POISONING & DIALYSIS

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Renal consultant

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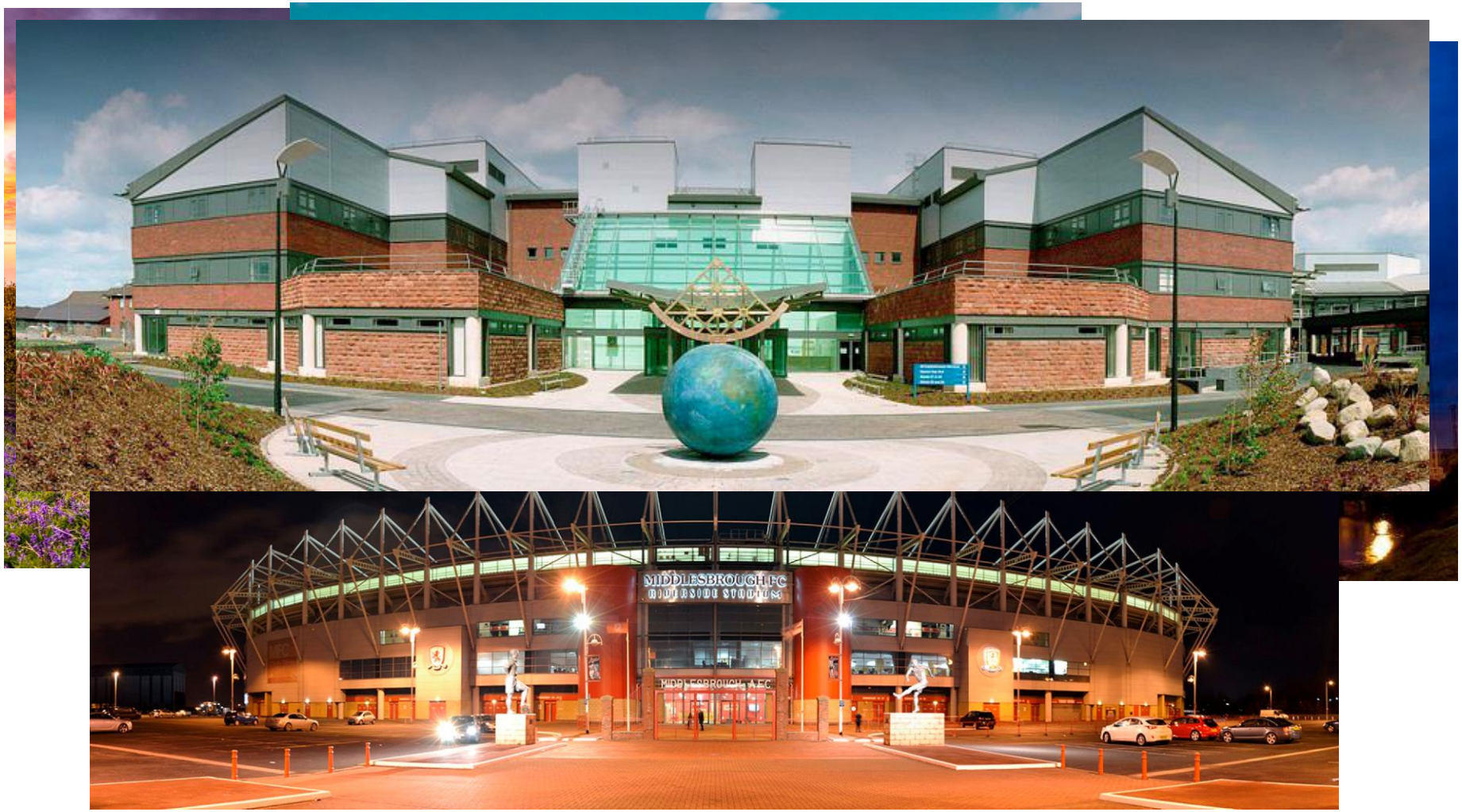
No declarations of interest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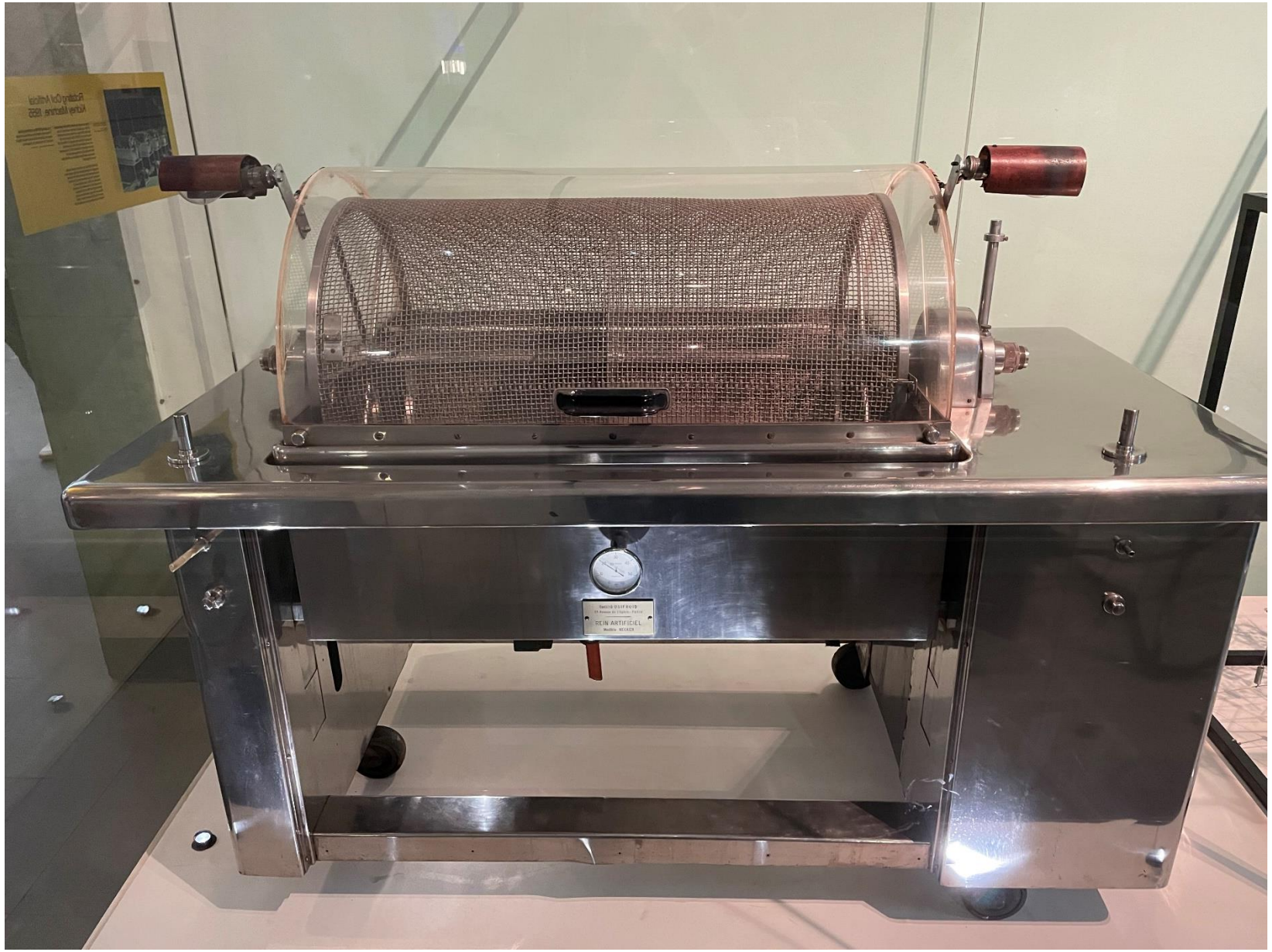
REIN ARTIFICIEL

