

Population Pharmacokinetics of Phenytoin in Saudi Patients

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Introduction

Chemistry

Hydantoin-derivative anticonvulsant

Insoluble in water

Soluble in hot alcohol

Pharmacology

Anticonvulsant agent.

Antiarrhythmic agent Class 1-B

Introduction

Pharmacokinetics

Absorption: Cap=92% (peak: 4 – 12 hr)

Sus=100% (peak: 1- 3 hr)

Distribution: V_{dss} : 0.6 – 1.2 L/kg

Crosses the Placenta

Crosses into Breast Milk

Half-life: 22 hr

Introduction

Pharmacokinetics

Metabolism Oxidation (Liver)

Elimination: As HPPH metabolite in bile & urine
 <5% unchanged in urine

Introduction

Therapeutic uses

- Generalized Tonic-Clonic (Grand mal)
- Simple and Complex Partial seizures.
- Prevention of seizures following trauma and neurosurgery.
- Status epilepticus.
- Ventricular Arrhythmia.

Adverse effects

Dizziness, insomnia, headache, N, V, constipation
Gingiva hyperplasia, Encephalopathy and nystagmus

Introduction

Dosage

Children

- Loading dose
 - 15-20 mg/kg/day (in 3 divided doses)
- Maintenance dose (mg/kg/day)
 - 6 m-3 yr: 8 - 10
 - 4-6 yr: 7.5- 9
 - 7-9 yr: 7 - 8
 - 10-16 yr: 6 - 7

Adults

- Loading dose
 - 15-20 mg/kg/day (in 3 divided doses)
- Maintenance dose
 - 300 mg/day (or 5-6 mg/kg/day, as tid)

Introduction

Precautions and contraindications

Hypersensitivity to phenytoin

Severe liver disease

Heart block, sinus bradycardia

Pregnancy (category D) and lactation

Use with caution in:

