Pharmacovigilance & Adverse Drug Reactions

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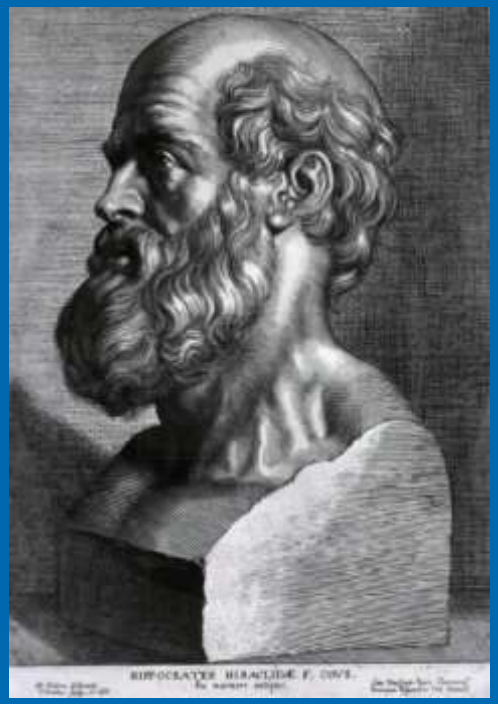
'First of all be sure you do no harm'

Hippocrates (460-370 BC)



Pharmacovigilance (PV)

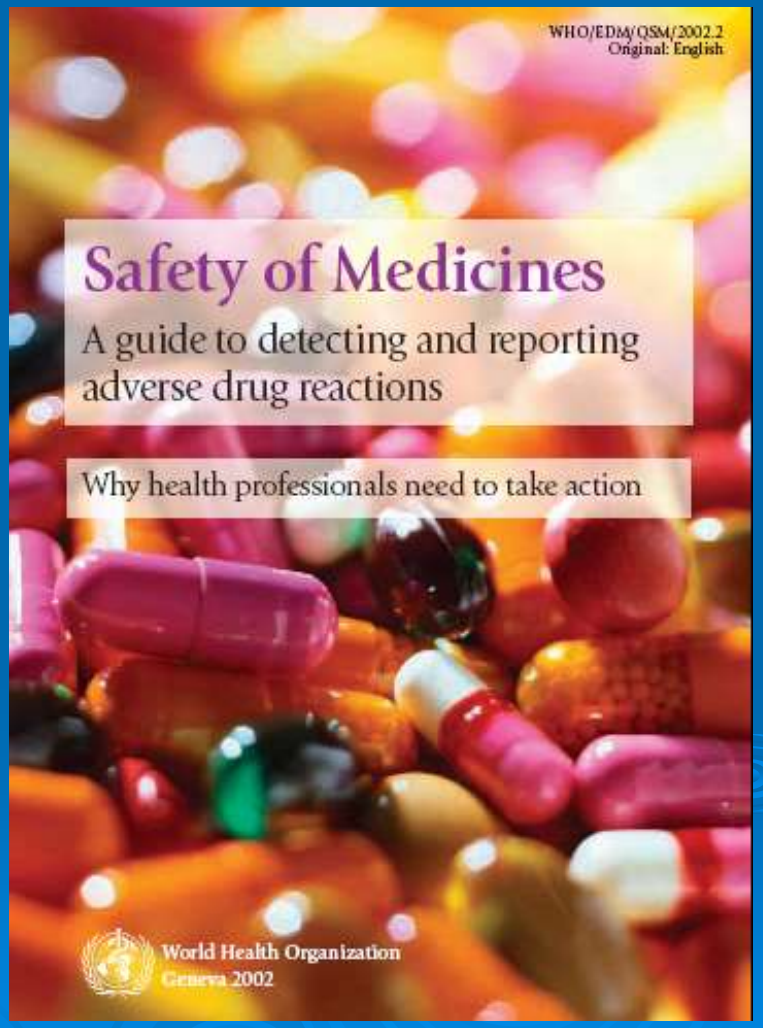
- **The root of pharmacovigilance:**

  Pharmaco (Greek)= **Drug**

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

Pharmacovigilance (PV)

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



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**

Why Pharmacovigilance?

