

General anaesthetics

Intravenous and inhalational agents that produce reversible loss of consciousness for surgery, each with a distinct mechanism and a distinct signature risk, from malignant hyperthermia to adrenal suppression.

Online guide: <https://www.medguideglobal.com/pharmacology/analgesia-and-anaesthesia/general-anaesthetics>

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Quick revision

One Liner: General anaesthetics produce reversible unconsciousness mainly by enhancing inhibitory GABA-A and glycine signalling and blocking excitatory NMDA and nicotinic signalling, and each agent's specific risk profile - malignant hyperthermia, adrenal suppression, or infusion syndrome - is what actually differentiates the class.

1. Inhalational agents work by augmenting inhibitory chloride-channel activity (GABA and glycine receptors) and inhibiting excitatory channels (NMDA, nicotinic acetylcholine, serotonin, glutamate) in the CNS; the precise mechanism remains incompletely understood. [1]
2. Minimum alveolar concentration (MAC) is the potency benchmark for inhalational agents: the concentration at which 50% of people do not move to a noxious stimulus. [1]
3. Propofol acts by binding GABA-A receptors and prolonging chloride-channel opening, hyperpolarising postsynaptic neurons. [2]
4. Ketamine acts by noncompetitive NMDA receptor antagonism, producing dissociative anaesthesia rather than the GABA-mediated unconsciousness of most other agents, and preserves airway reflexes and cardiovascular tone better than most alternatives. [3]
5. Etomidate causes dose-dependent inhibition of 11-beta-hydroxylase, suppressing cortisol synthesis for 6 to 12 hours after a single bolus; it is no longer given by continuous infusion because of the risk of sustained adrenal suppression. [4]
6. Malignant hyperthermia is a hereditary hypermetabolic reaction to halogenated inhalational agents or succinylcholine, caused by defective ryanodine receptors, and is treated with intravenous dantrolene. [5]
7. Propofol infusion syndrome is a rare but often fatal complication of prolonged high-dose propofol, involving mitochondrial dysfunction, cardiac and skeletal muscle injury, with reported mortality of about 18 to 32%. [2]
8. Ketamine emergence reactions - vivid dreams, hallucinations, confusion or agitation on waking - occur in roughly 12% of patients and are commonly reduced by co-administering a benzodiazepine. [3]

Overview

1. General anaesthetics produce a medically-induced, reversible loss of consciousness with concurrent loss of protective reflexes, given intravenously (propofol, ketamine, etomidate, thiopental) or by inhalation (sevoflurane, isoflurane, desflurane, nitrous oxide). Most agents converge on a shared mechanistic theme - augmenting inhibitory GABA-A and glycine chloride-channel activity while dampening excitatory NMDA, nicotinic, serotonergic and glutamatergic signalling in the CNS - though the precise molecular mechanism for the class as a whole is still incompletely understood. [1]
2. Ketamine is the clear exception, working chiefly through noncompetitive NMDA receptor antagonism rather than GABA enhancement, which is why it produces a dissociative state and tends to preserve airway reflexes and cardiovascular tone rather than depress them. Propofol acts by prolonging GABA-A chloride channel opening; etomidate does too, but is distinguished by a specific and clinically important side effect on adrenal steroid synthesis. [2][3][4]
3. What matters most for safe use of this class is not a shared toxicity but each agent's specific, well-defined hazard:

malignant hyperthermia with halogenated inhalational agents and succinylcholine, propofol infusion syndrome with prolonged high-dose propofol, and transient but real adrenal suppression with even a single etomidate bolus. Recognising which hazard belongs to which agent is the core clinical skill this class teaches. [5][2][4]

Classification and drug examples

Intro: Best learned by route and by the specific hazard each agent carries, since the shared 'produces unconsciousness' effect explains little about how each is actually used and monitored.

1. Name: Intravenous induction and maintenance agents

1. Note: Used to induce anaesthesia rapidly and, for some agents, to maintain it; each carries a distinct signature risk.

