An Introduction to Drug Safety/Pharmacovigilance

MotecLife AGM

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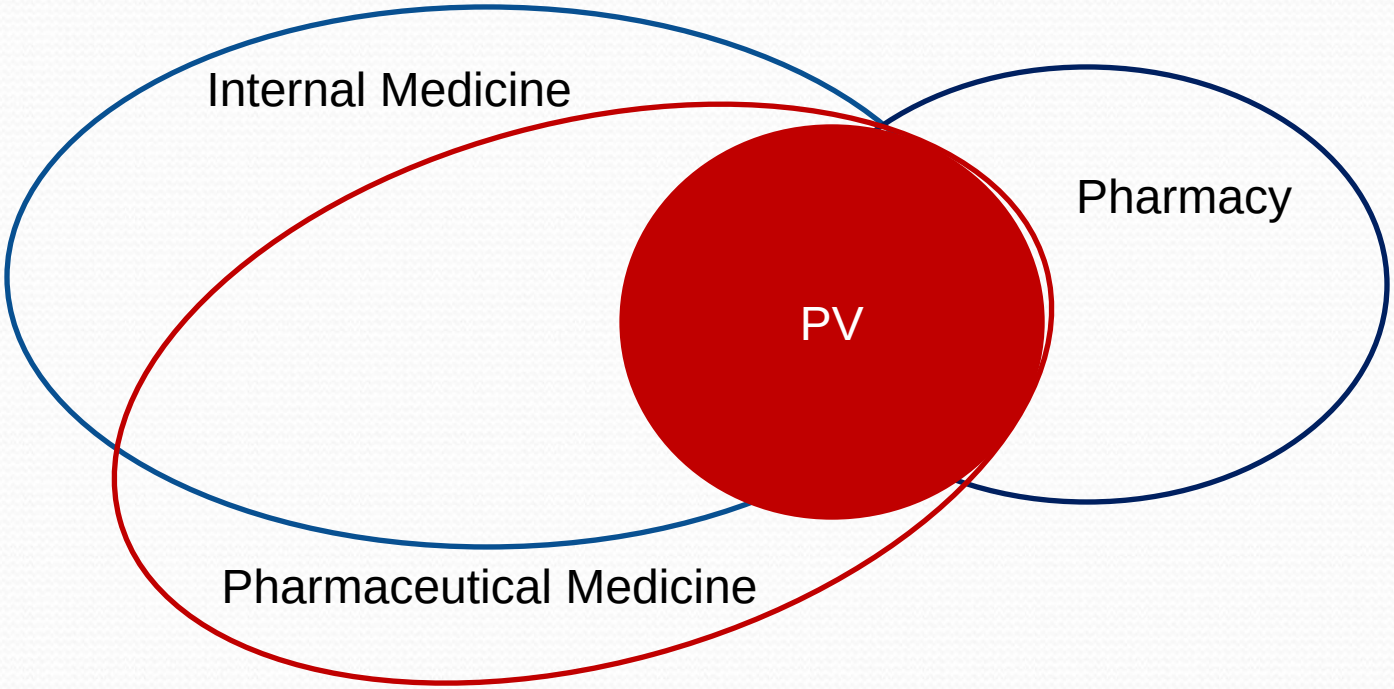
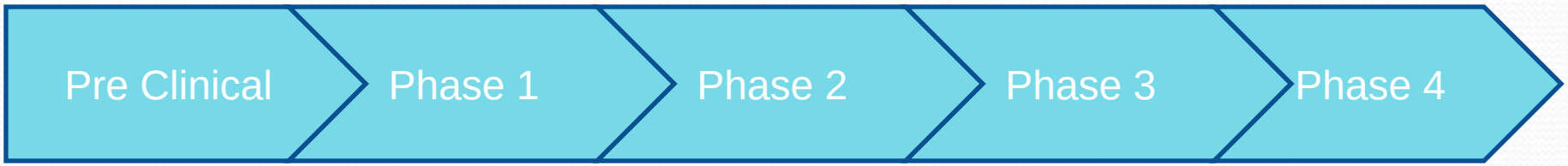
Pharmaceutical Medicine