- **In clinical trials:**

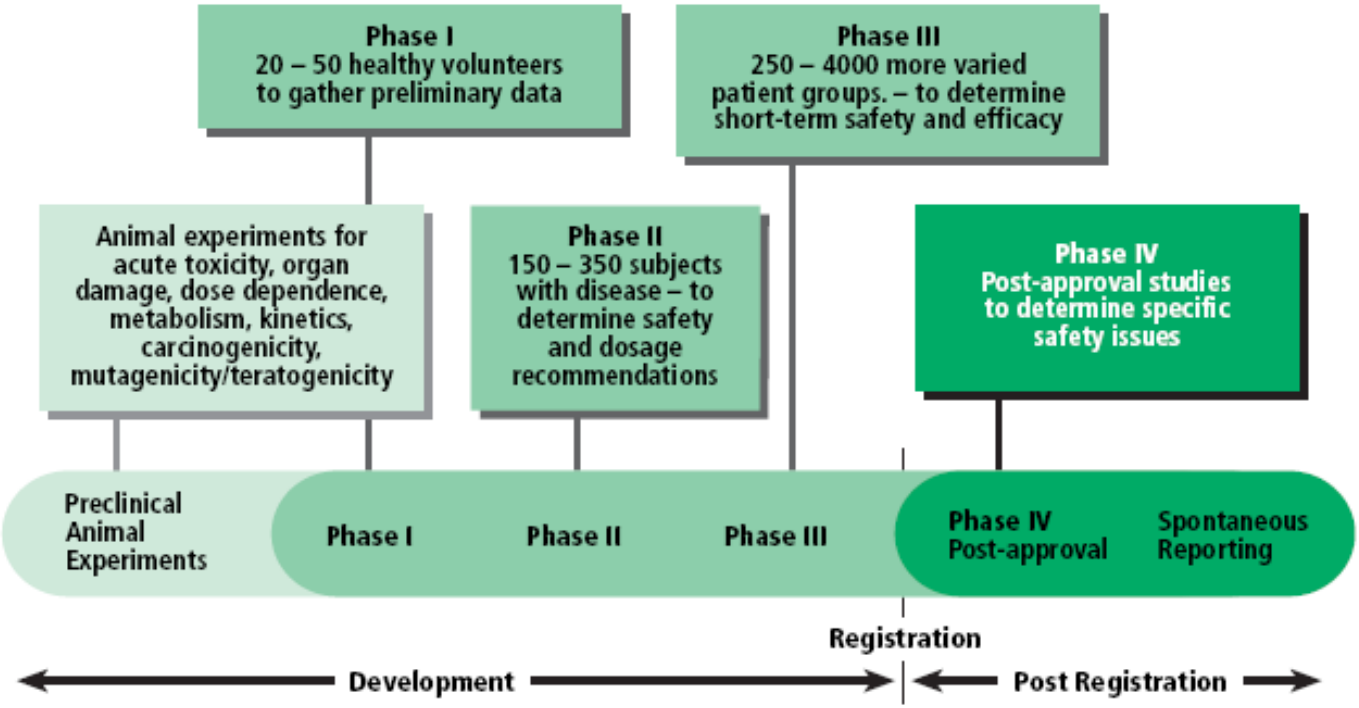
- Patients are limited in number
- Conditions of use differ from those in clinical practice
- Duration of trials is limited

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



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"

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

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):
  - ARBs (Valsartan, Losartan, Irbesartan) 2019
  - Reductil (Sibutramine) 2010
  - Valdecoxib (Bextra) 2005
  - Rofecoxib (Vioxx) 2004