1. Name: Propofol

1. Route: IV

1. Note: GABA-A agonist used for induction and maintenance and for procedural sedation; risk of propofol infusion syndrome with prolonged high-dose use. [2]

2. Name: Ketamine

2. Route: IV/IM

2. Note: NMDA antagonist producing dissociative anaesthesia; relatively preserves airway reflexes and haemodynamics; emergence reactions in roughly 12% of patients. [3]

3. Name: Etomidate

3. Route: IV

3. Note: Favoured for cardiovascular stability at induction; causes dose-dependent adrenal suppression via 11-beta-hydroxylase inhibition, so is not used as a continuous infusion. [4]

4. Name: Thiopental

4. Route: IV

4. Note: An older barbiturate induction agent, largely superseded by propofol in routine practice. [2] [2]

2. Name: Inhalational (volatile and gaseous) agents

2. Note: Used chiefly for maintenance of anaesthesia; potency is compared using MAC, and halogenated agents are the classic malignant hyperthermia trigger.

1. Name: Sevoflurane

1. Route: Inhaled

1. Note: A commonly used halogenated volatile agent; MAC approximately 2.6%. [1]

2. Name: Isoflurane

2. Route: Inhaled

2. Note: A halogenated volatile agent; MAC approximately 1.2%. [1]

3. Name: Nitrous oxide

3. Route: Inhaled

3. Note: A gaseous agent of low potency (MAC approximately 104%) used as an adjunct; contraindicated in bowel surgery, craniotomy and intraocular procedures because of expansion of closed air spaces. [1] [1]

Mechanism of action

Summary: Most general anaesthetics enhance inhibitory GABA-A/glycine chloride-channel signalling and dampen excitatory NMDA, nicotinic, serotonergic and glutamatergic signalling in the CNS. Ketamine is the notable exception, acting chiefly through NMDA receptor blockade. The precise molecular basis of general anaesthesia as a unified phenomenon remains incompletely understood.

Target: GABA-A and glycine receptors (most agents); NMDA receptors (ketamine); multiple additional excitatory channels depressed by inhalational agents

Cidal Static: Not applicable - this class produces reversible unconsciousness, not antimicrobial killing.

Kill Kinetics: Not applicable in the antimicrobial sense; effect tracks alveolar or plasma concentration and is titrated to

the desired depth of anaesthesia.

1. Step: 1

1. Title: Inhibitory chloride-channel activity is enhanced

1. Detail: Propofol and the inhalational agents augment signalling through GABA-A (and, for inhalational agents, glycine) receptors, prolonging chloride channel opening and hyperpolarising neurons in the CNS. [2][1]

2. Step: 2

2. Title: Excitatory signalling is suppressed

2. Detail: Inhalational agents also depress excitatory neurotransmission through NMDA, nicotinic acetylcholine, serotonin and glutamate receptors, contributing to the overall CNS depression. [1]

3. Step: 3

3. Title: Ketamine instead blocks NMDA receptors directly

3. Detail: Ketamine's anaesthetic and analgesic action is attributed to noncompetitive antagonism of NMDA receptors in the cortex, limbic system and hippocampus, producing a dissociative rather than a classically hypnotic state. [3]

4. Step: 4

4. Title: Depth of anaesthesia is titrated against a potency benchmark

4. Detail: For inhalational agents, minimum alveolar concentration (MAC) - the concentration at which 50% of patients do not move to a noxious stimulus - is the standard used to titrate and compare agents. [1]

5. Step: 5

5. Title: Consciousness and reflexes return as the agent clears

5. Detail: Because the effect tracks ongoing receptor occupancy rather than a lasting structural change, anaesthesia reverses as the drug is redistributed and eliminated, restoring consciousness and protective reflexes. [1]

Major clinical uses

1. Drug: Propofol

1. Indication: Induction and maintenance of general anaesthesia; procedural sedation

1. Line: first-line induction agent in routine practice

1. Note: Monitor for propofol infusion syndrome with prolonged high-dose administration. [2]

2. Drug: Ketamine

2. Indication: Induction of anaesthesia in haemodynamically unstable patients, procedural sedation, and analgesia

2. Line: targeted, especially where cardiovascular stability or airway reflex preservation matters

2. Note: Co-administer a benzodiazepine to reduce emergence reactions. [3]

3. Drug: Etomidate

3. Indication: Rapid-sequence induction, particularly in patients where cardiovascular depression from other agents would be poorly tolerated

