EDITORIAL

Happy 50th Anniversary Ketamine

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Guest editor for the special issue.

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In 1962, 50 years ago, a remarkable molecule was first synthesized by the team of Professor Calvin Lee Stevens, Ph.D., Professor of Organic Chemistry at Wayne State University and a chemical consultant to Parke Davis at that time. As soon as 1964, this molecule, ketamine (CI-581), a phencyclidine derivative, was evaluated during a clinical trial. It was rapidly introduced into clinical practice. Since this date, the medical and scientific world seems to have been divided into strong believers and ardent contenders. For its 50th anniversary, a special issue is dedicated to ketamine and features 10 reviews that will try to shade lights on the different characteristics of the molecule, a two-faced Janus, with both bad and good ones.

Numerous studies have tried to unravel the multiple ways by which ketamine exerts its actions. Mion and Villevieille will review the current knowledge. Ketamine is largely and safely used in anesthesia, both in prehospital and hospital settings as reviewed by Marland et al. The facts that it can be administered by different routes (im, iv or even, although rarely, orally), that it is not respiratory depressant, not always necessitating intubation and respiratory support, that it can be used in patients with a full stomach make it very attractive for anesthesia in difficult environments such as in the battlefield. Some of the untoward effects can be reduced by combination with other drugs. However, dissociative anesthesia induces signs that can be misinterpreted by nonregular users and lead to some prevention.

The opponents to ketamine will emphasize its adverse effects, such as its neurotoxicity in some age-groups, as reviewed by Wang et al., its psychotomimetic properties that led to its use in experimental models of schizophrenia as reviewed in this special issue by Kocsis et al., or its potentials for long-term neurological effects even after a single administration, even though no data support the latter, neither in

infants/children nor in adults. Similarly, although this is no longer truly valid, some will continue to mention that brain trauma is a contraindication for ketamine's use and Chang et al. will review "The emerging use of ketamine for anesthesia and sedation in traumatic brain injuries". Its potentials for use (abuse) as a recreational drug, which started as early as the late 60s, also probably participate to this unfavorable picture. Corazza et al. review this case of abuse as well as the emergence of the use of a ketamine derivative, methoxetamine.

Conversely, the molecule displays a wide array of interesting features usable in different areas of medical interventions, aside from anesthesia already mentioned. Indeed, a renewed interest for this molecule stemmed from reports showing its interesting properties in the field of analgesia (as reviewed by Persson), depression (as reviewed here by Salvatore and Singh) and for its neuroprotective properties after central nervous system insults. In the mind of many, ketamine, because of its very special properties, can induce seizures but a review of the literature fails to find a clear support for this. Uncoordinated movements have been reported as convulsions. Electroencephalographic features of ketamine's anesthesia have sometimes been misinterpreted. All this probably prevented neurologists to widely use ketamine in the treatment of seizures and *status epilepticus* (SE) although it is sometimes used as a third line of treatment for refractory SE. A wealth of preclinical studies, and some clinical reports, call for an extended use of ketamine to abate seizures and provide neuroprotection as reviewed by Dorandeu et al. Its peripheral antiinflammatory properties have also started to draw attention and will be presented by de Kock et al.

All in all, by the number of current publications on ketamine, it is clear that it remains a drug of remarkable interest. Happy anniversary ketamine!