ON THE REMOVAL OF DIFFUSIBLE SUBSTANCES FROM THE CIRCULATING BLOOD OF LIVING ANIMALS BY DIALYSIS

BY

JOHN J. ABEL, LEONARD G. ROWNTREE AND B. B. TURNER

From the Pharmacological Laboratory of the Johns Hopkins University

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Extracorporeal treatments for dialysis

- Haemodialysis
- Haemofiltration
- Haemoperfusion
- Plasma exchange

Evidence for ECTR in poisoning

Limited

No RCTs

Reliant on back-to-basics pharmacology, pharmacodynamics and toxicodynamics

Are there other treatments available?

- Corporeal treatments
  - Activated charcoal
- Antidotes
  - NAC, fomepizole
- Antibodies
  - Digibind
  - Snake bite anti-venom

Some basic principles

- *Risk vs benefit of ECTR*
  - What is the risk from the poison?
  - Will ECTR prevent death?
  - Will ECTR prevent serious injury/disability?
  - Will ECTR reduce the length of time spent on ITU?

Some basic principles

- *What characteristics of a poison make it amenable to ECTR?*

1. Lower molecular weight
2. Less protein bound
3. Lower endogenous clearance
4. Smaller volume of distribution

Extracorporeal treatments for dialysis

- Haemodialysis
- Haemofiltration
- Haemoperfusion
- Plasma exchange

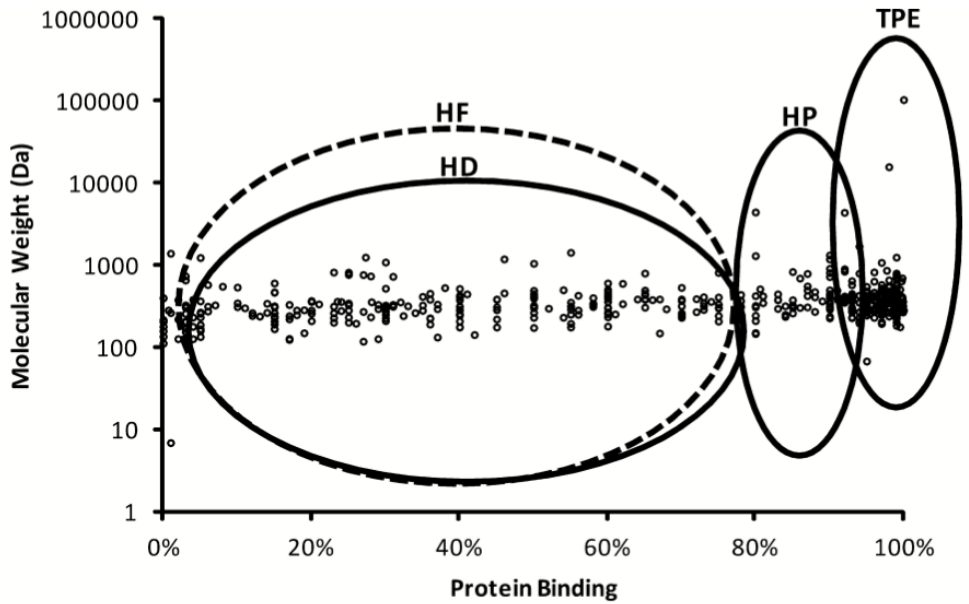


FIG. 1. Relationship between a drug's or poison's molecular weight and protein binding characteristics and the method of extracorporeal clearance that is anticipated to maximize clearance. Circles indicate for which poisons a specific ECTR is most useful. HD: Hemodialysis, HP: Hemoperfusion, HF: Hemofiltration, TPE: Therapeutic plasma exchange.

Seminars in Dialysis

BLOOD PURIFICATION IN POISONING

Marc Ghannoum,* Darren M. Roberts,† Robert S. Hoffman,‡ Georges Ouellet,§ Louise Roy,¶ Brian Scott Decker,** and Josee Bouchard††

Choice of ECTR modality

- Presence of AKI
- Need for anticoagulation
- Local availability & expertise
- What the patient is poisoned with

Specific poisons


galpharm
PARACETAMOL
500mg CAPLETS
EFFECTIVE
PAIN RELIEF
16


Prestone
EXCELS IN EXTREMES
READY TO USE
COOLANT
ANTIFREEZE
ALL MAKES, ALL MODELS
10 YEAR GUARANTEE
SUPERIOR PROTECTION
AGAINST CORROSION
LONGER ENGINE LIFE