DM

Elderly

Pts with porphyria

Introduction

Drug interactions

↑ PHT level

Eethosuximid
INH
Fluconazole
Diazepam
Estrogen

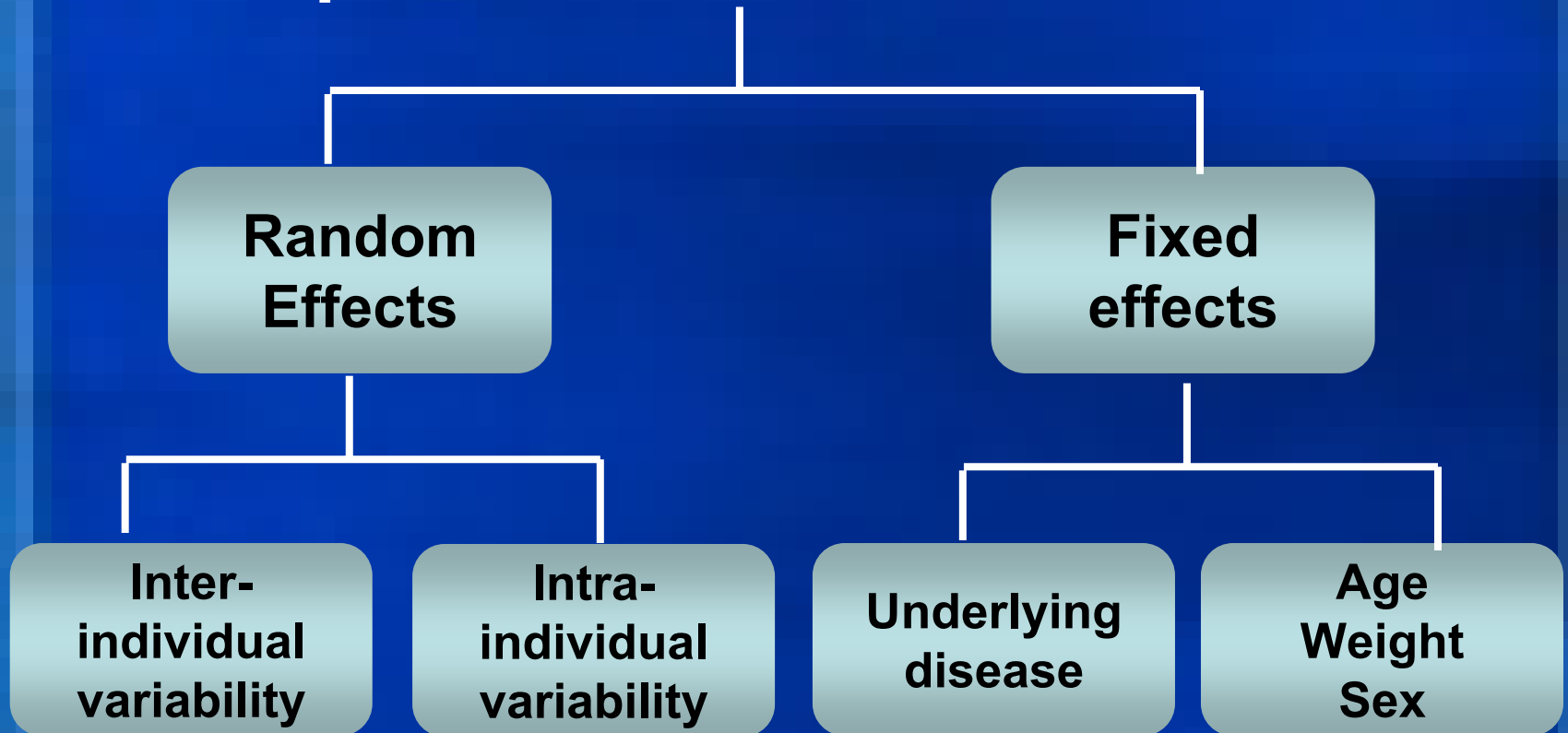
↓ PHT level

CBZ
Phenobarbital
Rifampin
Ethanol (Alcohol)

