

Example of multidisciplinary Mediterranean collaboration for forensic toxicological investigations: a case of fatal poisoning by vanadium



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Key points of multidisciplinary Mediterranean collaboration for forensic toxicological investigations

I- Benefits

- Material: savings in equipment and competence sharing
- Strategic: Overview of the specific emergent risks (Toxic agents) inherent to the Mediterranean area
- intellectual : Cross fertilization ideas and common scientific publications

II- Obstacles in the way of southern/northern Mediterranean collaboration

- Physical Distance (Algiers-Paris: 1300km)
- Intergovernmental and inter-institutional Policies
- Fear of confidentiality Lack

III- Conditions of success

- Recent improvements in transportation and communication technologies
- Good coordination and the presence of an efficient intermediary.
 - In compliance with:
 - GLP criteria: Pre analysis steps, traceability and transfer of the samples (refrigeration procedure)
 - Confidentiality criteria



Case report



Forensic Dpt.

Suspicion of vanadium intoxication

- **SYMPTOMS/** 10h30 p.m., a 24-year-old woman was admitted to the emergency department of the university hospital of Tizi-Ouzou (Algeria), for diffuse abdominal pain, nausea, vomiting, multiple daily diarrhoeas.
- **INITIAL CHEMISTRY/** tests were normal except for glucose 0.2g.L⁻¹ (1.1mmol.L⁻¹), alanine amino transferase: 114IU.L⁻¹ (normal 10-45 IU.L⁻¹).
- Acute renal failure (The glomerular filtration rate was estimated at 21ml.mn⁻¹) [creatinine 265 μmol.L⁻¹ (normal 49-90 μmol.L⁻¹)].
- A rapid urine drug of abuse panel was negative.
- **ANAMNESIS/** This patient had taken an undetermined amount of ammonium vanadate at about 10 a.m. the same day.
- **CLINICAL DEVELOPMENT/** She died on the following morning in the context of respiratory distress, despite intensive care and oxygen therapy.

AFPremed

Coordination & Toxicological Expertise



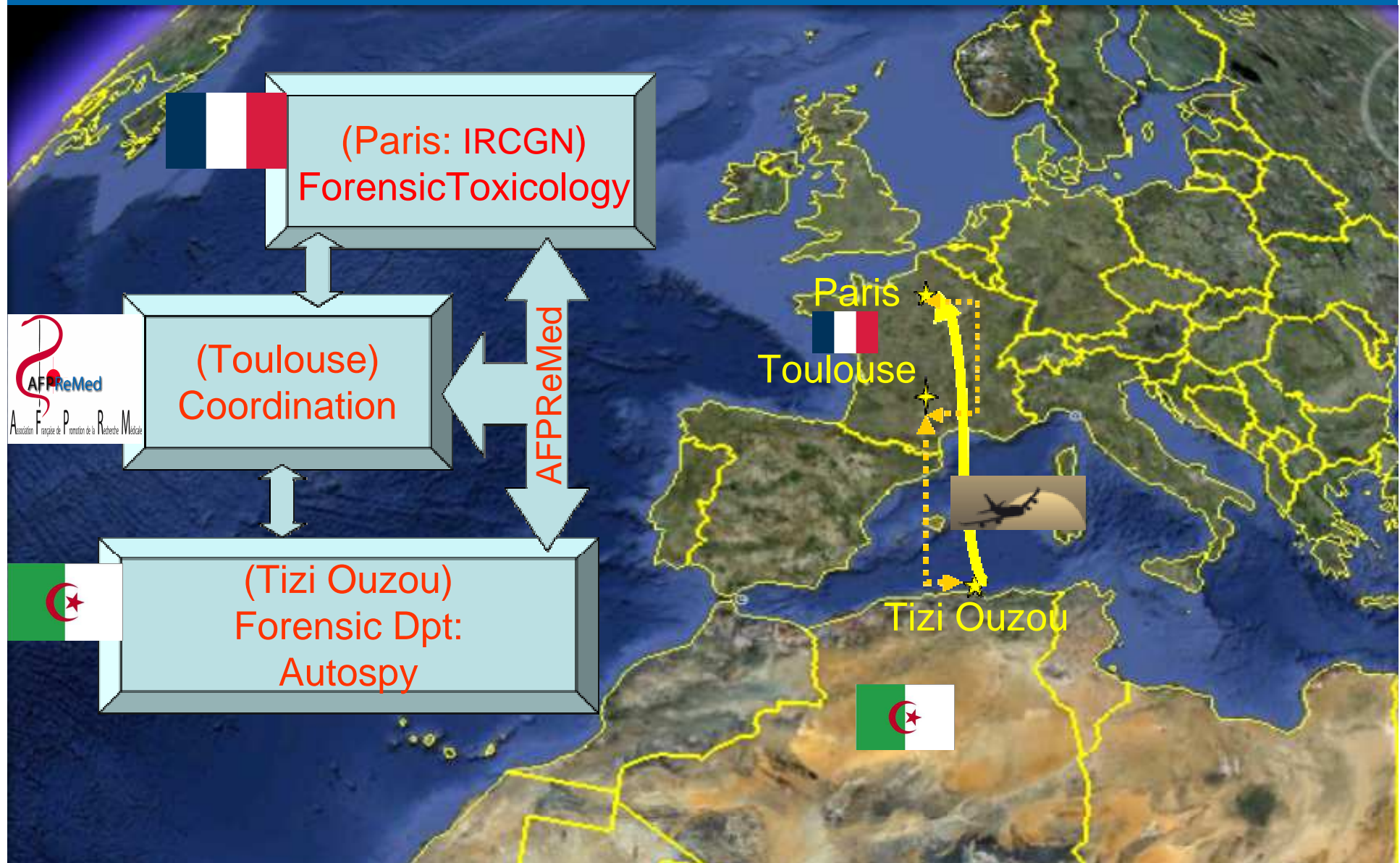
- Blood sample collected in vacuum tube with K₃EDTA, was stored at -18°C
- and transferred to IRCGN (France) for analysis.

