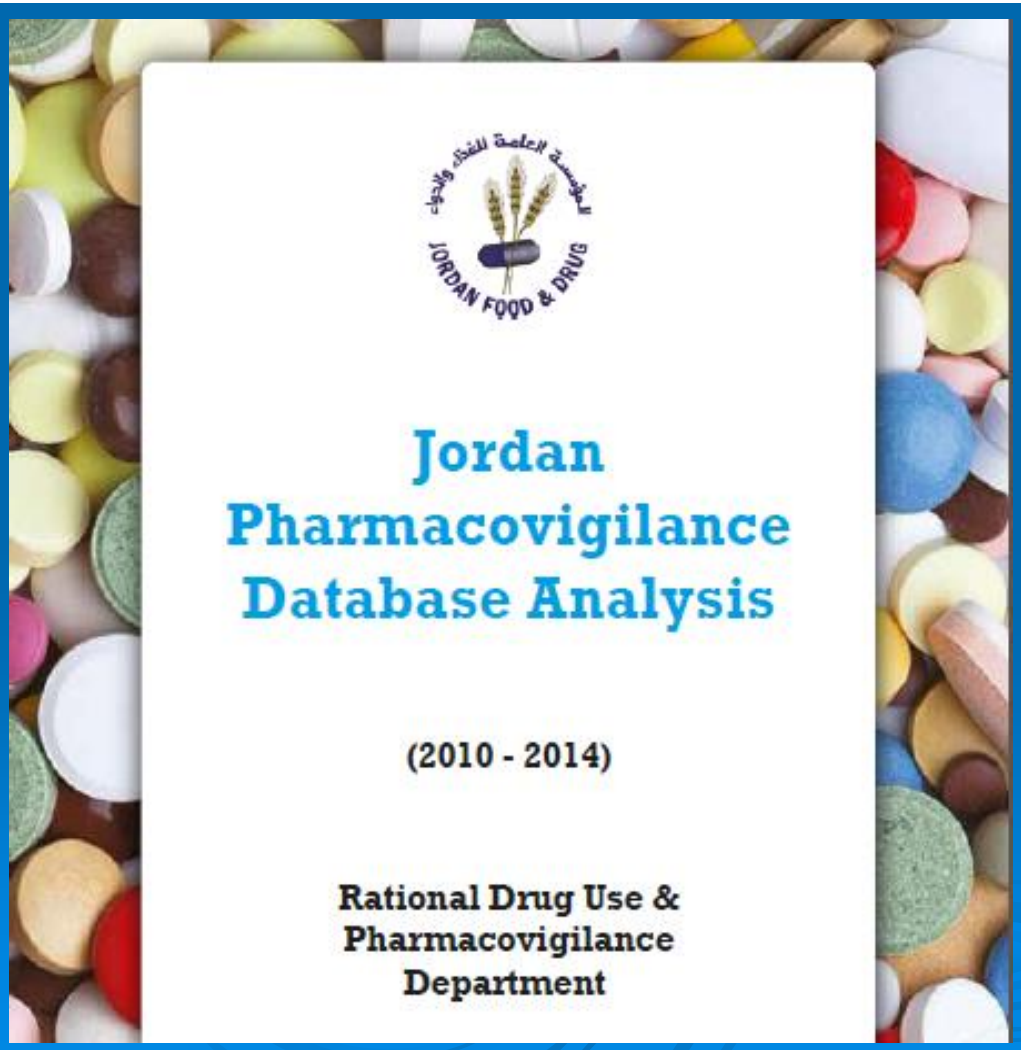
(J Med J 2010; Vol. 44 (4):442-446)

- **16 of 200 patients (8%)** suffered from one or more ADRs
- **50%** of ADRs were **avoidable**
- **One patient died** during admission and his death was contributed to an ADR

Biomedical & Pharmacology Journal Vol. **10**(1), 319-328 (2017)