Drug Development



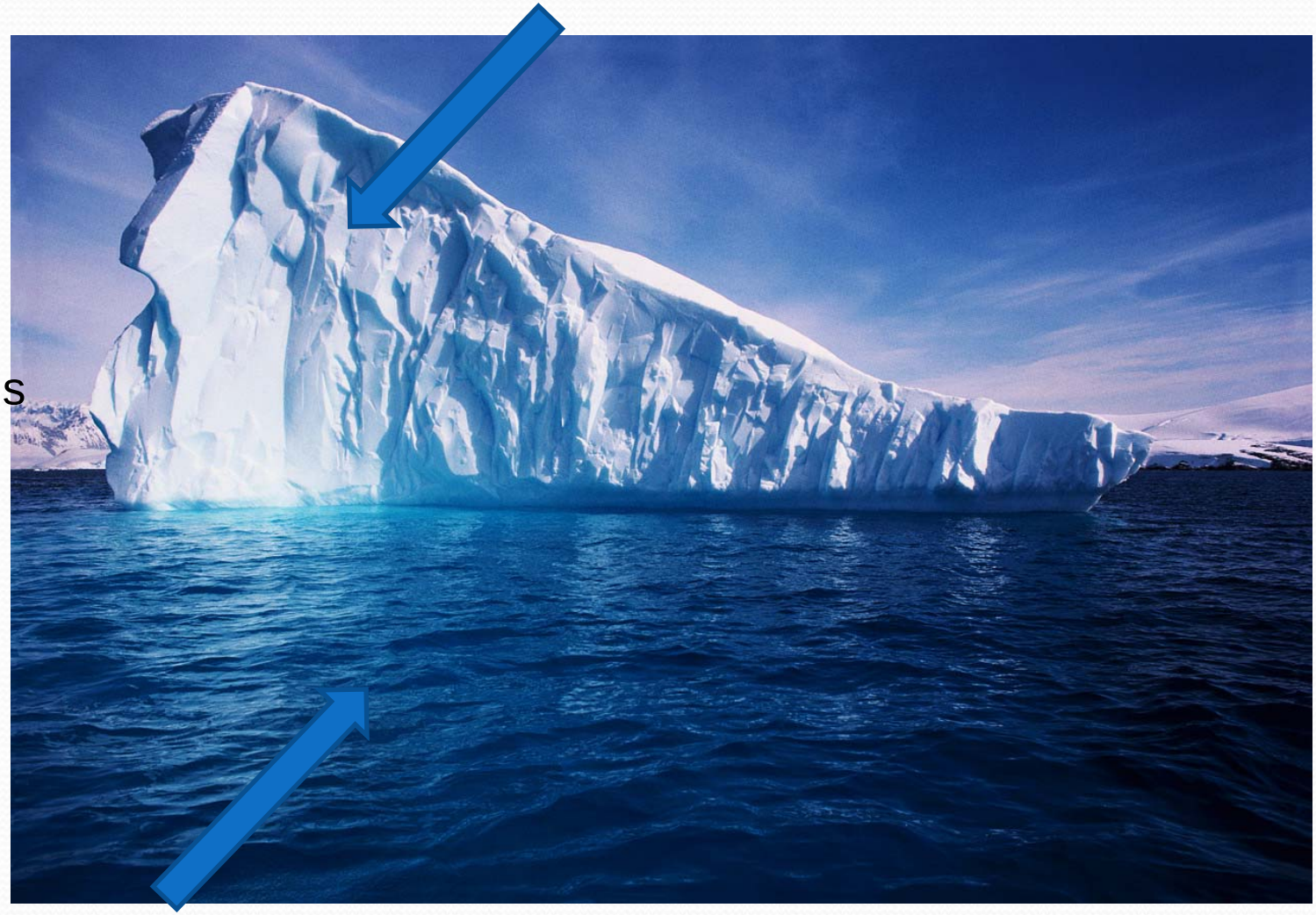
Entry into man

Post marketing

Pharmacovigilance

What we know at the end of the clinical trial programm

Most new drugs are not tested in Africans!