Forensic Toxicology

Confirmation of vanadium intoxication

- Determination of vanadium concentration in blood was carried out by means of a mass spectrometer (ICP-MS)

Coordination of the forensic investigations



Determination of vanadium concentration (Material)

- **Analysis of the vanadium in blood was performed using:**
 - a mass spectrometer (ICP-MS), (ThermoOptek, X7/CCT model, Courtaboeuf, France) equipped with a quartz torch and a quartz nebulizer
 - *PlasmaLab 2.0.as software.*
- **Instrumental parameters were as follow:**
 - **Rhodium (^{103}Rh) is used as an internal standard for the ICP method.**
 - *1200W plasma, argon flows: 15 L.mn⁻¹ in the plasma, 0.72 L.mn⁻¹ in the nebulizer.*
 - *The nebulizer was equipped with a Peltier effect cooler for regulating the temperature (with 3°C error).*
 - *The autosampler consisted of a CETAC ASX-500 and an ID100 autodiluter.*



Département toxicologie
Institut de recherche criminelle de la gendarmerie nationale



Determination of vanadium concentration (Method)

➤ *Sample preparation*

- 100 μL of the sample were added to 10 mL of a mineralising solution prepared as follows: Nitric acid 0.216 M, 0.5% (v/v) of 1-butanol and 0.01 % (v/v) of triton X100.
- The solution was then filtered on Millipore filters (0.45 μm) and injected into the ICP-MS.

➤ Blank samples, and calibrants [5 levels ranking from 0 to 107.14 $\mu\text{g/L}$],

- preparation by spiking a negative whole blood matrix with the multi elemental solution

	LOQ	LLOQ	accuracy	Bias
	0.4 $\mu\text{g/L}$	1 $\mu\text{g/L}$	89.9 %	1.49 %
			(at 50 $\mu\text{g/L}$ level)	

Results : Post mortem Findings

Autopsy



- The examination of body revealed the absence of violence.
- Labial mucosa showed a greenish colour.
- Widespread asphyxia syndrome of the viscera
- An erosive gastritis.

