KETAMINE
A phencyclidine derivative

Mechanism of Action
1. With repeated C fiber input, NMDA receptors increase C fiber activity and receptor field, which can contribute to phenomena like wind-up and sensitization
2. Ketamine’s non-competitive antagonism of NMDA type glutamate receptors in the brain and spinal cord prevents calcium influx which leads to decreased downstream nociceptive signaling

On WHO list of essential medicines
since 1985 due to its versatility and low cost

Dosing & indications
- Induction: 1-2mg/kg IV, 2-4 mg/kg IM
- Analgesia/prevention of opioid induced hyperalgesia: 3-5 mcg/kg/min
- Chronic pain: 0.35mg/kg bolus, or 8.33-33mcg/kg/min infusion (grade C)
- Analgesia (oral dosing): 0.5 - 1mg/kg daily to TID (under investigation)

Pharmacokinetics
- Low oral bioavailability due to flow dependent hepatic clearance
- Lipophilic with rapid distribution, large Vd and low protein binding
- Half-life 2-4 hours with short context sensitive half time
- Excretion: hepatic oxidation to norketamine and other minor metabolites, glucuronidation and excretion in bile > urine

Emergence reactions & side effects
- Emergence reactions less common with intraop dosing
- Not dose dependent
- Retrospective studies estimate 16% incidence but wide variability between studies, and concern for observer bias in non-blinded studies
- Indirect sympathomimetic and direct negative inotrope can increase myocardial work in at-risk patients
- Potent bronchodilator, preserved spontaneous respiration & airway reflexes, but increased secretions
- Potentially neurotoxic intrathecally
- Use caution with hepatic dysfunction and elevated ICP or IOP

Potency and onset time as antidepressant equal or superior to classical pharmacological treatments or ECT

Emergence reactions & side effects

References:
2. WHO model list of essential medicines, 2017
3. Papadimitropoulou, Vossen, Karabis, Donatti, & Kubitz, 2017
4. Cohen, et al., 2018
5. Barreved, et al., 2013
6. Abram, 2011
7. Schwenk, et al., 2016
8. Lemoel, et al., 2017
10. Choi, et al., 2015

In a double blinded prospective RCT (n>300) of chronic opioid using lumbar spine surgery patients.