3. Line: targeted, single-bolus use

3. Note: Not used as a continuous infusion because of adrenal suppression risk. [4]

4. Drug: Sevoflurane / isoflurane

4. Indication: Maintenance of general anaesthesia after intravenous induction

4. Line: maintenance

4. Note: Halogenated agents are malignant hyperthermia triggers in susceptible patients. [1][5]

5. Drug: Nitrous oxide

5. Indication: Adjunct to reduce the required dose of other anaesthetic agents

5. Line: adjunct

5. Note: Avoid in bowel surgery, craniotomy and intraocular procedures. [1]

Pharmacokinetics

1. Drug: Propofol

1. Route: IV
1. Absorption: Not applicable (parenteral)
1. Csf Penetration: Highly lipophilic; rapid CNS penetration explains fast onset
1. Metabolism: Hepatic and extrahepatic
1. Elimination: Renal, as metabolites
1. Half Life: See prescribing reference; rapid redistribution accounts for quick emergence from a single dose
1. Dose Adjust: Prolonged high-dose infusion raises propofol infusion syndrome risk [2]
2. Drug: Etomidate
2. Route: IV
2. Absorption: Not applicable (parenteral)
2. Csf Penetration: Rapid CNS penetration
2. Metabolism: Hepatic ester hydrolysis
2. Elimination: Renal, as metabolites
2. Half Life: See prescribing reference
2. Dose Adjust: Not used as continuous infusion because of adrenal suppression; caution with repeat or prolonged dosing [4]
3. Drug: Sevoflurane / isoflurane / nitrous oxide
3. Route: Inhaled
3. Absorption: Alveolar uptake governed by solubility and ventilation
3. Csf Penetration: Crosses to CNS, which is the site of action
3. Metabolism: Minimal to moderate hepatic metabolism, varies by agent
3. Elimination: Chiefly exhaled unchanged
3. Half Life: Not a standard pharmacokinetic parameter for inhaled agents; MAC governs dosing instead
3. Dose Adjust: Halogenated agent exposure is a malignant hyperthermia trigger in susceptible patients [1]
1. This page gives no dose regimens by design. Induction and maintenance dosing depend on the patient's physiology, the procedure, monitoring available and concurrent medications, and belong in a prescribing reference and anaesthetic protocol used by the treating clinician.
2. Every general anaesthetic requires personnel and equipment for airway management and resuscitation to be immediately available; this class is never given without that support in place. [1]

Adverse effects

1. Effect: Postoperative nausea and vomiting
1. Detail: The most common adverse effect reported with inhalational anaesthesia. [1]
2. Effect: Cardiovascular and respiratory depression
2. Detail: Dose-dependent with most agents; etomidate and ketamine are relative exceptions in typical dosing. [1]
1. Effect: Malignant hyperthermia
1. Detail: A hereditary hypermetabolic reaction to halogenated inhalational agents or succinylcholine, presenting with hyperthermia, tachycardia, muscle rigidity, hyperkalaemia and metabolic imbalance in genetically susceptible patients.
1. Action: Stop the triggering agent immediately, give IV dantrolene, and manage temperature, acidosis and hyperkalaemia. [5]
2. Effect: Propofol infusion syndrome
2. Detail: A rare complication of prolonged high-dose propofol, typically within about four days, involving mitochondrial dysfunction and cardiac/skeletal muscle injury; reported mortality roughly 18 to 32%.
2. Action: Limit dose and duration where possible and monitor for metabolic acidosis, rhabdomyolysis and cardiac dysfunction with prolonged infusions. [2]
3. Effect: Adrenal suppression
3. Detail: Etomidate causes dose-dependent inhibition of 11-beta-hydroxylase, suppressing cortisol synthesis for 6 to

12 hours after a single bolus.

