100 Years of Blood Purification in Poisoning: Closing the Gap Between Anecdotal Care And Evidence-Based Therapy

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It has now been just over 100 years since Abel and colleagues published their seminal paper on the successful use of a hemodialysis to remove salicylate from a poisoned dog (1). While it may be contrary to most clinicians’ perceptions of a technique (hemodialysis) that has become a mainstay in modern medicine, it is a fact that extracorporeal blood purification was designed as a temporizing measure to hasten the elimination of exogenous substances and speed the recovery of those patients who were intentionally or unintentionally poisoned. Years lagged before hemodialysis and peritoneal dialysis were accepted as maintenance therapies for patients with chronic kidney disease (CKD).

Abel’s choice of salicylate was an ideal test of concept as we now recognize that salicylates meet all a priori criteria for a drug that would be expected to be easily cleared by hemodialysis having a small molecular weight, an exceedingly small volume of distribution, and a lack of extensive protein binding in overdose. Likewise, the timing could not have been better for Abel’s work as intensive care medicine was essentially nonexistent and patients were dying of respiratory depression from overdoses of drugs like bromides, barbiturates, and others.

Medical toxicology was likewise in its infancy as a discipline and although a link between coma and death was easily recognized, care was predominated by misguided and potentially dangerous attempts to awaken patients with nonspecific analeptics like camphorated oil, strychnine, nikethamide, picrotoxin, and amphetamines (2–5). Aggressive use of gastrointestinal decontamination techniques (induced emesis and orogastric lavage) likely added to mortality in many victims by facilitating pulmonary aspiration in patients with depressed consciousness and unprotected airways. Extracorporeal blood purification was intuitively reasonable, filled a necessary treatment void, and was a clean and more efficient approach to older techniques such as bloodletting, which was still in common use for barbiturate poisoning in the 1920s.

By 1961, Clemmesen and Nilsson, two of the most important clinicians in modern toxicology, made the simple and brilliant observation that the treatment for respiratory depression was respiratory support and that if harmful analeptics were replaced by aggressive respiratory care including, at times, tracheostomy, the mortality from barbiturate poison could be significantly reduced (6). This concept, later known as the “Scandinavian Method” gave rise to the modern dictum of “treat the patient, not the poison” and ultimately heralded an era where good supportive (proactive) care alone could significantly reduce morbidity and mortality from poisoning.

Unfortunately, the proverbial horse was out of the barn with hemodialysis (and later hemoperfusion) becoming the mainstay of therapy for virtually any type of severe poisoning. Textbooks and review articles of that time published extensive tables of drugs and toxins that could be “cleared” by extracorporeal techniques (7). These recommendations were supported by anecdotal case reports and flawed animal models that used apparent half-lives of elimination and extraction ratios across filters as imperfect and inaccurate surrogates for actual drug removal from the body.

As the science of hemodialysis grew and techniques and equipment improved, so did the understanding of toxicokinetics, the treatment of poisoning, and the development of an evidence base to support clinical practices. Peritoneal dialysis was recognized as useless for toxin removal and has since been largely abandoned for that indication. Hemoperfusion has essentially been eliminated in many countries as a result of improvements in water preparation that limit aluminum exposure in patients with chronic kidney disease, abandoning the use of theophylline, and a sharp decline in pulmonary aspiration in patients with depressed consciousness and unprotected airways. Extracorporeal blood purification was intuitively reasonable, filled a necessary treatment void, and was a clean and more efficient approach to older techniques such as bloodletting, which was still in common use for barbiturate poisoning in the 1920s.

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the availability of hemoperfusion cartridges (8). Unfortunately, during all of these changes, golden opportunities were missed. Not a single human randomized controlled trial addressed the utility of extracorporeal elimination in patients with the most commonly dialyzed toxins; salicylates, methanol, ethylene glycol, lithium, or barbiturates. While today we can say with great certainty that 19,351 cases of extracorporeal treatments for toxin removal (ECTR) were reported to US poison centers from 1985 to 2005 (9), there are limited if any data in these cases to derive sound indications for ECTR or demonstrate its efficacy or safety.

The Extracorporeal Treatments in Poisoning (EXTRIP) workgroup was created not only to help bridge the gap between existing data and clinical practice patterns, but also to identify limitations of current publications and offer solutions to allow for more accurate interpretation as new information is gathered (10,11). Rather than gather simple efficacy data, EXTRIP’s approach is one of the more formal risks: benefit analysis that in addition to efficacy strives to understand the role of alternative therapies, availability, cost, and safety including modifications in compromised hosts. This current issue of Seminars should be considered mandatory reading for all trainees in Nephrology, Critical Care, Toxicology and perhaps many other disciplines. It provides an essential primer on critical decision-making by characterizing the general approach of a poisoned patient that may require blood purification. Both the description of available extracorporeal techniques for poison removal, and ways to optimize their clearance will be presented. The trends in case reporting of poisonings treated with extracorporeal treatments will be reviewed as well as those relating to toxic alcohol management in the US. This issue will also contain an overview of the heterogeneity in treatment approaches for lithium poisoning, a reappraisal on the lost art of hemoperfusion, and an introduction to one of the formal EXTRIP guidelines. Finally, since it is obvious that much of our understanding of extracorporeal elimination of new toxins will be largely driven by case reports, general guidance is offered for authors considering publication of their own experiences with hemodialysis such that appropriate inferences can be made and understood with regard to the utility of the technique in their report.

It is my sincere hope that you enjoy this issue as much as I will and that you keep it handy, share it with your colleagues, and refer to it often.

The EXTRIP group would like to recognize the valuable contribution of their peers who have been pioneers in expanding the difficult science of improving outcome of poisoned patients with extracorporeal treatments. Without their insight and dedication, our knowledge would still be in its infancy today. It is a tribute to their work that papers that were published 100 years ago still have meaning and value. We dedicate this issue to some of these giants: Thomas Graham, John Abel, Paul Doolan, Georg Haas, Willem J. Kolff, George Schreiner, Stefan Okonek, Jerry L. Rosenbaum, James F. Winchester, Günther Seyffarth, Miroslav Mydlik, Dag Jacobsen, Marc E. De Broe, Les Benet, Thomas P. Gibson, Bernd Grabensee, Chantal Bismuth, Evgeny Alekseevich Luzhnikov, and Thomas Tozer.

References