

Propofol: A Safer Future Forged from a Lethal Past

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Dear Editor,

In modern medicine, few pharmacological agents have been as transformative as propofol. Widely regarded as the gold standard for intravenous induction and maintenance of anaesthesia, it has reshaped perioperative care worldwide. Yet, behind its clinical use lies a lesser-known narrative: one shaped by the limitations of thiopentone, the tragedies of wartime medicine, and the pivotal role of Irish research in ensuring propofol's safe implementation.

Before propofol's introduction in the 1980's, anaesthetists relied heavily on thiopentone sodium, a barbiturate first synthesised in the 1930's. Although revolutionary for its rapid onset, thiopentone's pharmacology proved problematic. It is a haemodynamic depressant and cannot be used to maintain anaesthesia. After injection, thiopentone redistributes into highly perfused tissues (e.g., muscle) and once administration ceases, it diffuses back into the circulation, leading to prolonged drowsiness and unpredictable patient responses. This renders it impractical as a sole anaesthetic agent. During World War II, thiopentone, thought to be an ideal field anaesthetic, was used on American soldiers at Pearl Harbour. Tragically, many who might otherwise have survived, succumbed to its cardiac depressant effects.

By the late 1970's, the search for a safer alternative was underway. At Imperial Chemical Industries Pharmaceuticals (now AstraZeneca), Dr. John Glen, a Scottish veterinarian, identified 2,6-diisopropylphenol, later named propofol, as an agent with an ideal anaesthetic profile: rapid onset, short duration, minimal residual effects, and a wider safety margin than thiopentone.

Propofol's journey from discovery to clinical use began in the mid-1980's when a lipid emulsion formulation was trialled in centres across the United Kingdom, Belgium, France, and Ireland. The first hospital in the Republic of Ireland to publish research on the drug was the Coombe Lying-In Hospital (today The Coombe).

A team led by Dr. Liam Briggs, then consultant anaesthesiologist at the Coombe, conducted one of the earliest clinical studies of propofol. Their findings, published in the British Medical Journal in 1986 under the title *"Pharmacokinetics of Propofol in Female Patients: Studies Using Single Bolus Injections"*, offered vital data on absorption, distribution, metabolism, and

elimination in female patients. Using a three-compartment pharmacokinetic model, it demonstrated propofol's rapid distribution (half-life ~3 minutes) and high clearance (~1.91 L/min), explaining its fast onset, short duration, and controllability. Crucially, unlike thiopentone, propofol redistributes into poorly perfused tissue (e.g., fat) where it is gradually metabolised, allowing smoother recovery without rebound sedation.

This pioneering Irish contribution provided confidence in propofol's pharmacokinetics and safety, particularly in female patients. By offering real-world evidence, the study validated propofol's advantages, guided dosing strategies, and catalysed further research which spurred regulatory approval and the drug's eventual adoption internationally.

Despite minor adverse effects such as injection-site discomfort, propofol rapidly displaced thiopentone, offering superior safety and smoother recovery. While Dr. Glen led development, Irish clinicians were crucial in translating it into real-world practice.

The transition from thiopentone to propofol represented not only a pharmacological breakthrough but also advancement in quality and patient safety. This achievement stemmed from an Irish legacy of rigorous clinical research, which quietly but decisively shaped the course of modern anaesthesia.

Declarations of Conflicts of Interest:

None declared.

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