3. Action: Consider stress-dose steroid coverage in critically ill patients and avoid continuous infusion. [4]

1. Drug: Ketamine

1. Effect: Emergence reactions - vivid dreams, hallucinations, confusion or agitation on waking - in roughly 12% of patients. [3]

2. Drug: Nitrous oxide

2. Effect: Expansion of closed air-filled spaces from its high solubility, hazardous in bowel surgery, craniotomy and intraocular procedures. [1]

Contraindications, precautions and interactions

1. Known or strongly suspected malignant hyperthermia susceptibility, for halogenated inhalational agents. [5]

2. Nitrous oxide specifically: bowel surgery, craniotomy and intraocular procedures. [1]

1. Critical illness or physiologic stress states, where etomidate's adrenal suppression is a particular concern. [4]

2. Anticipated prolonged high-dose sedation with propofol, given propofol infusion syndrome risk. [2]

3. Conditions where ketamine's psychotomimetic emergence effects, or raised sympathetic tone, would be poorly tolerated. [3]

1. With: Succinylcholine, in a patient susceptible to malignant hyperthermia

1. Effect: Also a recognised trigger; combined use with a halogenated agent compounds the risk. [5]

2. With: Other CNS depressants

2. Effect: Additive sedative and cardiorespiratory depressant effect with most general anaesthetics. [1]

Comparison tables

Title: Each agent's signature risk

Caption: The differentiating hazard, not the shared property of producing unconsciousness. A prescribing reference and the treating anaesthetist govern actual therapy.

1. Key: drug

1. Label: Agent

1. Is Row Header: true

2. Key: mechanism_note

2. Label: Mechanistic note

3. Key: signature_risk

3. Label: Signature risk

1. Drug: Propofol

1. Mechanism Note: GABA-A chloride channel prolongation

1. Signature Risk: Propofol infusion syndrome with prolonged high-dose use [2]

2. Drug: Ketamine

2. Mechanism Note: NMDA receptor antagonism (dissociative)

2. Signature Risk: Emergence reactions in ~12% of patients [3]

3. Drug: Etomidate

3. Mechanism Note: GABA-A enhancement with cardiovascular stability

3. Signature Risk: Adrenal suppression via 11-beta-hydroxylase inhibition [4]

4. Drug: Sevoflurane / isoflurane

4. Mechanism Note: Halogenated inhalational, GABA/glycine plus excitatory-channel depression

4. Signature Risk: Malignant hyperthermia trigger in susceptible patients [1][5]

5. Drug: Nitrous oxide

5. Mechanism Note: Low-potency gaseous adjunct

5. Signature Risk: Expansion of closed air spaces; avoided in bowel, cranial and intraocular surgery [1]

High-yield exam pearls

1. Pearl: MAC is defined by movement, not by unconsciousness.
1. Why: Minimum alveolar concentration is specifically the concentration at which 50% of patients do not move in response to a noxious stimulus - a surgical-immobility endpoint, not directly a measure of hypnosis or memory suppression. [1]
2. Pearl: Ketamine is the outlier mechanism in the class.
2. Why: While most general anaesthetics work chiefly through GABA-A/glycine enhancement, ketamine works through NMDA receptor blockade, producing a dissociative rather than a purely hypnotic state - and, unusually for the class, it tends to preserve airway reflexes and haemodynamic stability. [3]
3. Pearl: Etomidate's cardiovascular stability comes with a hidden hormonal cost.
3. Why: Etomidate is prized for causing little cardiovascular depression, but even a single induction bolus measurably suppresses cortisol synthesis via 11-beta-hydroxylase inhibition for 6 to 12 hours - which is why it is no longer used as a continuous infusion. [4]
4. Pearl: Malignant hyperthermia is a receptor problem, not a drug-overdose problem.
4. Why: It results from a defective ryanodine receptor releasing calcium uncontrollably in genetically susceptible muscle when triggered by a halogenated agent or succinylcholine - dantrolene works by directly blocking that same receptor, not by reversing the anaesthetic. [5]
5. Pearl: Propofol infusion syndrome is a duration-and-dose phenomenon.
5. Why: It typically appears within four days of high-dose propofol infusion and reflects impaired mitochondrial fatty-acid metabolism rather than an acute allergic or idiosyncratic reaction - which is why prolonged high-dose sedation, more than a single induction dose, is the setting of concern. [2]
6. Pearl: Nitrous oxide's danger is about physics, not toxicity.
6. Why: Its high solubility allows it to diffuse into and expand air-filled spaces, which is why it is contraindicated in bowel surgery, craniotomy and intraocular procedures - a mechanical hazard rather than a pharmacological one. [1]