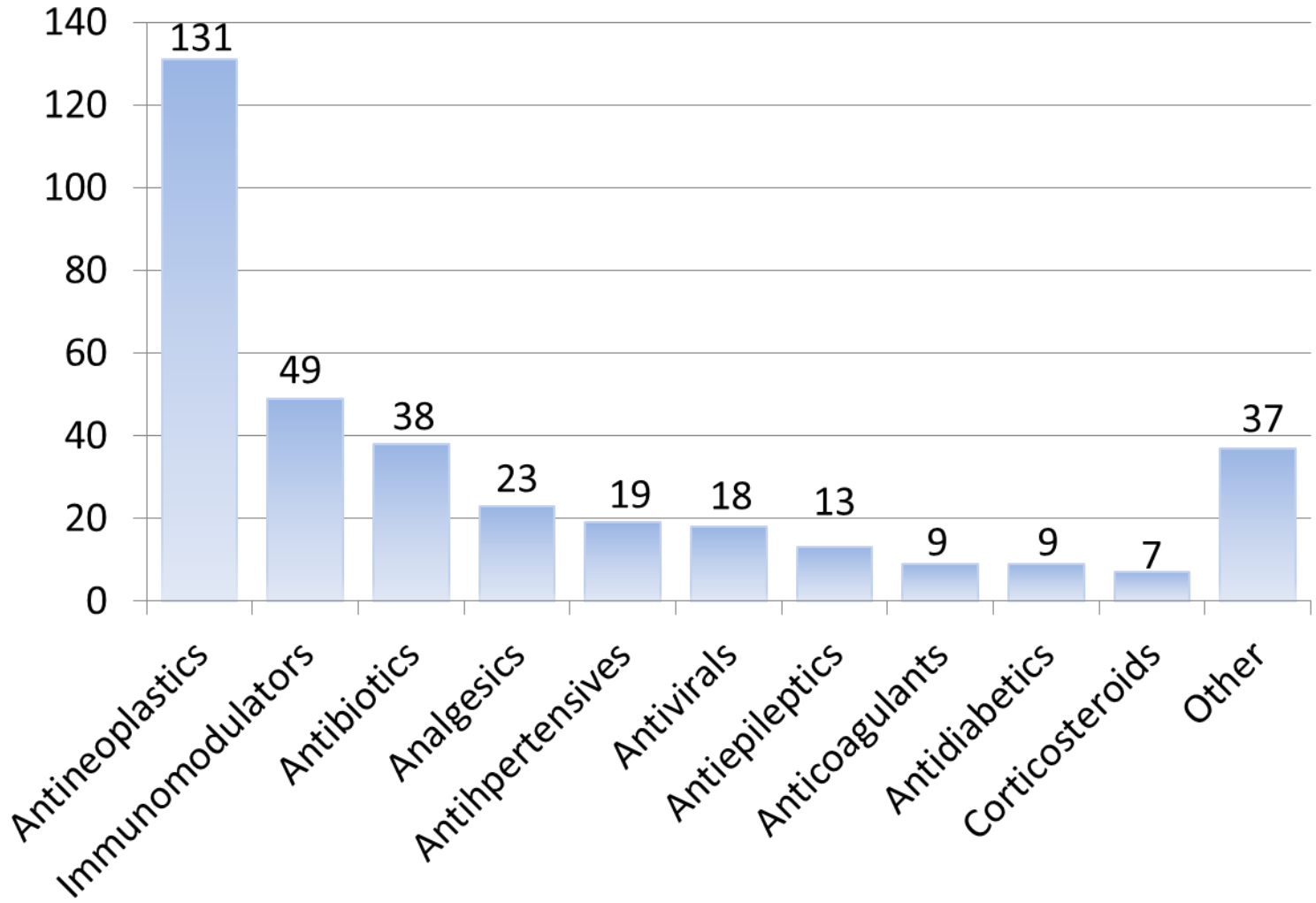
Analysis of the National Pharmacovigilance Database in Jordan (2010-2014)

MOHAMMED ALSBOU[1], GADEER ABDEEN[2], ADEL BATARSEH[3], NIDDA BAWARESH[4], JABER JABER[4], GADEER QAWASMI[4], TAQWA MAQATEF[4], HAYAT BANAT[4] and ABDELRAHMAN BATAYNEH[4]