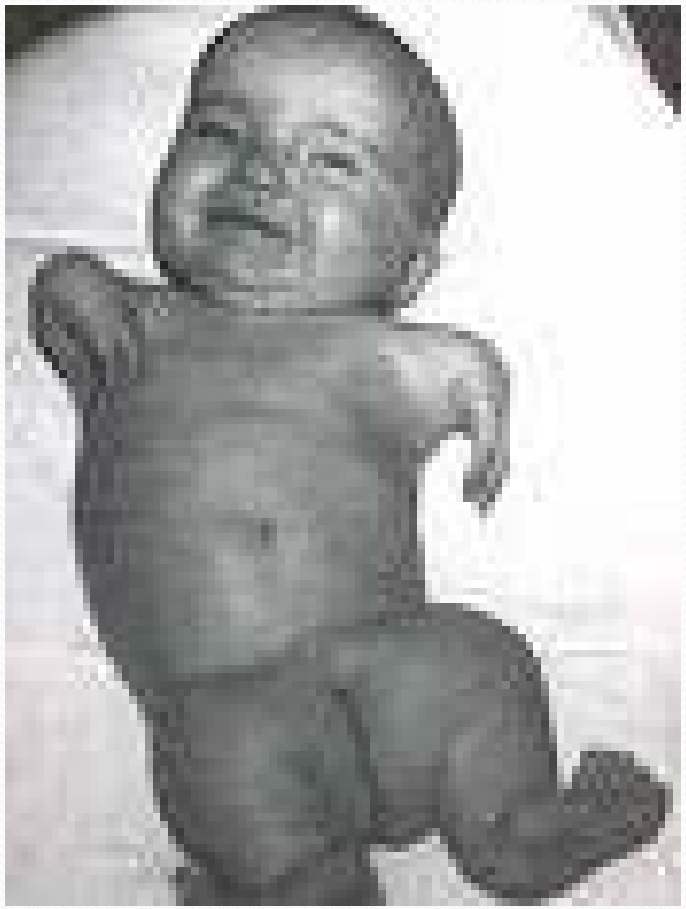


What happens when drug used in normal practice

Limitations of Clinical Trials

- Homogenous patient populations
- Restricted patient populations; one disease, and exclude many populations eg pregnancy, children, elderly
  - Do not reflect the ‘real’ world
- Inability to predict drug - drug interactions
- Small sample size
  - NB: At least 30,000 people need to use a drug in order to identify a rare AE with an incidence of 1:10,000 with 95% power
- Limited duration/Short follow up

Yellow Card System



- Vital public health mechanism
- Essential component in Regulatory Authority's pharmacovigilance work
- To date, more than 500,000 UK reports submitted
- Reports submitted ***in confidence*** by healthcare professionals & patients

- www.yellowcard.gov.uk

Black Triangle Scheme

- A black triangle indicates intensive monitoring by the Regulators
- Assigned if the drug/vaccine is a new active substance.
- Products containing previously licensed active substances may also be monitored:
  - a new combination of active substances
  - administration via a new route of administration or drug delivery system
  - a significant new indication which may alter the established benefit/risk profile of that drug
- Assessment is usually made following 2 years of post-marketing experience

What is Drug Safety or Pharmacovigilance?

Pharmacovigilance is the science & activities relating to the

- detection,
- assessment,
- understanding
- prevention

of adverse effects of any other drug related problems

WHO 1992

Definition of an Adverse Event

- Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. - ICH

- Adverse Drug **Reaction** (ADR) implies a **causal relationship** between the event and the drug.