Common exam traps

1. Trap: "All general anaesthetics work through the same GABA mechanism."
1. Correction: Ketamine is the clear exception: its anaesthetic and analgesic action is attributed to noncompetitive NMDA receptor antagonism, not primarily to GABA-A enhancement, which is why its clinical profile - preserved airway reflexes, dissociative state, emergence reactions - differs so much from propofol or the inhalational agents. [3]
2. Trap: "Malignant hyperthermia is treated by giving more anaesthetic to deepen the plane and suppress the reaction."
2. Correction: Malignant hyperthermia is treated by stopping the triggering agent immediately and giving intravenous dantrolene, which blocks the defective ryanodine receptor directly. Continuing a triggering agent worsens the hypermetabolic crisis. [5]
3. Trap: "Etomidate's adrenal suppression only matters with prolonged infusion."
3. Correction: A single induction bolus already causes measurable, dose-dependent adrenal suppression lasting 6 to 12 hours, with roughly 80% of patients showing inhibition at 12 hours in the cited data - the concern is real even after one dose, which is exactly why continuous infusion was abandoned. [4]
4. Trap: "Nitrous oxide is contraindicated because it is directly toxic to the bowel or eye."
4. Correction: The mechanism is physical, not toxic: nitrous oxide's high solubility lets it diffuse into closed air spaces faster than nitrogen leaves, expanding them - which is why it is avoided in bowel surgery, craniotomy and intraocular procedures specifically. [1]

Self-test questions

1. Question: What does minimum alveolar concentration (MAC) actually measure?

1. The blood concentration at which 50% of patients become unconscious
 2. The alveolar concentration of an inhaled anaesthetic at which 50% of people do not move in response to a noxious stimulus
 3. The maximum safe concentration before respiratory arrest occurs
 4. The concentration required for complete amnesia in all patients
1. Explanation: MAC is specifically defined as the minimum alveolar concentration at which 50% of people do not move in response to a noxious stimulus. It is a potency and surgical-immobility benchmark, used to compare inhalational agents, not a direct measure of unconsciousness or amnesia. [1]
2. Question: How does ketamine's mechanism differ from that of propofol?
1. Both work identically through GABA-A receptor enhancement
 2. Ketamine acts through noncompetitive NMDA receptor antagonism producing dissociative anaesthesia, while propofol acts by prolonging GABA-A chloride channel opening
 3. Ketamine blocks voltage-gated sodium channels, exactly like a local anaesthetic
 4. Propofol works through NMDA antagonism and ketamine through GABA enhancement - the reverse of the true mechanisms
2. Explanation: Propofol binds GABA-A receptors and prolongs chloride-channel opening, hyperpolarising neurons. Ketamine instead works mainly through noncompetitive NMDA receptor antagonism, producing a dissociative anaesthetic state with relatively preserved airway reflexes and haemodynamics. [2][3]
3. Question: Why is etomidate no longer given as a continuous infusion?
1. It causes unacceptable cardiovascular depression with prolonged use
 2. It causes dose-dependent inhibition of 11-beta-hydroxylase, suppressing cortisol synthesis, and sustained infusion risks prolonged adrenal suppression
 3. It has too short a duration of action to be infused
 4. It causes malignant hyperthermia when infused continuously
3. Explanation: Even a single etomidate bolus measurably suppresses cortisol synthesis via 11-beta-hydroxylase inhibition, an effect lasting 6 to 12 hours. Continuous infusion was abandoned because sustained suppression of the adrenal stress response is a genuine safety concern. [4]
4. Question: What is the underlying defect responsible for malignant hyperthermia?
1. An acquired liver enzyme deficiency that prevents anaesthetic metabolism
 2. A hereditary defect in the ryanodine receptor causing uncontrolled calcium release in skeletal muscle in response to a triggering agent
 3. An allergic IgE-mediated reaction to inhalational anaesthetic vapour
 4. Excess circulating cortisol triggered by surgical stress
4. Explanation: Malignant hyperthermia is a hereditary pharmacogenetic disorder in which a defective ryanodine receptor in the skeletal muscle sarcoplasmic reticulum releases calcium uncontrollably when triggered by a halogenated anaesthetic or succinylcholine, producing a hypermetabolic crisis. Dantrolene treats it by directly antagonising that receptor. [5]
5. Question: What best describes propofol infusion syndrome?
1. An immediate anaphylactic reaction occurring within minutes of the first propofol dose
 2. A rare complication, typically appearing within about four days of prolonged high-dose propofol infusion, involving mitochondrial dysfunction and cardiac/skeletal muscle injury, with reported mortality of roughly 18 to 32%
 3. A benign, self-limiting rash seen with any propofol exposure
 4. A withdrawal syndrome occurring after propofol is stopped
5. Explanation: Propofol infusion syndrome typically develops within about four days of prolonged high-dose administration. Its proposed mechanism involves impaired mitochondrial fatty-acid metabolism and an energy-demand mismatch leading to cardiac and skeletal muscle necrosis, and reported mortality is substantial at roughly 18 to 32%. [2]