Classification of ADRs

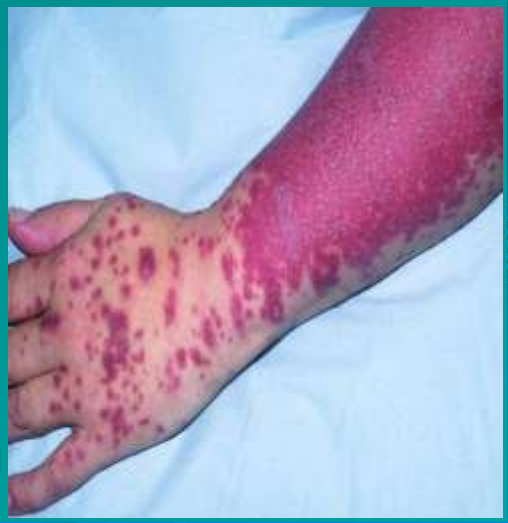
- **Classification of Rawlins & Thompson**

Type A reactions

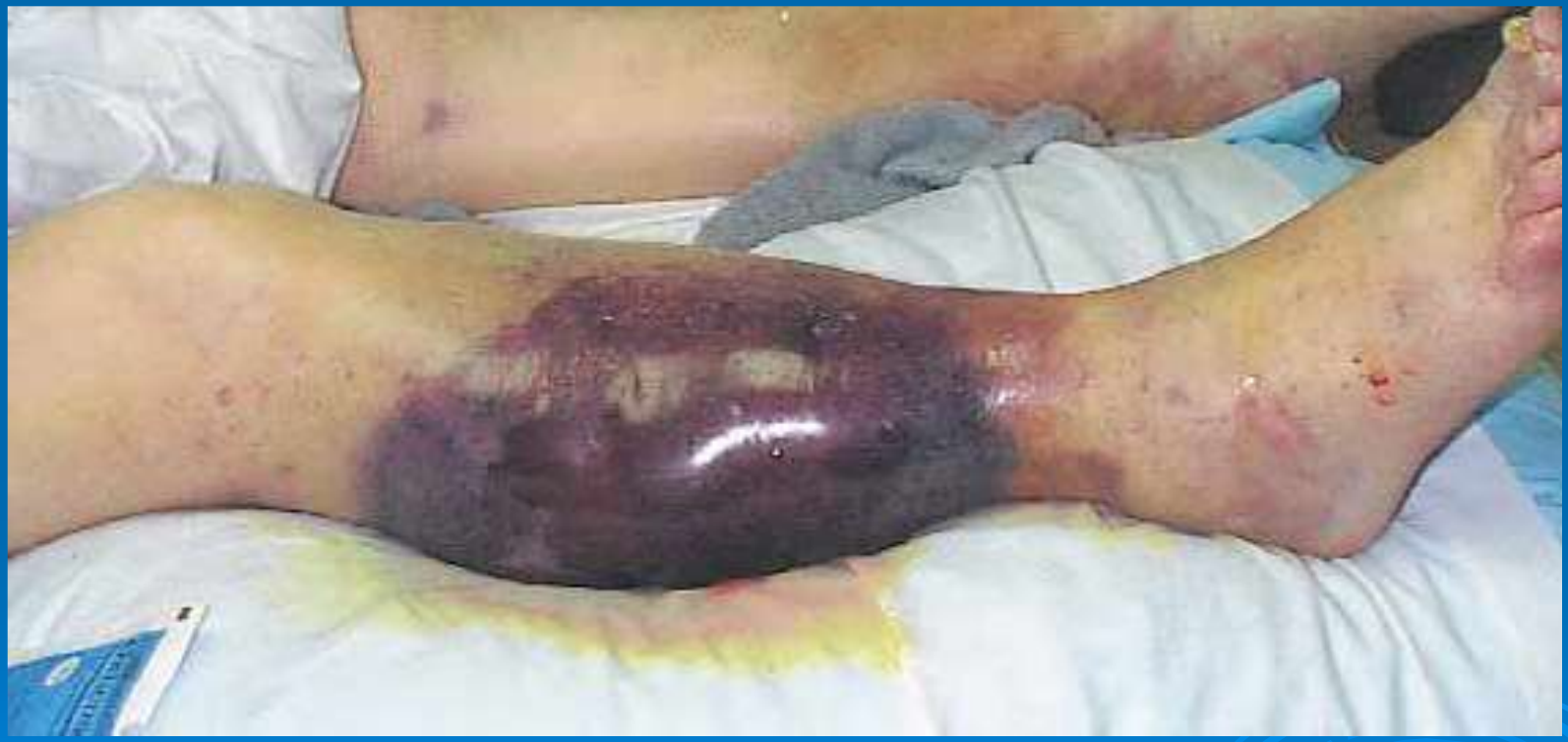
- Augmentation of known pharmacological effect of drug
- Predictable
- Dose related
- **e.g. warfarin causing bleeding**

