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Original Research

Anaesthesia Under Scrutiny: A Contemporary Insight into Its Untold Adverse Effects

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ABSTRACT:
Anaesthesia has revolutionized modern surgery by providing reliable pain relief, inducing unconsciousness, and ensuring immobility, thereby enabling complex surgical procedures. Despite significant advances in pharmacology, monitoring, and perioperative care, anaesthetic practice carries a spectrum of potential adverse effects that extend beyond immediate physiological disturbances. This review explores both well-recognised and underappreciated complications, including respiratory and cardiovascular instability, postoperative nausea and vomiting, malignant hyperthermia, neurological and cognitive dysfunction, organ-specific impairments, chronic post-surgical pain, immunological alterations, and microbiome-related effects. Special attention is given to vulnerable populations such as the elderly, neonates, pregnant patients, and those with significant comorbidities. Furthermore, the review highlights the roles of anaesthetic equipment, human factors, and advances in monitoring and risk mitigation, including enhanced recovery protocols, neuromuscular and depth-of-anaesthesia monitoring, and emerging precision-based strategies.

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INTRODUCTION

Evolution of Anaesthesia: Progress and Persisting Concerns

Anaesthesia has undergone remarkable advances since its formal introduction in the mid-19th century, evolving from rudimentary ether inhalation to sophisticated multimodal techniques that enable complex surgical interventions. Modern anaesthetic practice now integrates refined pharmacology, advanced monitoring systems, and enhanced perioperative care pathways to improve patient safety and procedural success.Despite these achievements, anaesthesia is not without risk. Although adverse events have become less common, the expanding surgical population—including elderly patients, neonates, and individuals with substantial comorbidities—has heightened awareness of both immediate and long-term complications. Contemporary research continues to uncover subtle neurocognitive, immunological, and systemic effects that were previously under-recognized, prompting renewed scrutiny of anaesthetic exposures.

Rationale for Re-examining Anaesthetic Safety

With global surgical volumes increasing each year, understanding the full spectrum of anaesthesia-related risks has become more important than ever. Historically, perioperative morbidity was predominantly attributed to surgical factors, but a growing body of evidence highlights the significant contribution of anaesthesia itself. Concerns regarding postoperative cognitive dysfunction (POCD), delirium, chronic pain syndromes, and potential long-term organ-specific effects have sparked debate about the true safety profile of commonly used agents.Furthermore, advances in neuroimaging,

biomarker discovery, and long-term cohort studies are revealing mechanistic insights that were previously obscured. These developments necessitate a contemporary re-evaluation of anaesthetic practices to ensure informed decision-making, personalised care, and improved patient outcomes. This review therefore aims to synthesise emerging evidence on both recognised and underappreciated adverse effects of anaesthesia, offering a comprehensive perspective on its evolving risk landscape.[1-2]

OVERVIEW OF ANAESTHETIC AGENTS AND TECHNIQUES

General Anaesthetics

General anaesthesia induces a reversible state of unconsciousness, amnesia, analgesia, and immobility through a combination of intravenous and inhalational agents. Common intravenous agents such as propofol, etomidate, and ketamine act primarily through modulation of GABAergic or NMDA pathways, providing rapid induction and favourable pharmacokinetics. Volatile anaesthetics—including sevoflurane, desflurane, and isoflurane—are often used for maintenance due to their titratability and widespread familiarity among clinicians.Balanced anaesthesia, which incorporates opioids, neuromuscular blockers, and adjuncts such as dexmedetomidine or magnesium sulfate, aims to reduce the dose dependence and potential toxicity of any single agent. Despite the effectiveness of these techniques, growing evidence highlights concerns over neurocognitive effects, hemodynamic instability, and organ-specific toxicity, particularly in vulnerable populations.

Regional and Local Anaesthetics

Regional anaesthesia involves targeted blockade of peripheral nerves or neuraxial pathways to provide surgical anaesthesia and postoperative analgesia. Techniques include spinal and epidural anaesthesia, brachial plexus blocks, and peripheral nerve blocks performed under ultrasound guidance. These methods offer benefits such as reduced opioid consumption, improved postoperative pain control, and lower risk of systemic adverse effects associated with general anaesthesia.Local anaesthetics—such as lidocaine, bupivacaine, and ropivacaine—achieve reversible inhibition of nerve conduction by blocking sodium channels. While generally safe, adverse events ranging from hypotension and nerve injury to local anaesthetic systemic toxicity (LAST) remain important considerations, necessitating careful dosing, monitoring, and timely management strategies.