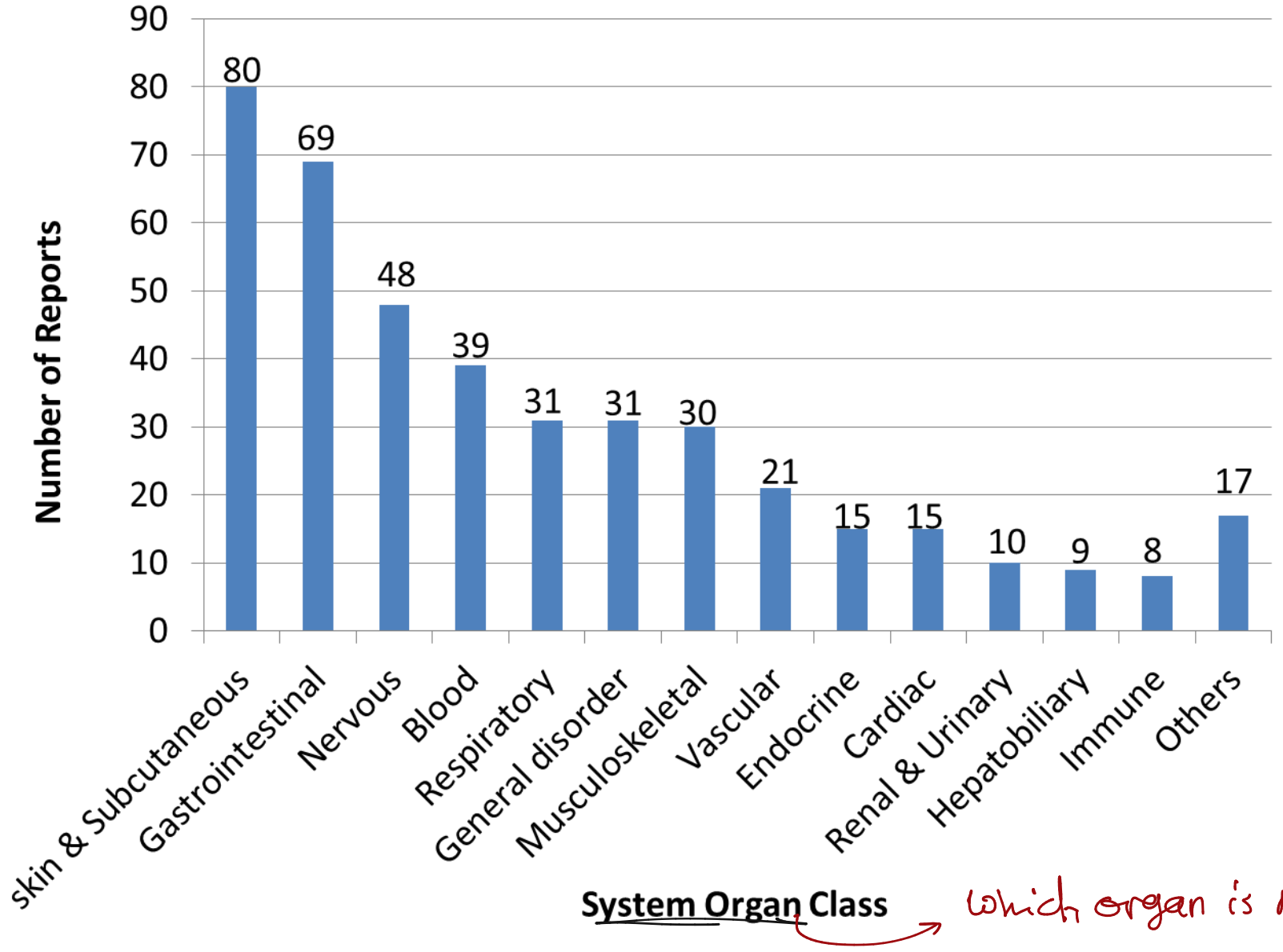


Number of ADR Reports / Drug Class

Based on



Number of ADR Reports / System Organ Class



Why report suspected ADRs?

- **Documentation of ADRs** in patients' records is often poor => Not good for greater good, why?
- **Physicians fear** that reporting of ADR may **put them at risk**
- **Under-reporting** is common phenomenon

Any Health Provider

even if it is mild ADR => report it!

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Methods of Reporting ADRs

- **Spontaneous reporting:**

  ‘Yellow Card system’