↑ or ↓ PHT level

Valproic acid
Sodium valproate
TCA,s

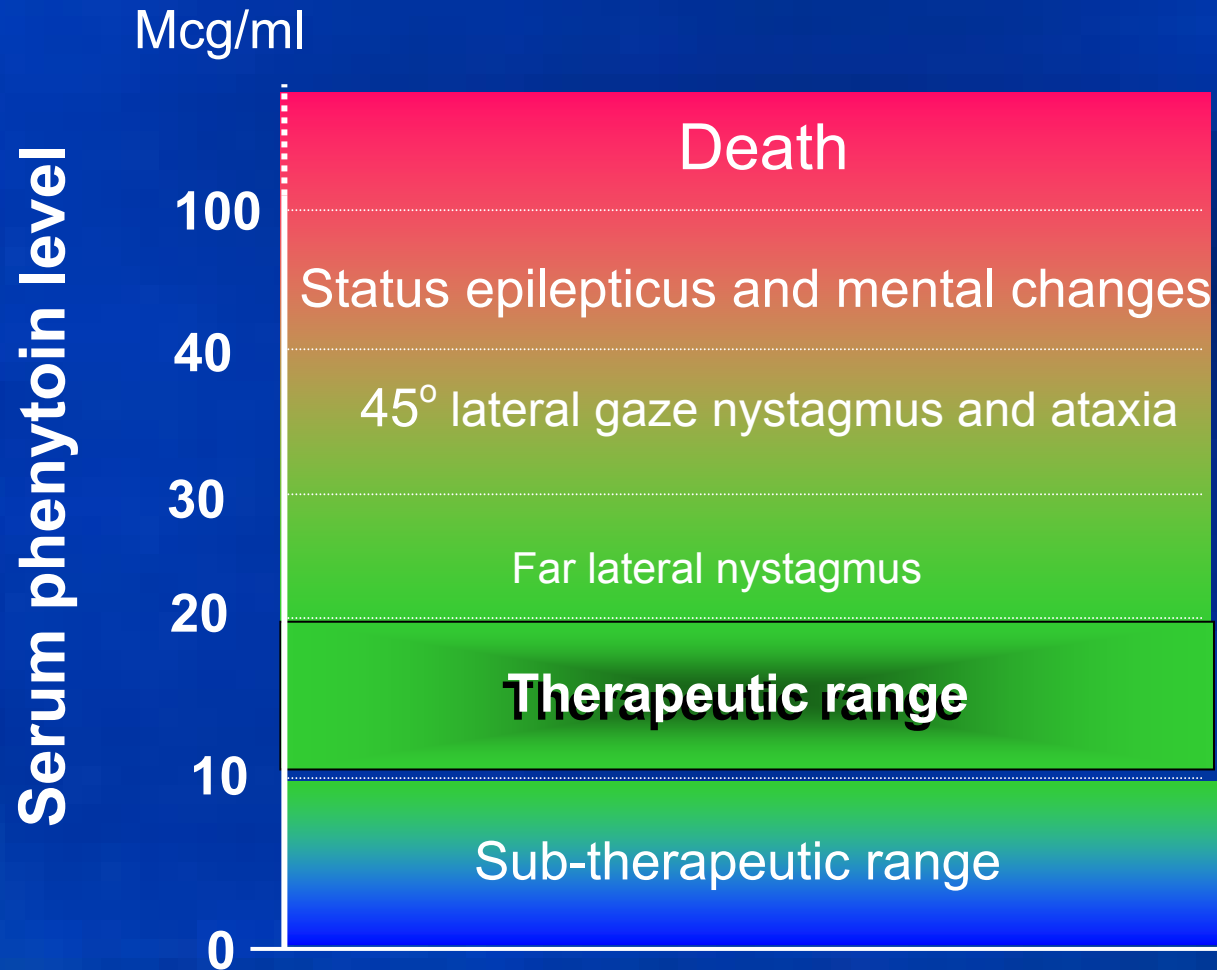
Population Pharmacokinetics



Importance of Phenytoin monitoring

- Narrow therapeutic index
- Wide inter&intra-
Individual differences
- Seizures development

Introduction



South African

$$K_m = 13.6 \mu\text{mol/L}$$