Sedation Practices

Sedation provides a continuum of altered consciousness, ranging from minimal anxiolysis to deep sedation, while maintaining varying degrees of patient responsiveness. Agents commonly used include benzodiazepines, propofol, dexmedetomidine, and short-acting opioids. Sedation is widely utilised in endoscopic, interventional radiologic, dental, and minor surgical procedures, and may be administered by anaesthetists or trained non-anaesthetist professionals depending on local guidelines.

Although sedation is often perceived as safer and less invasive than general anaesthesia, it carries its own set of risks—such as respiratory depression, airway obstruction, hemodynamic instability, and paradoxical reactions. The growing use of procedural sedation amplifies the need for updated safety protocols, appropriate monitoring standards, and competency-based training.[3-5]

IMMEDIATE ADVERSE EFFECTS OF ANAESTHESIA

Respiratory and Cardiovascular Instability

Anaesthetic agents exert profound effects on the respiratory and cardiovascular systems, often resulting in immediate physiological instability. Respiratory compromise may arise from hypoventilation, airway obstruction, laryngospasm, or bronchospasm, particularly during induction and emergence. Depressant effects of agents such as propofol and opioids reduce respiratory drive, while volatile anaesthetics can impair airway reflexes. Cardiovascular instability—manifesting as hypotension, arrhythmias, or myocardial depression—commonly occurs due to vasodilation, reduced cardiac contractility, or autonomic suppression. Patients with pre-existing cardiac disease, hypovolemia, or advanced age are at heightened risk. Rapid detection through continuous monitoring and timely corrective measures such as fluid resuscitation, vasopressor support, or airway interventions remain essential to mitigating these complications.

Post-operative Nausea and Vomiting (PONV)

PONV is one of the most frequent and distressing immediate complications of anaesthesia, affecting 20–30% of patients overall, with higher rates in females, non-smokers, and individuals with prior susceptibility. Volatile anaesthetics, nitrous oxide, and opioids are known triggers due to their effects on the chemoreceptor trigger zone and vestibular pathways.Although often self-limiting, PONV can lead to dehydration, electrolyte imbalance, surgical wound dehiscence, and delayed recovery or discharge. Prophylactic strategies—including multimodal antiemetic therapy, minimisation of emetogenic agents, and optimisation of hydration—play a central role in reducing incidence. Enhanced Recovery After Surgery (ERAS) protocols further support structured prevention and evidence-based management.[6]

Malignant Hyperthermia and Allergic Reactions

Malignant hyperthermia (MH) is a rare but life-threatening pharmacogenetic disorder triggered by volatile anaesthetics and depolarising neuromuscular blockers such as succinylcholine. It results in

uncontrolled calcium release within skeletal muscle, producing hypermetabolism, muscle rigidity, hypercapnia, acidosis, and rapidly rising core temperature. Early recognition and prompt administration of dantrolene significantly improve outcomes, making readiness and staff training critical components of perioperative safety.Allergic reactions, including anaphylaxis, represent another acute and potentially fatal complication of anaesthesia. Common culprits include neuromuscular blocking agents, antibiotics, latex, and chlorhexidine. Clinical manifestations range from urticaria and bronchospasm to cardiovascular collapse. Rapid diagnosis, cessation of suspected agents, airway support, and administration of epinephrine form the foundation of effective management.[7]

NEUROLOGICAL AND COGNITIVE COMPLICATIONS

Anaesthesia can contribute to a spectrum of neurological and cognitive complications, ranging from acute postoperative delirium to longer-term impairments such as post-operative cognitive dysfunction (POCD). Older adults and patients with pre-existing cognitive deficits are particularly vulnerable, with delirium linked to prolonged hospitalisation, functional decline, and increased mortality. Emerging evidence also raises concerns about neurotoxicity in neonates and young children, where prolonged or repeated exposure may affect synaptogenesis and neurodevelopment. While the association between anaesthesia and long-term cognitive decline or dementia remains inconclusive, perioperative stress, inflammation, and comorbidities may interact with anaesthetic agents to influence brain health, underscoring the importance of preoperative assessment, tailored anaesthetic planning, and postoperative cognitive monitoring.[6]