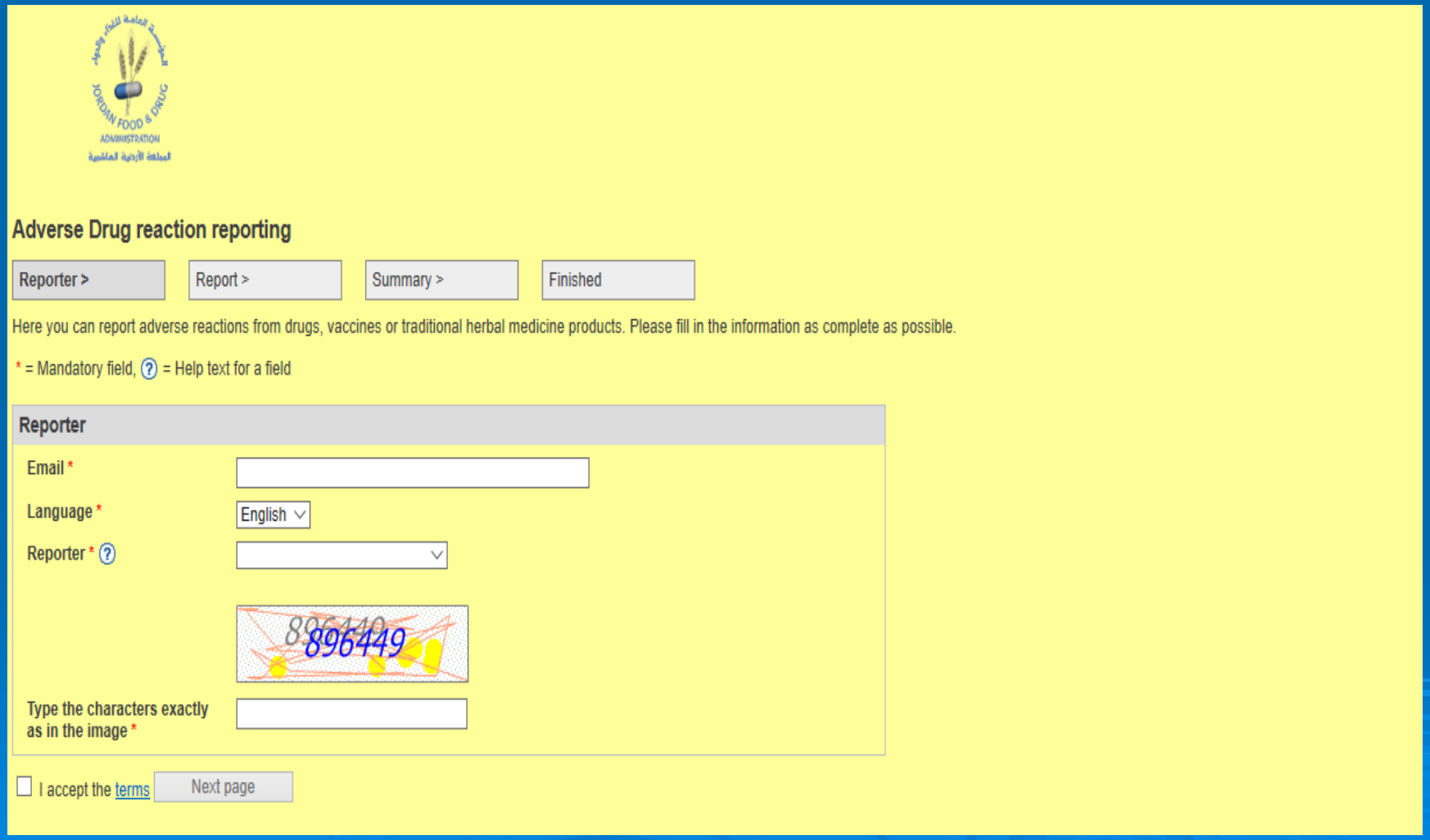
Reporting Methods

1- Spontaneous reporting: (Voluntary)

- Doctors, nurses & pharmacists are **supplied with forms** to record suspected ADRs
- Regional PV centers at hospitals
- Reporting ADRs to **National Pharmacovigilance Centre**
- **In UK** & jordan this is called **'Yellow Card system'**

→ All the reports goes there for documentation.

Online ADRs reporting form



Paper Form

نموذج رصد الآثار الجانبية للأدوية المشتبه بحدوثها والمشاكل المتعلقة بالمستحضرات الصيدلانية

ملاحظة : المعلومات المتعلقة بشخص كل من المبلغ، المريض، المؤسسة المعنية ستبقى سرية

رقم الملف الطبي : ..... ☐ذكر : ..... الوزن : ..... كغم الطول : ..... سم العمر : ..... سنة

الأحرف الأولى من اسم المريض : ..... ☐انثى هل المريضة حامل:؟ ☐ نعم ☐ لا إذا كنت حامل فأي مرحلة؟

	اسم الدواء/الأدوية (الاسم التجاري) التي يتناولها المريض	اسم المصانع ورقم التشغيلية	شكل الدواء وطرقة استخدامه	الجرعة والتركيز	تاريخ ابتداء تناول الدواء	تاريخ توقف عن تناول الدواء	دواعي استعمال الدواء
الأدوية المشتبه بها	١ -						
	٢ -						
	٣ -						
الأدوية الأخرى	١ -						
	٢ -						
	٣ -						

الآثار الجانبية المشتبه بحدوثها والمشاكل المتعلقة بالدواء (نقص في فاعلية الدواء، عيوب تصنيعة ... الخ	تاريخ ظهور الأثر الجانبي أو المشكلة	الفترة الزمنية للأثر الجانبي أو المشكلة أو تاريخ توقف الأثر الجانبي أو المشكلة
١ -		
٢ -		
٣ -		

ملاحظات : (تاريخ سابق متعلق بالمرض، حساسية، استعمال مسبق للدواء ..... الخ).