$$V_{\text{max}} = 6.5 \text{ mg/kg/day}$$

Prospective study
For 1 year

37 pts
21 male
16 female

Japan

$K_m = 3.67 \text{ mg/L}$

$V_{max} = 369 \text{ mg/day}$

Retrospective study

220 pts
120 male
100 female

Chinese

Objectives

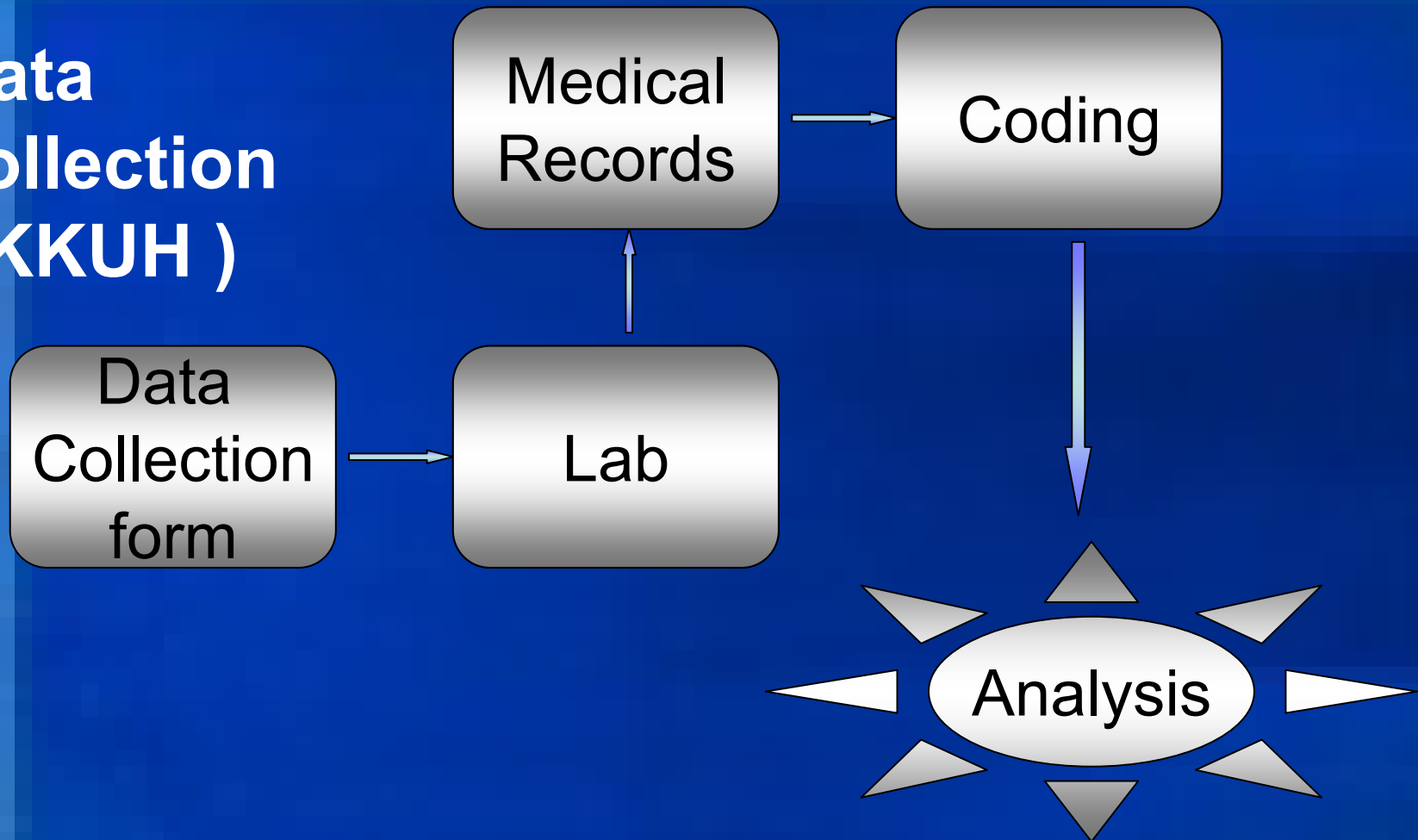
Determine the population pharmacokinetic parameters of phenytoin