ANAESTHESIA-RELATED ORGAN DYSFUNCTION

Hepatic and Renal Impairment

Anaesthetic agents can exert direct and indirect effects on hepatic and renal function, particularly in patients with pre-existing organ impairment. Volatile anaesthetics such as halothane—though less commonly used today—are historically associated with immune-mediated hepatotoxicity, while modern agents like sevoflurane may generate fluoride ions, raising concerns about nephrotoxicity under prolonged exposure. Hypotension, reduced hepatic blood flow, and impaired renal perfusion during anaesthesia can further exacerbate organ dysfunction, contributing to postoperative cholestasis, acute kidney injury (AKI), or delayed drug clearance. Patients with liver cirrhosis or chronic kidney disease are at heightened risk due to altered pharmacokinetics and reduced reserve. Optimising haemodynamic stability, careful selection and dosing of anaesthetic drugs, and perioperative monitoring of liver and kidney function are essential to mitigating these risks.[7,8]

Pulmonary Complications

Anaesthesia significantly affects respiratory mechanics and gas exchange, predisposing patients to several pulmonary complications. Atelectasis develops in a majority of patients during general anaesthesia due to alveolar collapse, impaired diaphragmatic tone, and high inspired oxygen concentrations. This can contribute to postoperative hypoxaemia and predispose to pneumonia, particularly in elderly patients or those undergoing major abdominal or thoracic surgery.

Other complications include bronchospasm, aspiration, hypoventilation, and postoperative respiratory failure, often exacerbated by opioid-induced respiratory depression or underlying pulmonary disease. Lung-protective ventilation strategies, optimal positioning, adequate pain control, and early mobilisation are key measures to reduce pulmonary morbidity in the perioperative period.

Endocrine and Metabolic Disturbances

Anaesthesia and surgery trigger complex endocrine and metabolic responses driven by activation of the hypothalamic–pituitary–adrenal axis and sympathetic nervous system. These responses result in elevated cortisol, catecholamines, and inflammatory mediators, which can lead to hyperglycaemia, insulin resistance, electrolyte disturbances, and impaired thermoregulation.

Anaesthetic agents themselves can also influence hormonal balance—for example, etomidate suppresses adrenal steroidogenesis, while volatile agents may impair glucose homeostasis. Patients with diabetes, endocrine disorders, or severe physiological stress are particularly vulnerable to these disturbances. Careful intraoperative monitoring of glucose, temperature, and electrolytes, along with tailored fluid and metabolic management, is essential to maintaining physiological stability and reducing postoperative complications.[9-12]

CHRONIC AND UNDER-RECOGNIZED ADVERSE EFFECTS

Chronic post-surgical pain (CPSP), lasting beyond three months after surgery, can be influenced not only by surgical factors but also by anaesthetic management, with inadequate acute pain control contributing to central sensitisation and persistent pain. Anaesthetic agents also exert immunomodulatory effects, potentially suppressing innate and adaptive immune responses and altering inflammatory pathways, which may increase susceptibility to infections, delay wound healing, or, in cancer patients, affect tumour surveillance. Emerging evidence further suggests that anaesthesia and perioperative interventions can disrupt the gut microbiome, leading to systemic inflammation,

impaired gastrointestinal function, and prolonged recovery. Collectively, these chronic and under-recognised effects highlight the need for strategies such as multimodal analgesia, regional techniques, careful drug selection, and microbiome-conscious perioperative care to optimise long-term outcomes.[13]

SPECIAL POPULATIONS AT HIGHER RISK

Certain patient groups exhibit heightened vulnerability to the adverse effects of anaesthesia due to physiological, developmental, or comorbid factors. Neonates and pediatric patients are particularly susceptible because of immature organ systems, altered pharmacokinetics, and developing neural networks that may be sensitive to neurotoxic effects of anaesthetic agents. Airway management challenges, limited physiological reserve, and rapid metabolic changes further increase perioperative risk. Careful dosing, vigilant monitoring, and judicious selection of anaesthetic techniques are essential in this population. Older adults represent another high-risk group, with age-related declines in cardiac, pulmonary, renal, and hepatic function. Polypharmacy, frailty, and pre-existing cognitive impairment increase the risk of postoperative complications such as delirium, POCD, and cardiovascular instability. Tailored anaesthetic plans, preoperative geriatric assessment, and proactive postoperative monitoring are key strategies to minimise morbidity.