تبعات الأثر/الآثار الجانبية:

- هل تبعات الأثر الآثار الجانبية خطيرة؟ ☐ نعم ☐ لا إذا كانت خطيرة، فما هي:

☐وفاة المريض (تاريخ الوفاة:..... سبب الوفاة: .....)

☐تهديد الحياة للمريض ☐ دخول مستشفى ☐ إطالة مدة إقامة المريض في المستشفى

☐إعاقة مستديمة ☐ ظهور عيب خلقي

☐تبعات أخرى (اذكرها .....)

- حالة المريض يوم كتابة التقرير :

☐شفاء تام ☐ الشفاء التام متوقع ☐ شفاء مع ظهور نقص وظيفي

☐وفـــاة ☐ غير معلوم النتائج ☐ تبعات أخرى (اذكرها:.....)

- هل تم إيقاف استخدام أي من الأدوية المشتبه بها ؟ ☐نعم ☐ لا إذا كانت الإجابة نعم، أي دواء تم إيقافة ؟

- هل توقف الأثر الجانبي بعد توقف استخدام الدواء ؟ ☐نعم ☐ لا ☐ غير معروف

- ما هو الأثر /الآثار الجانبية التي توقفت ؟..... بعد إعادة تناول ؟

☐نعم ☐ لا ☐غير معروف

- اسم المبلغ ووصفه الوظيفي: (طبيب، طبيب أسنان، صيدلي، ممرض):

عنوان العمل :..... توقيع المبلغ : ..... التاريخ :..... رقم الهاتف :..... الصندوق : .....

البريدي :..... البريد الألكتروني : ..... رقم الفاكس :.....

خاص بالمؤسسة العامة للغذاء و الدواء

- تاريخ استلام التقرير :..... - رقم التقرير الخاص بالبرنامج : .....

ملاحظة : عند وجود الحاجة إلى حيز أكبر ، أرفق تقرير آخر

المؤسسة العامة للغذاء والدواء

ص.ب : ٨١١٩٥١ جبل عمان ١١١٨١ - هاتف : ٤٦٠٢٠٠٠ / ٠٦ - فاكس : ٥٦٢٦٣٢٥ / ٠٦

البريد الالكتروني : jpc@jfda.jo - العنوان على الانترنت : www.jfda.jo

يقبل بدون طوابع على
حساب المؤسسة العامة
للغذاء والدواء

For JFDA Use Only

لاستخدام المؤسسة العامة للغذاء والدواء

Question	Yes	No	Do not Know or not Done
1. Are there previous conclusive reports on this reaction?	(+1)	(0)	(0)
2. Did the adverse event appear after the suspected drug was given?	(+2)	(-1)	(0)
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	(+1)	(0)	(0)
4. Did the adverse reaction appear when the drug was readministered?	(+2)	(-2)	(0)
5. Are there alternative causes that could have caused the reaction?	(-1)	(+2)	(0)
6. Did the reaction reappear when a placebo was given?	(-1)	(+1)	(0)
7. Was the drug detected in any body fluid in toxic concentrations?	(+1)	(0)	(0)
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	(+1)	(0)	(0)
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	(+1)	(0)	(0)
10. Was the adverse event confirmed by any objective evidence?	(+1)	(0)	(0)

World Health Organization

International Collaboration

⇒ Also Responsible to documentary these reports.

- **WHO International Drug Monitoring programme, 86 member nations** have systems **to record & report ADRs**
- Member countries send their report to **Uppsala Monitoring Centre (Sweden)** where they are entered into **WHO Database**

⇒ Location

- **WHO** database **(vigibase)** include **15 million** case reports

U.S. Food and Drug Administration

- **MedWatch** is **FDA** reporting system in U.S. for adverse effects of drugs

Jordan Food & Drug Administration (JFDA)

Jordan Pharmacovigilance Centre

Pharmacovigilance Center for South Jordan/ Alkarak Governmental Hospital

لا تتردد

بالإعلام عن أي آثار جانبية للدواء المستخدم

Don't Hesitate

to inform about any adverse reactions of your medicine


Jordan National Drug Formulary
(JNDF)
USAID
Ministry of Health
Royal Medical Services


BNF
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