Type B reactions

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



Warfarin-induced calf haematoma



Carbamazepine-induced Stevens Johnson Syndrome (SJS)

- 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

Risk Factors Predisposing to ADRs

- Age
- Long duration of treatment
- Polypharmacy
- Liver, kidney diseases

Causes of ADRs

1. Patient
2. Drug
3. Prescriber
4. Environmental factors

Causes of ADRs

1. The patient:

- Age (over 60)
- Genetic factors (e.g. polymorphisms in CYP450)
- Previous history of ADR
- 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
- At a critical phase in pregnancy
- Given with other drugs **(drug-drug interactions)**

4. Environmental factors:

- Diet, smoking, alcohol

Drugs Most Commonly Causing ADRs

- Warfarin
- Diuretics
- Digoxin
- Antibacterials
- Steroids
- 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.

Burden of Adverse Drug Reactions

Admission

Drug-induced admissions to medical wards at Jordan University Hospital

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

In patients

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

Mohammed Alsbou[*1]

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

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]

Int J Clin Pharm (2015) 37:1188–1193

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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]

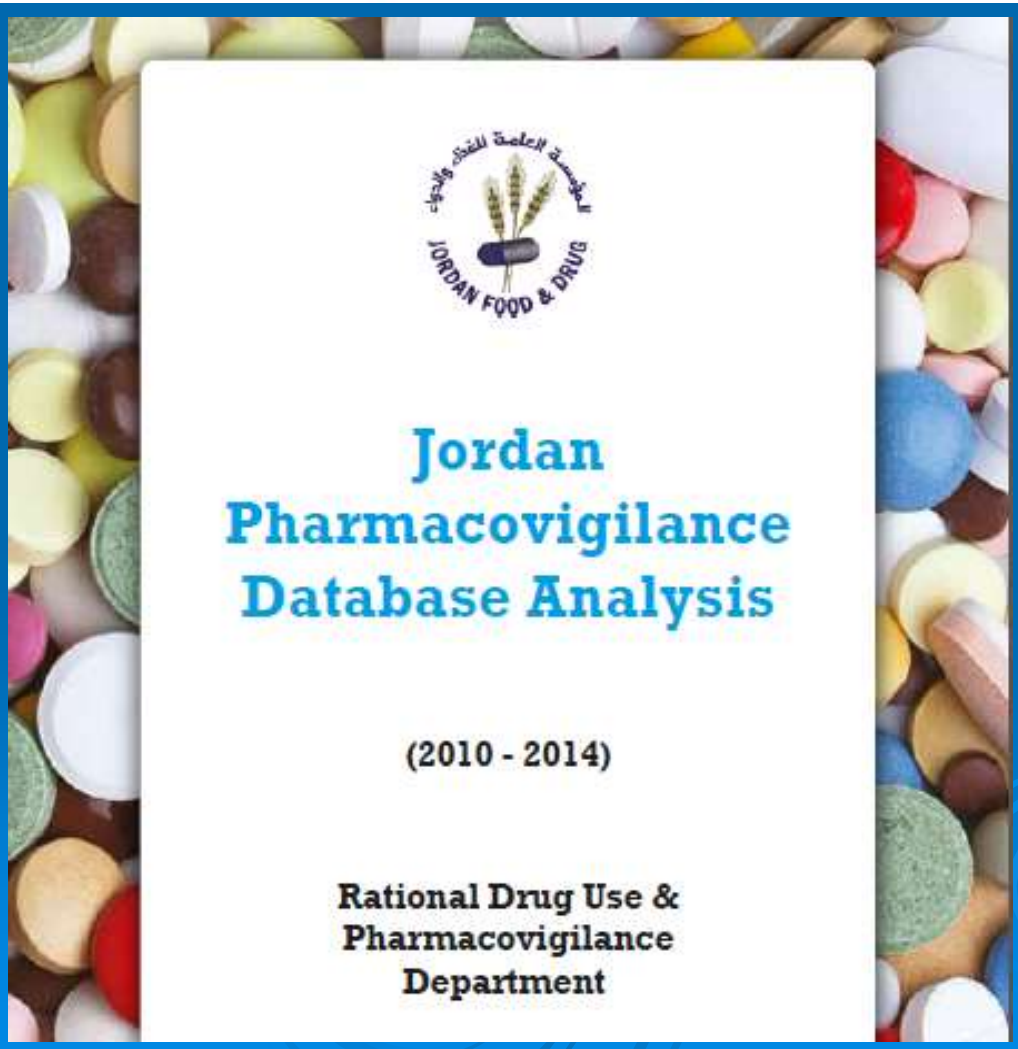
(J Med J 2010; Vol. 44 (4):442-446)

- **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

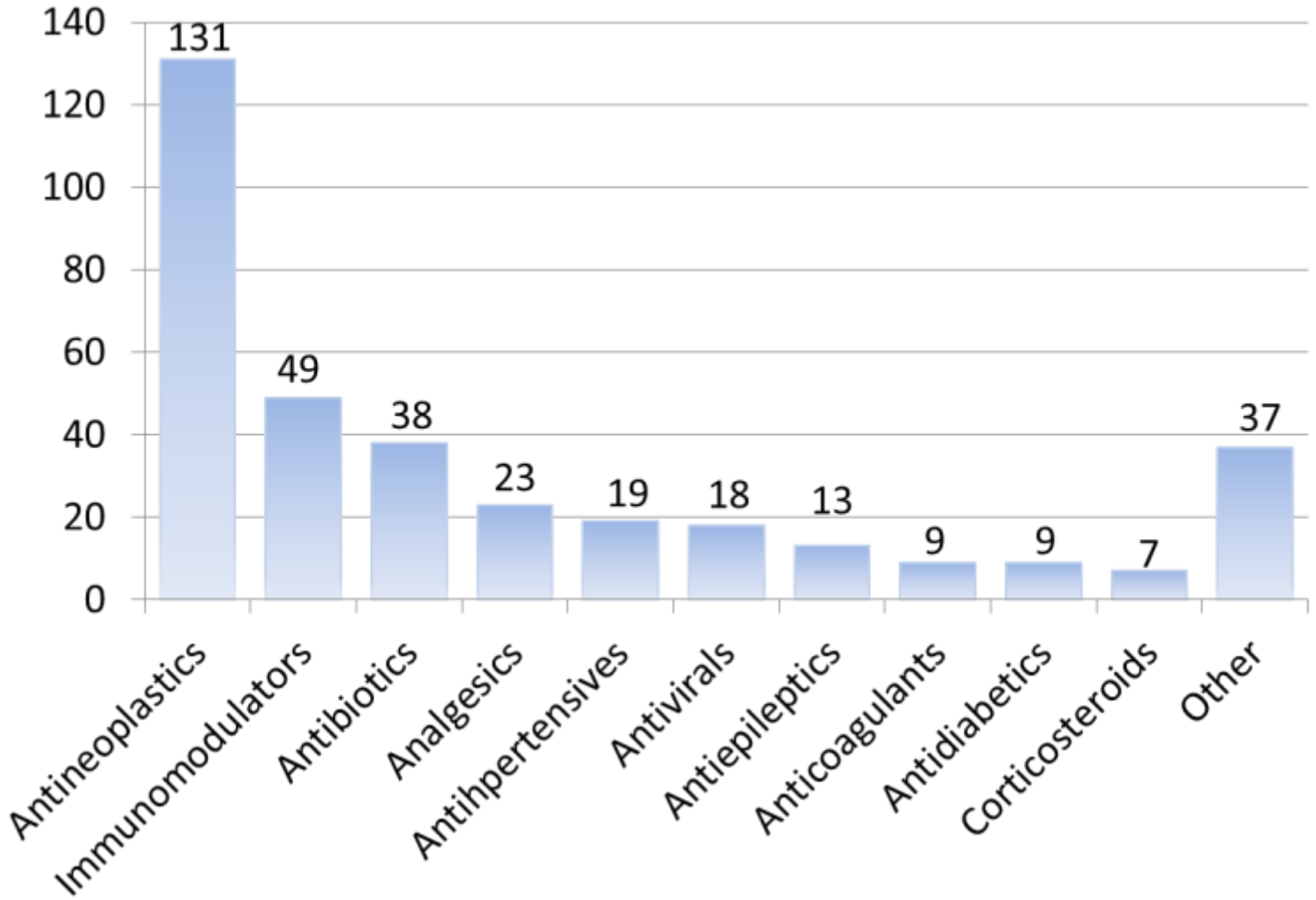
Biomedical & Pharmacology Journal Vol. **10**(1), 319-328 (2017)