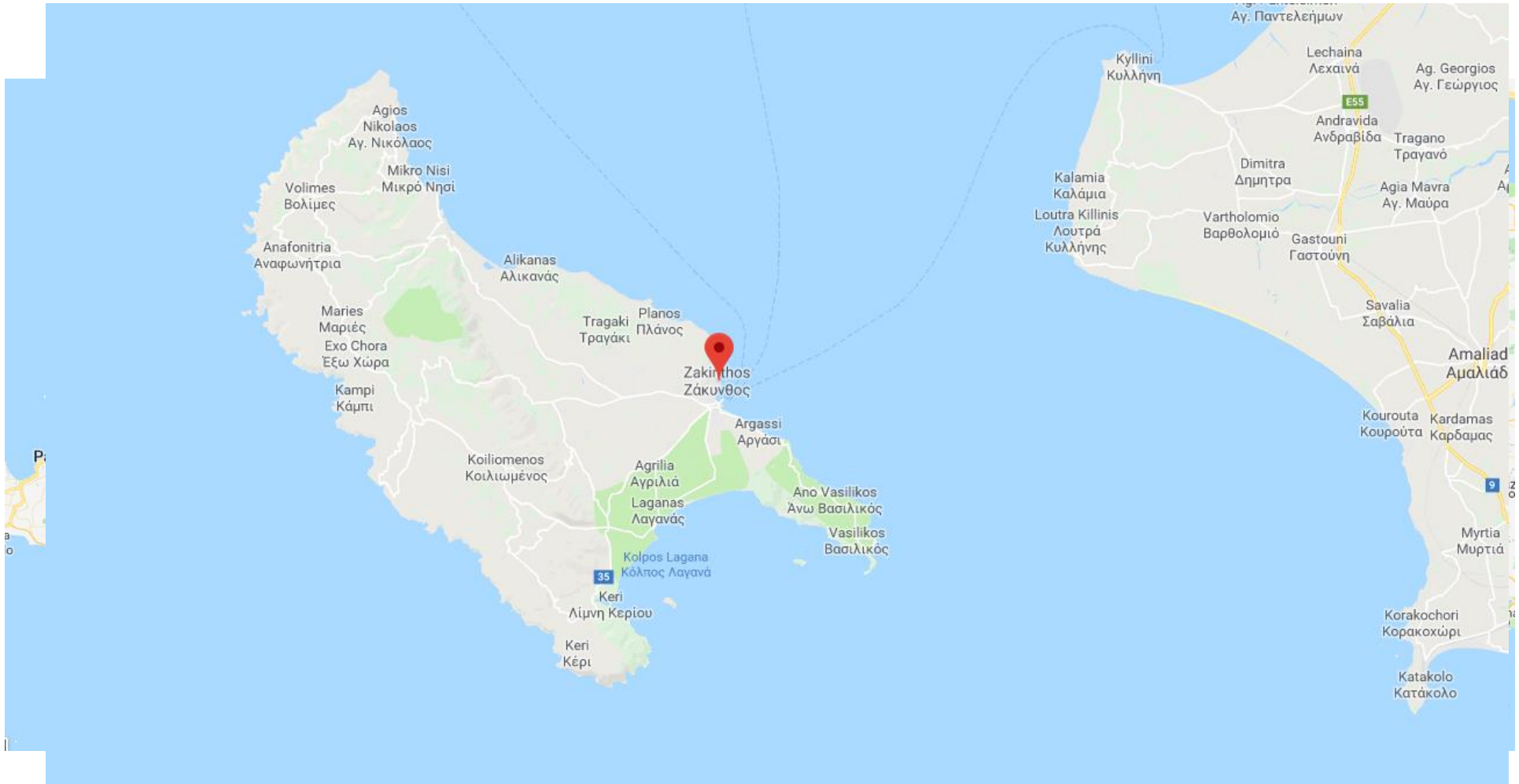

ASPIRIN 75 mg
GASTRO-RESISTANT TABLETS
Enteric-Coated
28
Tablets
BRISTOL


actavis
Metformin
Tablets
Metformin hydrochloride
500
mg
84 Film-Coated Tablets


LITHIUM


Theophylline S.R.
Theophylline Anhydrous
Bronchodilator
20 tablets


INDIE BAR
INDIE BAR
WILD COYOTE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Αλικανάς
Maries
Μαριές
Exo Chora
Έξω Χώρα
Tragaki
Τραγάκι
Planos
Πλάνος
Zakinthos
Ζάκυνθος
Kampi
Κάμπι
Argassi
Αργάσι
Koiliomenos
Κοιλιωμένος
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Ανω Βασιλικός
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Kalamia
Καλάμια
Agia Mavra
Αγ. Μαύρα
Loutra Killinis
Λουτρά Κυλλήνης
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Gastouni
Γαστούνη
Savalia
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Amaliad
Αμαλιάδ
Kourouta
Κουρούτα
Kardamas
Καρδαμας
9
Myrtia
Μυρτιά
Korakochori
Κορακοχώρι
Katakolo
Κατάκολο