6. Question: Why is nitrous oxide avoided in bowel surgery, craniotomy and intraocular procedures?

1. It is directly neurotoxic to those tissues
 2. Its high solubility lets it diffuse into and expand closed air-containing spaces faster than nitrogen can leave them, raising pressure in those spaces
 3. It causes malignant hyperthermia specifically in those procedures
 4. It has no relevant contraindication in these settings
6. Explanation: Nitrous oxide is highly soluble and diffuses into closed gas-filled spaces (bowel lumen, intracranial or intraocular air) faster than the nitrogen already there can be washed out, expanding those spaces and raising pressure - a mechanical rather than toxic hazard. [1]

Frequently asked questions

1. Question: Why does the same class of drugs cause both unconsciousness and dangerous reactions like malignant hyperthermia?

1. Answer: Most general anaesthetics act broadly on CNS inhibitory and excitatory receptors to produce unconsciousness, which is a separate mechanism from malignant hyperthermia. That reaction comes from a hereditary defect in a specific muscle calcium-release channel (the ryanodine receptor) that a halogenated agent or succinylcholine can trigger in genetically susceptible people - it is a patient-specific vulnerability, not an expected effect of the anaesthetic itself. [5]

2. Question: Is ketamine 'safer' than propofol because it does not depress breathing as much?

2. Answer: Ketamine does tend to preserve airway reflexes and cardiovascular tone better than many alternatives, which makes it useful in specific situations such as haemodynamic instability. But it carries its own distinct risk - emergence reactions in roughly 12% of patients - so it is a different risk profile, not a uniformly safer one; the right agent depends on the clinical situation. [3]

3. Question: Why is etomidate avoided for ongoing sedation in intensive care?

3. Answer: Even a single dose measurably suppresses cortisol production for 6 to 12 hours by inhibiting an adrenal enzyme. A continuous infusion would sustain that suppression, which is a real safety concern in critically ill patients who depend on an intact stress response - this is why etomidate infusions were abandoned in practice. [4]

4. Question: What is malignant hyperthermia and how is it treated?

4. Answer: It is a hereditary reaction in which a defective muscle calcium-release channel is triggered by a halogenated anaesthetic or succinylcholine, causing dangerous hyperthermia, muscle rigidity and metabolic derangement. It is a medical emergency treated by stopping the triggering drug immediately and giving intravenous dantrolene alongside supportive care. [5]

References

[1] Inhalational Anesthetic (StatPearls). StatPearls Publishing / NCBI Bookshelf 2025.

<https://www.ncbi.nlm.nih.gov/books/NBK554540/>

[2] Propofol (StatPearls). StatPearls Publishing / NCBI Bookshelf 2025. <https://www.ncbi.nlm.nih.gov/books/NBK430884/>

[3] Ketamine (StatPearls). StatPearls Publishing / NCBI Bookshelf 2025. <https://www.ncbi.nlm.nih.gov/books/NBK470357/>

[4] Etomidate (StatPearls). StatPearls Publishing / NCBI Bookshelf 2023. <https://www.ncbi.nlm.nih.gov/books/NBK535364/>

[5] Malignant Hyperthermia (StatPearls). StatPearls Publishing / NCBI Bookshelf 2025.

<https://www.ncbi.nlm.nih.gov/books/NBK430828/>

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