

ACE Question

Which of the following mechanisms is MOST likely responsible for the analgesic effects of gabapentin?

- (A) Acting as an agonist at the γ -aminobutyric acid (GABA) receptor (B) Blocking *N*-methyl-D-aspartate (NMDA) receptors
(C) Blocking voltage-gated calcium channels

Though gabapentin and pregabalin are structural analogs of GABA, they are not active at the GABA receptor. Gabapentin is extensively used for the treatment of neuropathic pain conditions. Its mechanism of action is thought to be mediated by blocking voltage-gated calcium channels and reducing calcium influx. By blocking calcium influx, gabapentin reduces the release of excitatory neurotransmitters like glutamate, substance P, norepinephrine, and calcitonin gene-related peptide from primary nociceptive afferents, thereby modulating nociceptive transmission. Gabapentin has been used to treat neuropathic pain conditions associated with diabetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, complex regional pain syndrome, and painful peripheral neuropathies associated with cancer.

Gabapentin was initially approved by the U.S. Food and Drug Administration as an anticonvulsant, but it is now widely



used off-label in conjunction with other medications for the management of pain. The use of gabapentin in enhanced recovery protocols has become more

controversial given recent data suggesting that the opioid-sparing effect is minimal, while the risk for postoperative respiratory depression may be increased.

Gabapentin does not block the NMDA receptor. ■

References:

1. Gropper MA, Cohen NH, Eriksson LI, Fleisher LA, Leslie K, Wiener-Kronish JP, eds. Miller's Anesthesia. 9th ed, 2020:742-6.
2. Hardman JG, Hopkins PM, Struys MMRF, eds. Oxford Textbook of Anaesthesia. 2017:318-9.

Answer: C

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Complexities of Physician-Assisted Dying

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must be given to the physician's own moral agency. (asamonitor.pub/3Tn-FIIA; *Surg Endosc* 2021;35:2217-22). The question of whether a patient's autonomy outweighs a physician's obligation to nonmaleficence is central to such discussions.

Some readers may remember an anonymous physician's experience of providing medical assistance in dying titled "It's Over, Debbie," which was published in *JAMA* in 1988 (*JAMA* 1988;259:272). The case described an exhausted resident cross-covering on the gynecology-oncology service at a private hospital. The resident was called to the bedside overnight for a young woman with intractable vomiting and end-stage ovarian cancer. In response, the resident personally administered 20 milligrams of intravenous morphine with the intention to "give her rest." The patient became apneic shortly thereafter. The essay, and the decision to publish the essay in the

journal, engendered an enormous response (*JAMA* 1988;259:2142-3). Then, as now, this conversation is reasonable; more broadly, the conversation needs to encompass how patient-centered care can be best provided at the end of life, which is our aim in the present essay. Debbie's case exposed the lack of patient-oriented safeguards when medical assistance in dying was done without a strong patient-physician relationship, patient education, or psychological evaluation.

The ethical doctrine of double effect can be used to evaluate treatments for patients at the end of their life. The principle describes how an unintended negative consequence can be permissible if an action is the means to a separate, intended outcome (*Philos Ethics Humanit Med* 2023;18:7; St. Thomas Aquinas *Summa Theologica: Complete English Edition* in Five Volumes. 2000). It is classically applied in the administration of opioids, either to provide analgesia or relieve air hunger, in perimortem patients. By considering the character of the positive effect (comfort), a clinician

may be able to tolerate a negative side effect (apnea) so long as the intention is not euthanasia. The doctrine includes four criteria to justify a negative, unintended effect:

1. The act itself (in this case, prescription) must be a moral good, or at least indifferent
2. The decision-maker must not *intend* the negative effect but may *allow* it
3. The negative effect must not be the means to achieving the positive effect
4. The intended effect must be proportionally desirable to accept the negative effect's severity.

In considering the clinical status of moribund patients, maybe with widespread

metastases or other incurable symptoms, physicians will approach each patient individually. Strong respect for colleagues' moral boundaries in this area can minimize disruptions to care and ensure the patient's wishes remain the focus of management discussions. Regardless of one's subspecialty or the legal status of physician-assisted dying locally, anesthesiologists may need to discuss these end-of-life scenarios with patients, colleagues, and families. ■

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