Forensic Toxicology

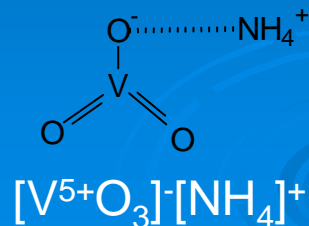


- The vanadium concentration found is 6.22 mg.L^{-1}
 - corresponding to 6000 times higher than the normal concentration in the non-exposed population

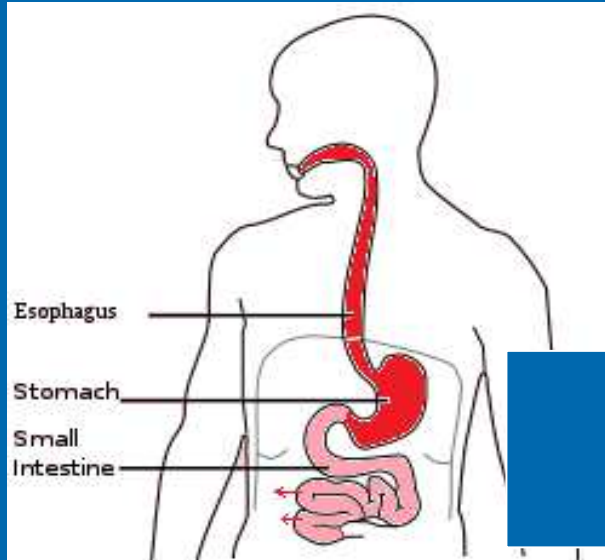
Expert's Report:

(Ammonium vanadate (VO_3NH_4))

- salt of pentavalent vanadium (+V) : CAS N° (7803-55-6),
- Molecular weight (116.97g); Density (2.32) and water solubility (5.1g/L at 20°C) .
- Uses: as catalyst in reactions involving the oxidation of sulfur oxide, oxides of nitrogen and other compounds.
- Vanadium is ubiquitous in the environment.
- Exposure through food is estimated at 11-30 μg per day.
- Vanadium is considered as an essential trace element for mammals and probably for humans.
- Occupational exposure to vanadium occurs mainly by inhalation of dust and smoke.



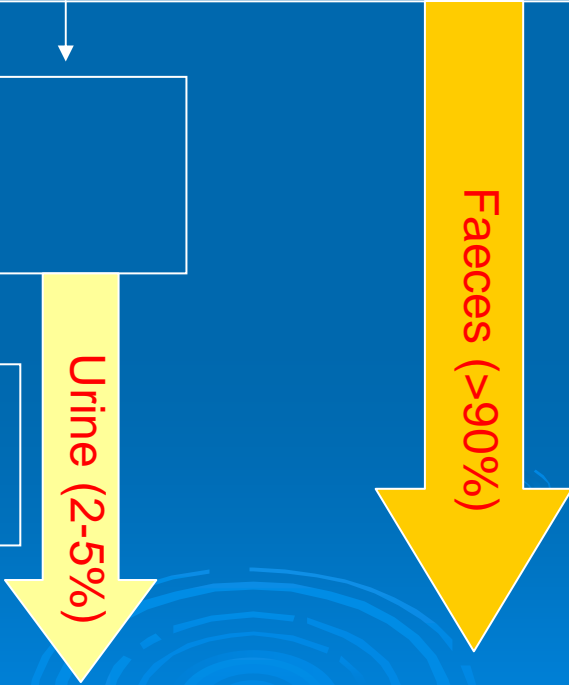
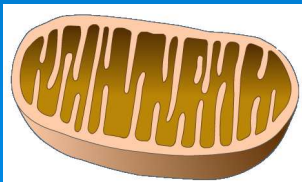
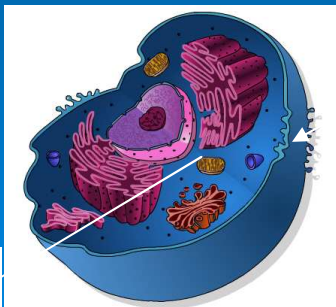
Expert's Report: Toxicokinetics of the vanadium



gastrointestinal tract
 Stomach $2VO_3^- + 4H^+ \rightarrow 2VO_2^+ + 2H_2O$
 Bowel : absorption (5%)