Compare the pharmacokinetic parameters for Saudi patients with other populations

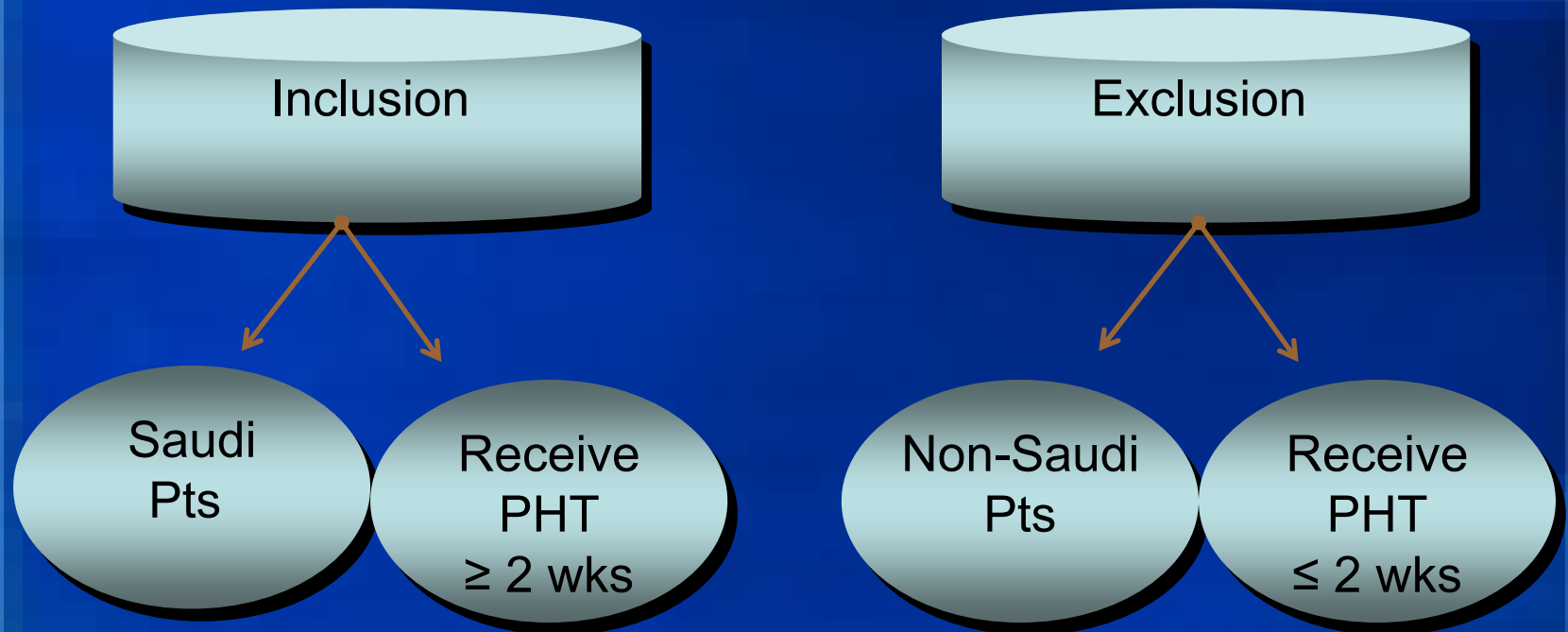
Methodology

Methodology

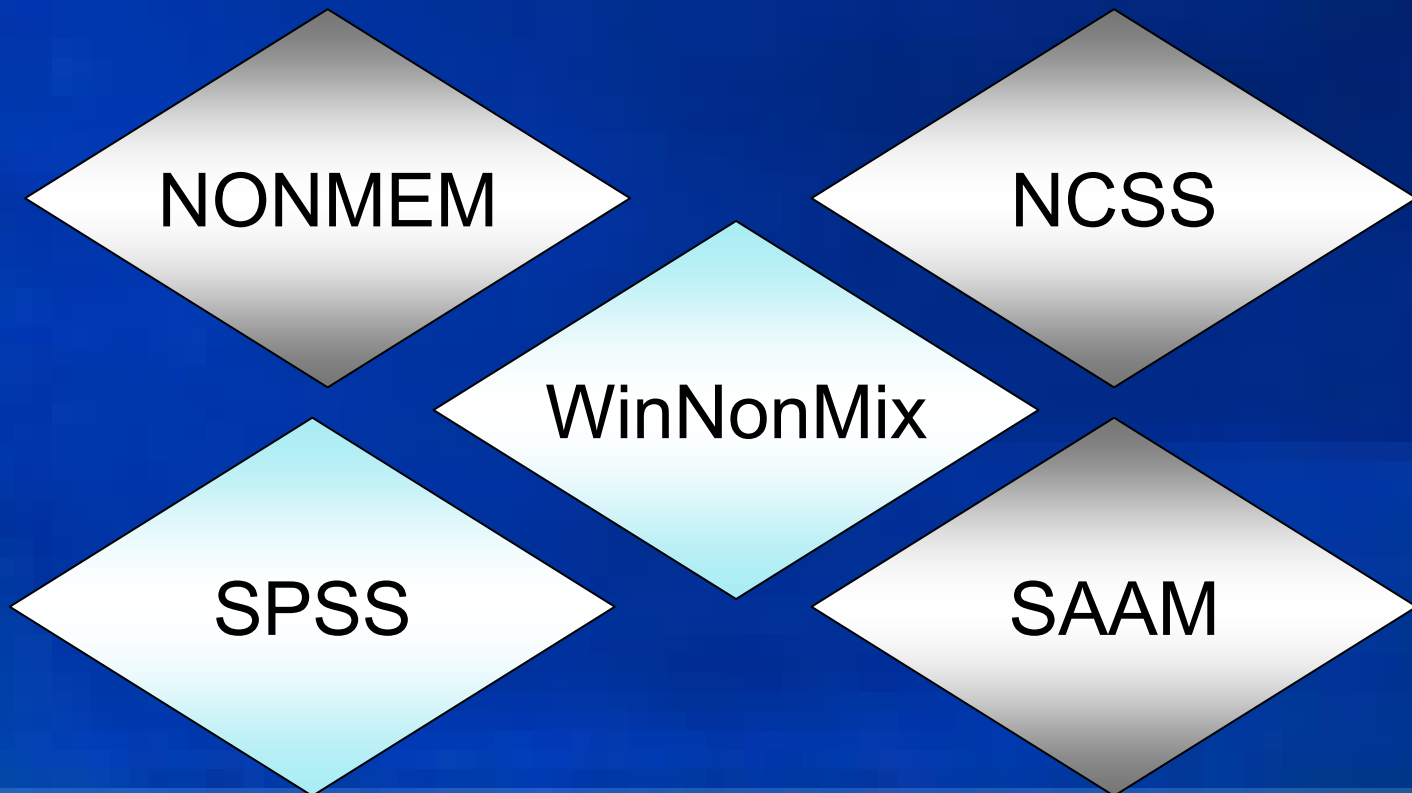
**Data
collection
(KKUH)**



Inclusion and Exclusion criteria



Data Analysis



Results and Discussion

DEMOGRAPHIC CHARACTERISTICS

101 Patients

58 Males (57.4%)

43 Females (42.6%)

Item	Value
	Mean \pm S.D
Age (yr)	38.87 \pm 20.22
Weight	60.49 \pm 24.74
Height	1.52 \pm 0.27

Japan

Vm
369 mg/day

Km
3.67 mg/L

S.A

Vm
6.5 mg/kg/
day

Km
13.6 μ mol/l

Saudi

Vm

Km

Chinese