MIAMI

The morning after

- Felt unwell

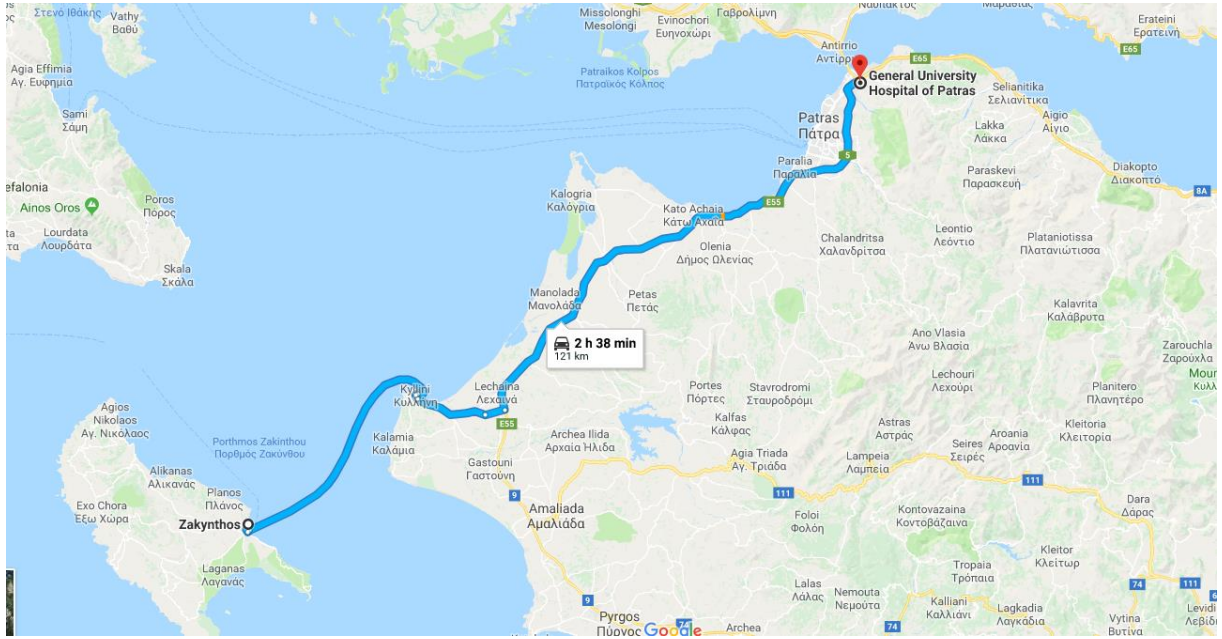
- Headache
- Tired
- Nauseated

By Monday

- Acutely unwell

- Admitted to local hospital

- Abdominal pain
- Vomiting
- AKI
- Severe acidosis
- Visual loss


General University Hospital of Patras
Zakynthos
2 h 38 min
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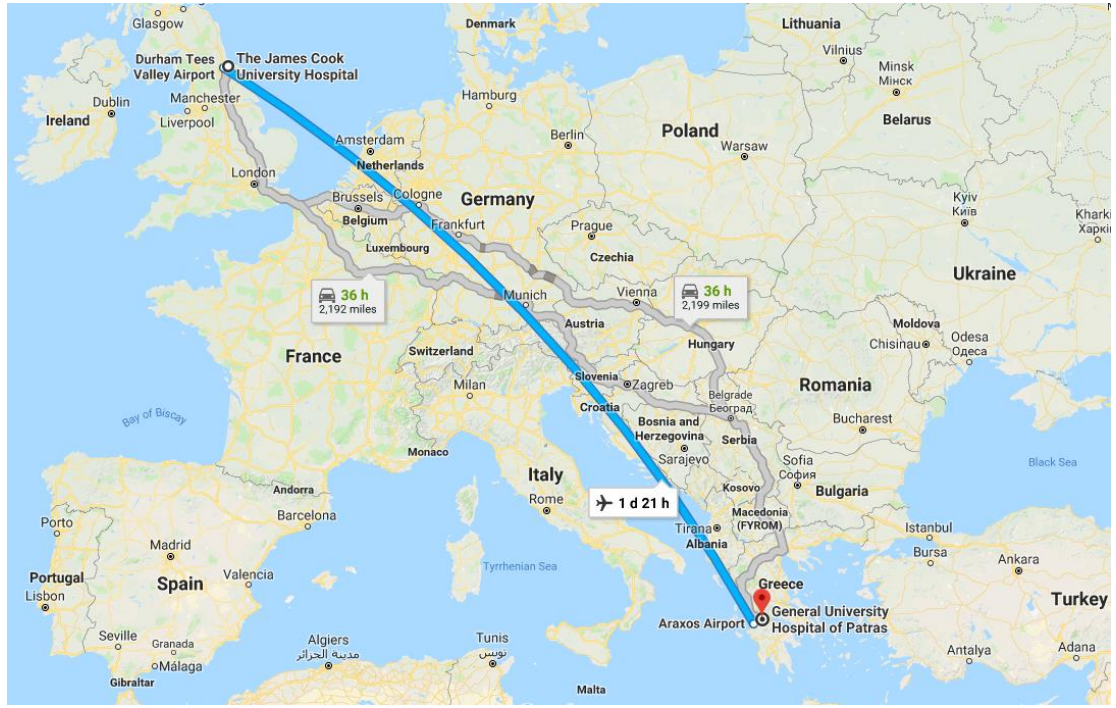
Pyrgos
Πύργος
Google