Classification of Adverse Drug Reactions

Type A: Most common type of reaction

- Usually predictable from the known pharmacological properties of a drug
- (augmented reaction). Generally less serious
- Eg Dehydration with diuretics; postural hypotension with antihypertensives

Type B: Uncommon, "bizarre" reaction

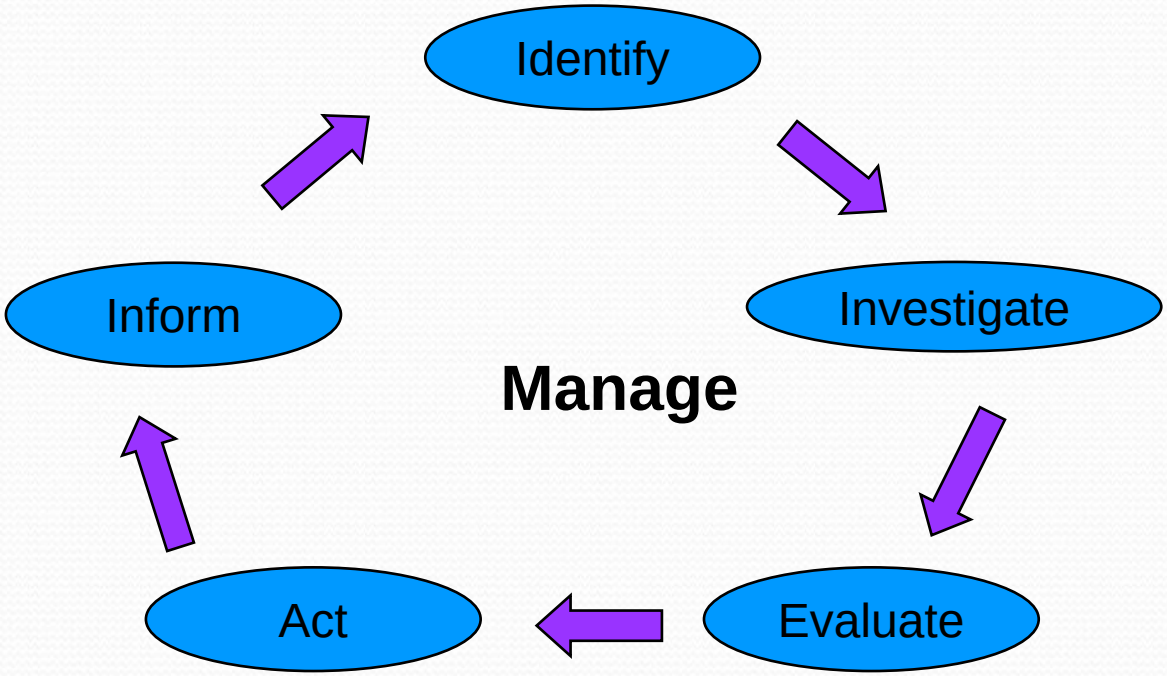
- Unpredictable & unrelated to known pharmacological properties of the agent.
- More likely to have serious consequences than Type A
- Eg Torsades de pointes with terfenadine; agranulocytosis with carbimazole

Examples of known ADRs

- **Teratogenesis:** Anti-epileptic phenytoin causing craniofacial malformation
- **Delayed:** Endometrial polyps or carcinoma with long term tamoxifen
- **Allergic:** Type IV hypersensitivity reaction: contact dermatitis with penicillin
- **Withdrawal reaction:** Abrupt withdrawal of high dose corticosteroids: adrenal insufficiency
- **Drug interactions:** Concomitant use of potassium-sparing diuretic with an angiotensin-converting enzyme inhibitor risks hyperkalaemia.

Pharmacovigilance: A Risk Management Process

- The key players are regulatory authorities, pharmaceutical companies and health professionals. :



Adapted from material produced by Drug Safety Research Unit

Thank you