Pregnant patients require careful anaesthetic consideration to balance maternal and fetal safety. Physiological changes—such as increased blood volume, reduced functional residual capacity, and heightened sensitivity to anaesthetic drugs—necessitate precise titration. Regional anaesthesia is often preferred to minimise systemic drug exposure, while maintaining uteroplacental perfusion remains critical.[14,15]

Finally, patients with significant comorbidities, including cardiovascular, pulmonary, renal, hepatic, or metabolic disorders, face compounded risks. Reduced organ reserve, altered drug metabolism, and increased susceptibility to hemodynamic instability or respiratory compromise necessitate meticulous preoperative optimisation, personalised drug selection, and continuous intraoperative monitoring. Recognising these vulnerable populations allows anaesthesiologists to implement targeted interventions, improving both safety and postoperative outcomes.

ANAESTHETIC EQUIPMENT AND HUMAN FACTORS

Anaesthetic safety is heavily influenced by the reliability of equipment and the performance of the clinical team operating it. Equipment-related issues—such as ventilator malfunctions, vaporiser leaks, circuit disconnections, or inadequate airway devices—can lead to hypoventilation, hypoxia, or accidental awareness if not promptly recognised. Regular maintenance, pre-use checks, and adherence to standardised protocols remain essential safeguards. Human factors play an equally critical role, with cognitive overload, fatigue, communication lapses, and hierarchical barriers contributing to preventable errors. Complex operating room dynamics increase the likelihood of slips and omissions, particularly during high-stress or emergent scenarios. Simulation training, checklists, standardised handovers, and fostering a culture of open communication are proven strategies that enhance team performance and reduce adverse events.[16]

ADVANCES IN MONITORING AND RISK MITIGATION

Recent years have seen substantial progress in monitoring technologies designed to improve perioperative safety. Quantitative neuromuscular monitoring allows precise titration of muscle relaxants and reduces the risk of residual paralysis. Depth-of-anaesthesia monitors, although not infallible, offer valuable insights into consciousness levels and may help reduce the incidence of intraoperative awareness and excessive anaesthetic dosing. Advanced hemodynamic monitoring—ranging from minimally invasive cardiac output devices to goal-directed fluid therapy algorithms—supports optimised cardiovascular management in high-risk patients. Artificial intelligence and predictive analytics are playing an increasingly important role by identifying early signs of deterioration and guiding real-time decision-making. Enhanced Recovery After Surgery (ERAS) pathways further integrate evidence-based practices to minimise complications, shorten hospital stays, and support holistic perioperative risk mitigation.[17-18]

FUTURE DIRECTIONS IN SAFE ANAESTHESIA PRACTICE

The future of anaesthetic safety is driven by a shift toward personalised, precision-based care. Pharmacogenomics promises to improve drug selection and dosing based on individual genetic profiles, potentially reducing adverse reactions and improving efficacy. Emerging agents with more favourable safety profiles, such as ultra-short-acting opioids and next-generation intravenous anaesthetics, may further reduce systemic toxicity.Advances in closed-loop anaesthesia delivery systems—where drug administration is guided automatically by patient responses—offer the potential for more stable anaesthetic depth and reduced human error. Integration of machine learning into perioperative decision support systems may improve outcome prediction, optimise monitoring, and enhance early complication detection. In addition, growing interest in non-pharmacological adjuncts such as neuromodulation, hypnosis, and enhanced patient education reflects a movement toward more holistic, multimodal anaesthetic care.

CONCLUSION

Anaesthesia has evolved into an increasingly sophisticated and safer domain of modern medicine, yet a comprehensive understanding of its potential adverse effects remains critical for improving patient outcomes. From immediate physiological disturbances to chronic, under-recognised complications, the spectrum of anaesthesia-related risks spans multiple organ systems and patient populations. Vulnerable groups—such as the elderly, infants, pregnant patients, and individuals with significant comorbidities—require personalised strategies and heightened vigilance.

Continued progress in technology, monitoring, human-factor optimisation, and research into long-term effects will be essential to refining anaesthetic practice. As surgical demands grow worldwide, prioritising safety, innovation, and evidence-based care will ensure that anaesthesia remains both effective and increasingly secure for patients across diverse clinical settings.

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