Durham Tees Valley Airport
The James Cook University Hospital
36 h
2,192 miles
36 h
2,199 miles
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General University Hospital of Patras
Araxos Airport
Ireland
France
Germany
Poland
Italy
Spain
Portugal
Greece
Turkey
Ukraine
Romania
Belarus
Bulgaria
Albania
Netherlands
Belgium
Switzerland
Austria
Hungary
Czechia
Slovenia
Croatia
Bosnia and Herzegovina
Serbia
Kosovo
Macedonia (FYROM)
Monaco
Andorra
Malta
Gibraltar
Bay of Biscay
Tyrrhenian Sea
Black Sea

What happened?

METHANOL POISONING

KILLS

ARE YOU GOING TO INDONESIA OR BALI?

IF SO, KEEP CLEAR OF COUNTERFEIT ALCOHOL.

ONE OF THESE BOTTLES CONTAINS 25% METHANOL AND IS DEADLY.
IT IS NEARLY IMPOSSIBLE TO TELL WHICH ONE.*

BE WARY OF SPIRIT BASED DRINKS IN BARS, HOTELS AND SHOPS

DO NOT DIE FOR A DRINK

THIS POSTER WAS PRODUCED BY THE 'CHEZ – SAVE A LIFE CAMPAIGN'

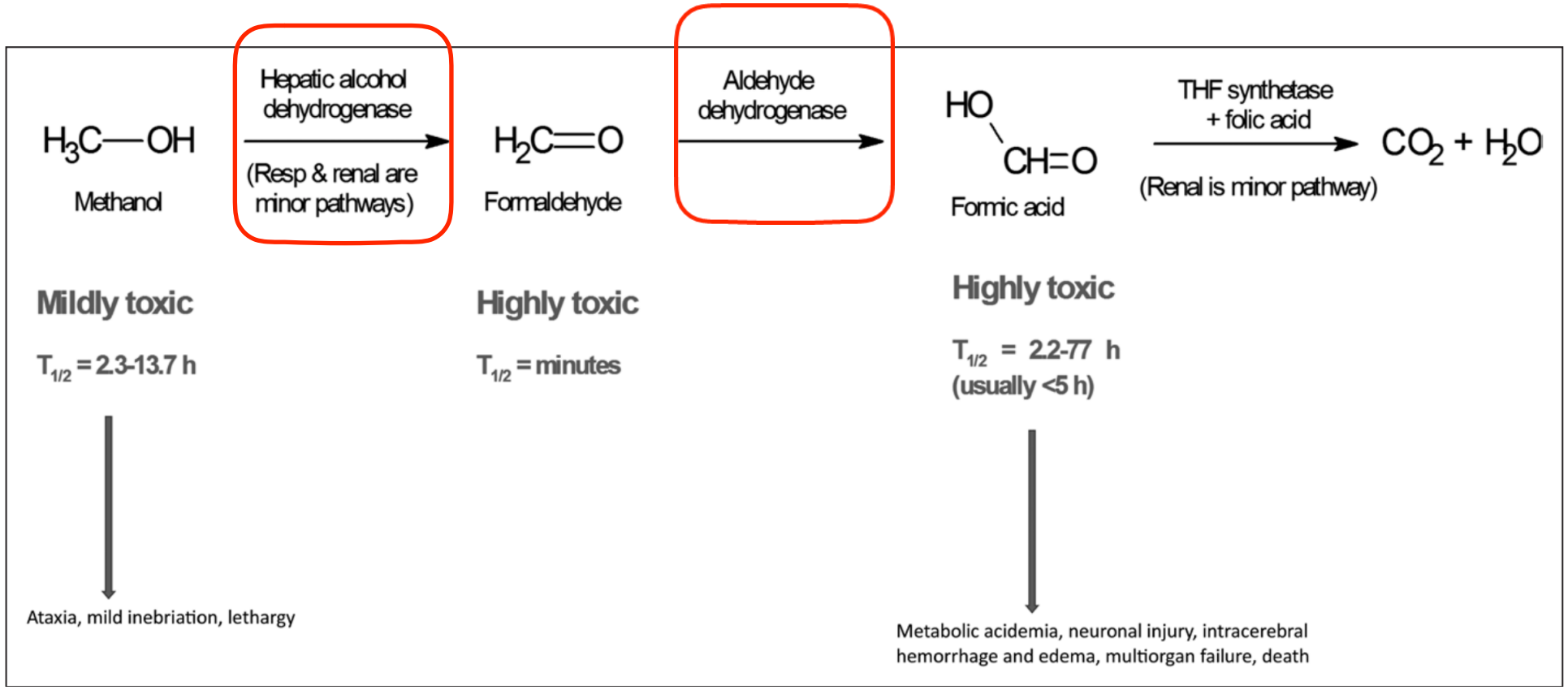
CHEZNYE EMMONS 1989 - 2013