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

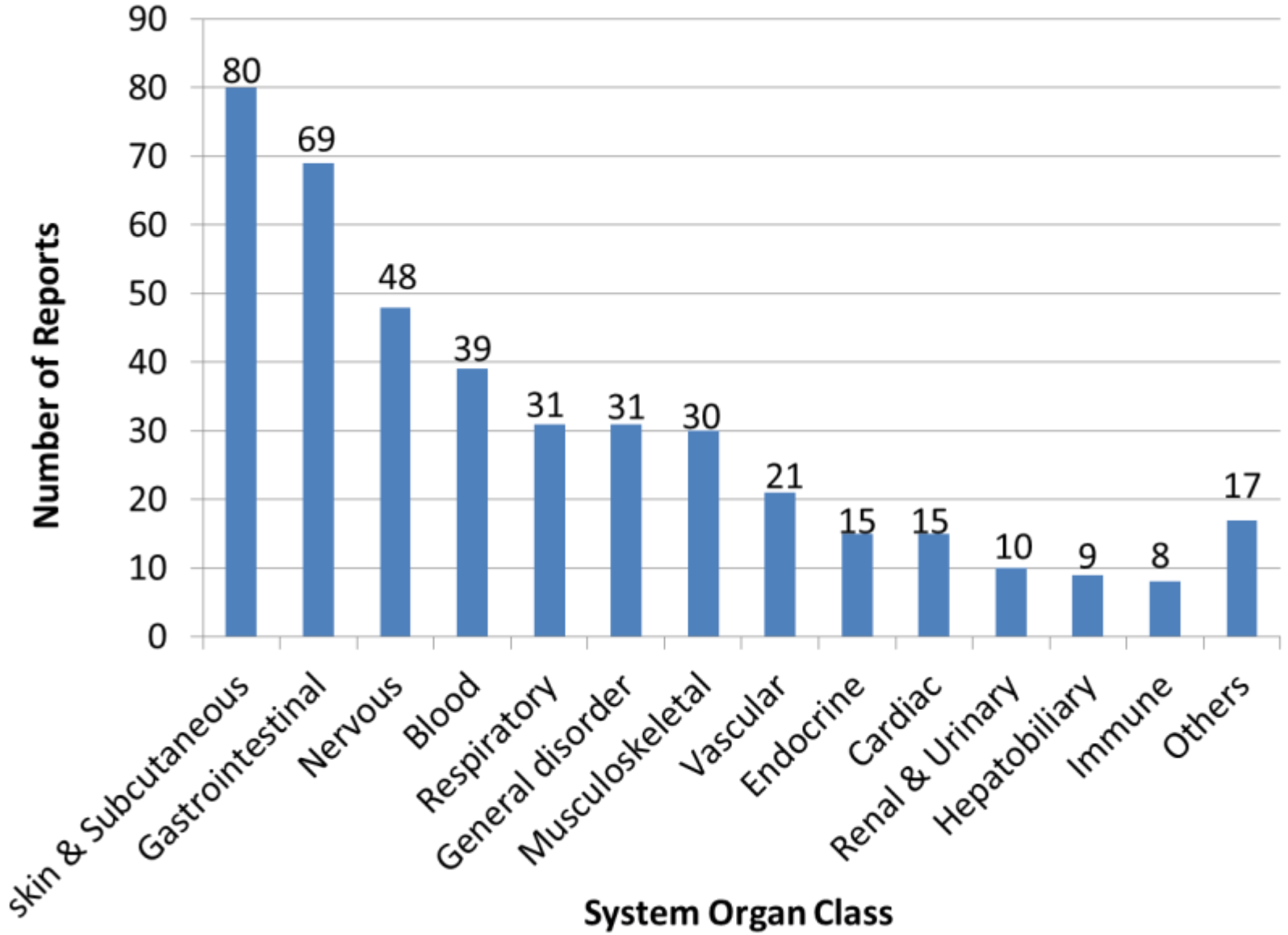
MOHAMMED ALSBOU[1], GADEER ABDEEN[2], ADEL BATARSEH[3], NIDDA BAWARESH[4], JABER JABER[4], GADEER QAWASMI[4], TAQWA MAQATEF[4], HAYAT BANAT[4] and ABDELRAHMAN BATAYNEH[4]



Number of ADR Reports / Drug Class



Number of ADR Reports / System Organ Class



Why report suspected ADRs?

- **Documentation of ADRs** in patients' records is often poor
- **Physicians fear** that reporting of ADR may put them at risk
- **Under-reporting** is common phenomenon

Methods of Reporting ADRs

- Spontaneous reporting:

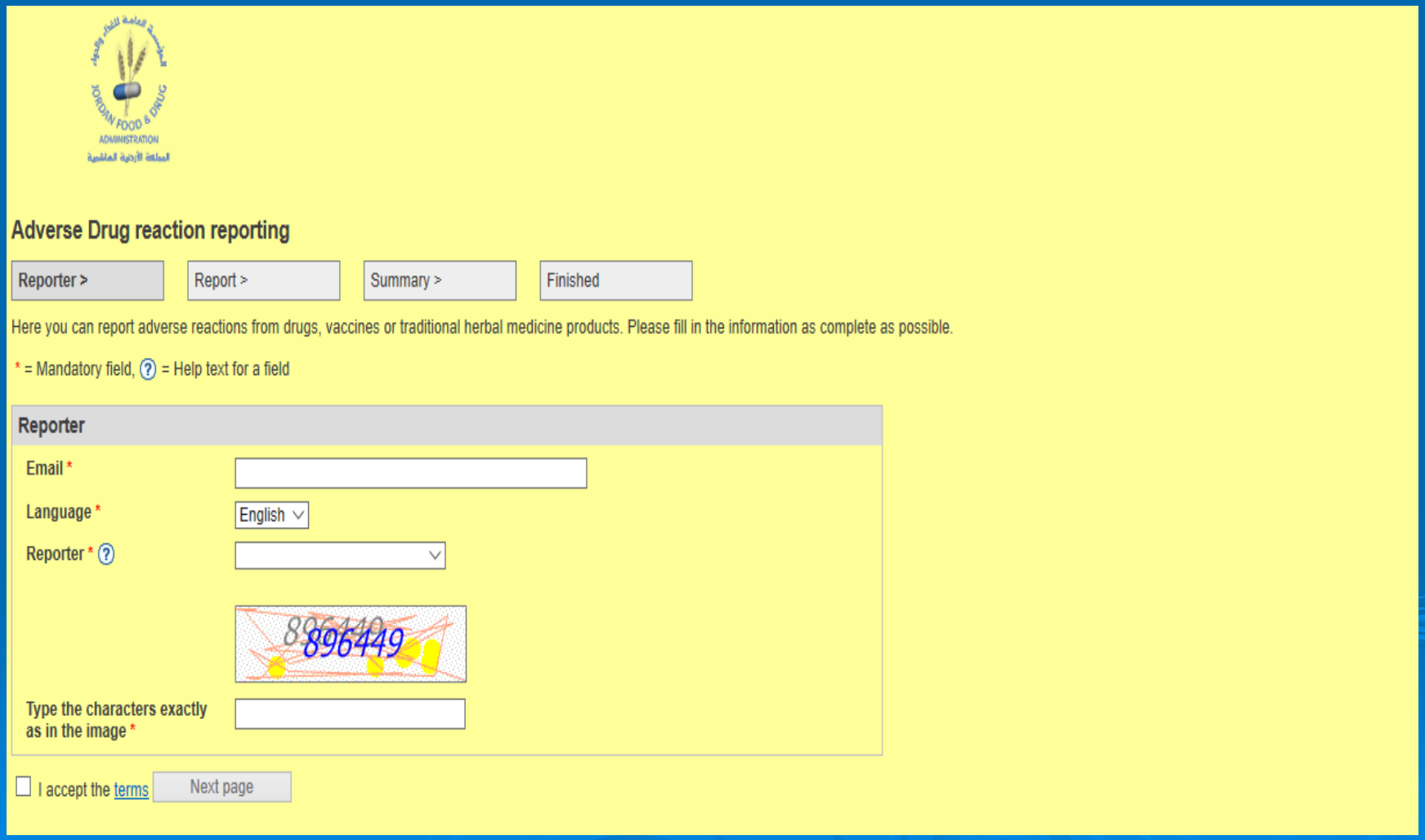
  'Yellow Card system'

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'**

Online ADRs reporting 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 ☐ أنثى الوزن : _____ كلغ الطول : _____ سم العمر : _____ سنة

الأحرف الأولى من اسم المريض : _____ هل المريضة حامل؟ ☐ نعم ☐ لا إذا كانت حامل فأي مرحلة؟

	اسم الدواء(الأدوية (الاسم التجاري) التي يتناولها المريض	اسم المصانع ورقم التشغيلة	شكل الدواء وطريقة 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 سيئ 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 أو من الأدوية المشتبه بها ؟ ☐ نعم ☐ لا إذا كانت الإجابة نعم، أي دواء تم إيقافه ؟

- 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

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حساب المؤسسة العامة
للغذاء والدواء

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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

- **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**

- **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

JPC

منظمة الصحة العالمية

يمكنك تعبئة نموذج الإبلاغ عن أية آثار جانبية للأدوية أو المستلزمات الطبية استخدم النموذج المتوفر في أي مستشفى أو اقرب مركز صحي لديك والاتصال بنا على هاتف رقم (4602000) لاستلامه باليد. كما يمكنك تحميل التقرير من الموقع الالكتروني www.jfda.jo

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