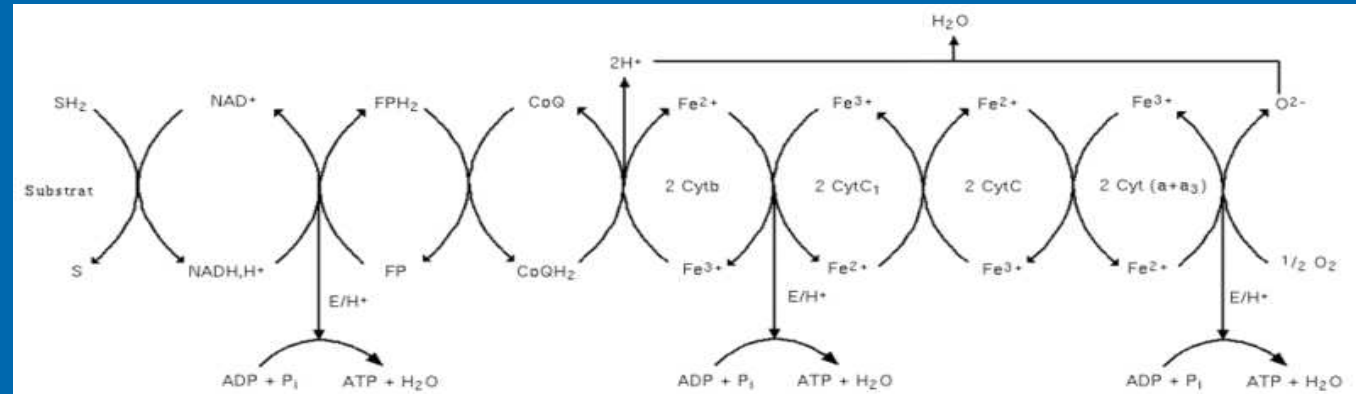
blood compartment
 plasma protein binding (90%)
 half-life about 1 hour;

Tissular compartment

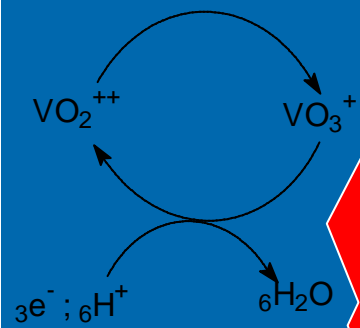


•Vanadium and its salts are poorly absorbed orally.

Expert's Report: mechanisms of vanadium toxicology



Redox vanadyl/vanadate ions interaction (E° Vanadyl/Vanadate: 1.0 V)
 → inhibition of the cellular respiratory processes by VO_3^-



Inhibition

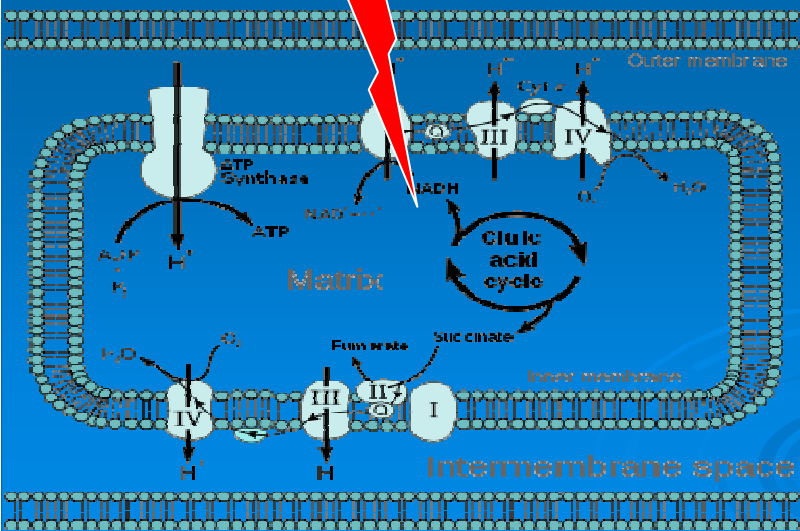


Table: Redox Systems respiratory chain

redox Systemes	Standard Potential (pH :7; 25° C)
NAD ⁺ /NADH	-0,32 V
FP/FPH ₂	-0,14 V
CoQ/CoQH ₂	-0,09 V
Cytb Fe ³⁺ /Cytb Fe ²⁺	+0,04 V
CytC1 Fe ³⁺ /CytC1 Fe ²⁺	+0,22 V
CytC Fe ³⁺ /CytC Fe ²⁺	+0,26 V
Cyt(a+a ₃) Fe ³⁺ /Cyt(a+a ₃) Fe ²⁺	+0,29 V
1/2O ₂ /O ²⁻	+0,82 V

Conclusion

- This documented case is of great importance for understanding the mechanisms of vanadium toxicology leading to widespread asphyxia syndrome.
- This interesting result argues that multidisciplinary collaboration between many mediterranean countries may enhance the forensic research
- Such collaborations require a good coordination



The authors dedicate this project in honor of :
Mrs Djamila Belhadj-Tahar (1932-2010)