* The bottle on the right has enough methanol in it to kill three grown men and was bought in Indonesia

Ethylene Glycol & Methanol

Ethylene Glycol & Methanol

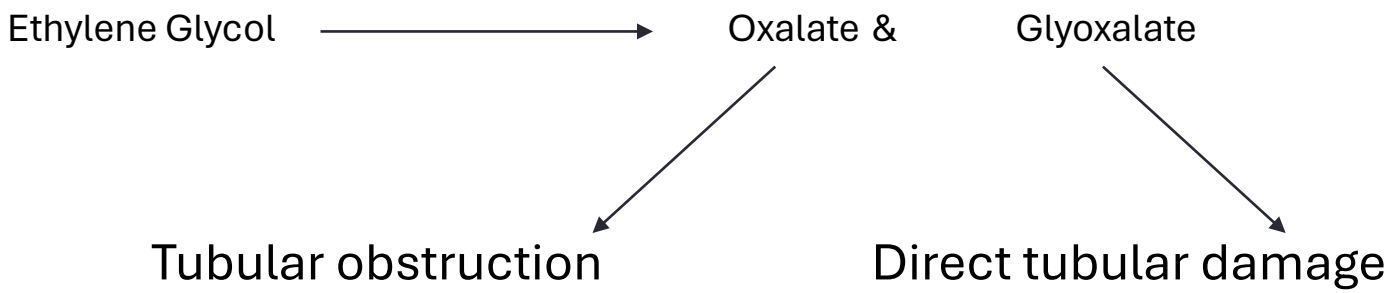
- Anti-freeze, de-icers & varnishes
- 50ml can lead to death
- Symptoms
  - Similar to being drunk
  - Usually 12-24 hours after ingestion
  - Abdominal pain
  - Headaches
  - Seizures
  - Methanol causes retinal oedema & white matter demyelination (“blind drunk??”)


$H_3C—OH$
Methanol
Hepatic alcohol dehydrogenase
(Resp & renal are minor pathways)
$H_2C=O$
Formaldehyde
Aldehyde dehydrogenase
HO
CH=O
Formic acid
THF synthetase + folic acid
(Renal is minor pathway)
$CO_2 + H_2O$
Mildly toxic
$T_{1/2}$ = 2.3-13.7 h
Highly toxic
$T_{1/2}$ = minutes
Highly toxic
$T_{1/2}$ = 2.2-77 h
(usually <5 h)
Ataxia, mild inebriation, lethargy
Metabolic acidemia, neuronal injury, intracerebral hemorrhage and edema, multiorgan failure, death

Ethylene Glycol

- Oxidated by alcohol dehydrogenase and aldehyde dehydrogenase in liver

- Toxic metabolites → kidney and nerve damage



Treatments

- Inhibit alcohol dehydrogenase

Low MW
Not highly protein bound
Water soluble

Indications for dialysis in methanol poisoning

- Severe poisoning
  - Coma
  - Seizures
  - New vision defects
  - Severe acidosis pH < 7.1
  - Anion gap > 24
- Very high methanol concentration
  - >700mg/L after fomepizole
- Renal failure

Haemodialysis

Indications for dialysis in EG poisoning

- Coma
- Siezures
- Very elevated anion gap
- Glycolate levels >12mmol/L
- AKI/renal impairment

In collaboration with:

http://www.extrip-workgroup.org/

Lithium

- Effective treatment for affective disorders
- Narrow therapeutic window
- Long term use associated with chronic renal failure

Acute Lithium Toxicity

Symptoms

Neuromuscular irritability

Confusion

Drowsiness

Measure lithium level

1.5 - 2.5mmol/L – mild toxicity

2.5 – 3.5mmo/L – moderate toxicity

>3.5mmo/L – severe toxicity

Dialysis in Lithium OD

Lithium effectively removed by dialysis

- “The most dialysable toxin”
- Low MW
- Negligible protein binding

Much higher clearance than in the urine

Indications for dialysis

HAEMODIALYSIS

LITHIUM LEVEL > 5MMOL/L

LEVEL > 4 IN PRESENCE RENAL FAILURE

SEIZURES, REDUCED GCS OR LIFE-THREATENING DYSRHYTHMIAS

Cautions

- Delay in equilibration between intracellular and extracellular lithium
  - Rebound can occur after 1st dialysis
- May need extended dialysis time or multiple sessions
- Possible role of CVVH to avoid repeat HD sessions
- Beware SR preparations

Salicylates

- In therapeutic doses
  - Rapidly broken down to salycylic acid
  - Highly protein bound
  - Metabolised in the liver
  - Small amount renally excreted

- In overdose, protective mechanisms are overwhelmed

In overdose

- Protein binding reduced
- Hepatic detoxification saturated
- Body relies more on renal excretion, which is slow
- 10 - 20g can be fatal in adults

Salicylate poisoning

- ECTR recommended in severe poisoning
  - Salicylate level >7mmol/L
  - Level > 6.5mmol/L and renal impairment
  - Altered mental state
  - Worsening hypoxia
  - Failure of medical treatment
- Recheck levels @ 2 hours and consider repeat HD

LOW MW
PROTEIN BINDING REDUCES IN OVERDOSE

HAEMODIALYSIS

Beta Blockers

High dialyzability

- Atenolol
- Metoprolol

Low dialyzabitlity

- Carvedilol
- Bisoprolol
- Propranalol

Theophylline

Narrow therapeutic window

Moderate → severe toxicity level >25mg/L

Features

- Seizures
- Tachyarrhythmias
- Electrolyte disturbances

Theophylline & dialysis

- ECTR recommended in severe poisoning
  - Level > 100mg/L
  - Seizures
  - Dysrhythmias
  - Shock
  - Rising levels despite medical management

LOW MW
40 – 60% PROTEIN BOUND
LOW VOL OF DISTRIBUTION

HAEMODIALYSIS

Metformin

- ECTR recommended for severe poisoning
  - Lactate >20
  - pH < 7.0
  - Shock
  - Failure of medical treatment

LOW MW
NOT PROTEIN BOUND
SMALL VOL OF DISTRIBUTION

HAEMODIALYSIS

Valproate

- ECTR recommended for severe poisoning
  - Level > 1300mg/L
  - Shock
  - Cerebral oedema
  - Severe acidosis

LOW MW
PROTEIN BINDING REDUCES IN OVERDOSE
SMALL VOL OF DISTRIBUTION

HAEMODIALYSIS

Digoxin

- Large volume of distribution
- High molecular weight

- **ECTR IS NOT A GOOD TREATMENT FOR DIGOXIN OD**

Take home messages

- Weight up risks & benefits of ECTR in poisoning

- Poisons that are amenable to ECTR are
  - Low MW
  - Not highly protein bound
  - Water soluble with a low volume of distribution

- Choice of ECTR depends
  - Poison
  - Local expertise & resource

In collaboration with:

EXTRIP

THE EXTRACORPOREAL TREATMENTS IN POISONING WORKGROUP

NEPHROLOGY SOCIAL MEDIA COLLECTIVE EST 2015

http://www.extrip-workgroup.org/

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