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The impact of anaesthesia on the immune system: understanding mechanisms and clinical implications – part II**Andrea Ortiz-Domínguez¹, José R. Ortiz-Gómez²**¹ Service of Immunology, Jiménez Díaz Foundation University Hospital, Madrid, Spain² Service of Anaesthesiology, University Hospital of Navarre, Pamplona, Spain**Abstract**

Anaesthesia plays a crucial role in modern medicine. Recent research suggests that anaesthesia may also have significant effects on the immune system. This article provides a comprehensive review of the current understanding of how anaesthesia affects immune function. It is divided in two parts. The first one, explores the underlying mechanisms and discussing the clinical implications of leukocyte function, cell-mediated immunity, humoral immunity, gut microbiota and cytokine signaling pathways. The second part review the inflammatory response modulation, stress response and cancer recurrence rates. By elucidating these complex interactions, we aim to enhance our understanding of anaesthesia-related immunomodulation and facilitate the development of strategies to mitigate potential adverse effects. Advancing our knowledge of anaesthesia's immunomodulatory effects is a cornerstone to improve patient safety and the effectiveness of perioperative management. *Anestezjologia i Ratownictwo* 2025; 19: 172-184. doi:10.53139/AIR.20251918

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Introduction

This article is the second part of a review on the impact of anaesthesia on the immune system. We analyzed in the first part the mechanisms and clinical implications on leukocyte function, cell-mediated immunity, humoral immunity, gut microbiota and cytokine signaling pathways.

The second part focuses on the inflammatory response modulation, stress response and cancer recurrence rates and also exposes the effects of the different anaesthesia drugs on the immune system.

The literature search criteria are the same that described in the first part.

Inflammatory response modulation

The immune system is a complex defense mechanism that activates different immune cell lineages at the

infection site and initiates an inflammatory response to contain and eliminate pathogens. Noninfectious stimuli such as major surgery can also induce this response, causing tissue damage, sometimes in an uncontrolled manner. The reasons why the usually moderate post-surgical inflammatory reaction causes an exaggerated inflammatory response are unknown. A multifactorial process occurs that includes immune cell recruitment, proinflammatory peptide release, endothelial and tissue damage. The recruitment of immune cells such as leukocytes and platelets (whose role as inflammatory mediators appears to be more active than traditionally recognized [1]) is activated by tissue damage and the release of Damage-Associated Molecular Patterns (DAMPs) [2], closely related with Pathogen-Associated Molecular Patterns (PAMPs).

Peptides released with proinflammatory effects include cytokines (from macrophages, natural killer (NK) cells, B cells, and T lymphocytes), interferons,

interleukins (ILs), tumor necrosis factors, colony-stimulating factors, and others such as Transforming Growth Factor β (TGF- β) and prostaglandins. Inflammatory cell recruitment, cytokines, and the release of Reactive Oxygen Species (ROS) induce endothelial dysfunction and glycocalyx damage, facilitating leukocyte and platelet adhesion to the endothelium, neutrophil activation, and ultimately tissue and multisystem organ damage, with the release of chemokines involved in neutrophil infiltration [3].

Anaesthesia can modulate the inflammatory response, leading to alterations in the production and release of inflammatory mediators, and should be considered when assessing perioperative inflammatory status and other measures such as pharmacologic agents (tables 1 to 3) [4], remote ischemic preconditioning protocols, cytokine blockade or clearance, and surgical and anaesthetic procedure optimization. It is important to note that tables 1 to 3 include published results from in vitro and in vivo studies, both in animals and humans. Controversial results from different studies have also been included, especially those affecting tumor progression or antimicrobial activity.

These effects appear in several clinical situations, such as ischemia-reperfusion injury [5], cancer progression [5-7], and perioperative infections [5]. Sevoflurane alleviates perioperative cognitive dysfunction [5] and improve immune function in elderly patients when compared with propofol [8]. Immunomodulation is particularly relevant in transplant surgery outcomes. Volatile anaesthetics exert immunomodulatory effects that could influence postoperative outcomes through interactions with GABA_A (Gamma-aminobutyric acid)_A, glycine, nicotinic acetylcholine, serotonin and N-methyl-D-aspartate (NMDA) receptors, potassium and sodium channels and β 2 integrin [5].

Desflurane (vs. sevoflurane) induces peripheral blood regulatory T cells to increase with better kidney transplant tolerance and graft function [9] and dexmedetomidine is associated with improved cardiac transplant outcomes [10].

Patient characteristics and the magnitude of the surgery may be more important factors than anaesthesia itself in some cases. Thus, it has been reported that the effect of general anaesthesia on cytokines in the immune system in healthy patients and short-term surgeries is not significant, and changes in the immune system are related to surgical trauma, particularly in major surgery [11].

Stress response

Surgery and anaesthesia induce a systemic stress response in patients, releasing cortisol, adrenaline, and noradrenaline, and impairing immune function by modulating leukocyte activity and cytokine production. Chronic exposure to stress hormones during surgery and anaesthesia may contribute to immune suppression and an increased susceptibility to infection. Several combinations of anaesthetic techniques, especially those involving regional anaesthesia, try to reduce the surgical stress-induced immunosuppression, with different reported favorable outcomes (e.g., interscalene block for shoulder surgery [12], general anaesthesia combined with epidural anaesthesia for colon cancer [7], total intravenous anaesthesia vs. balanced anaesthesia in neurosurgery [13] or propofol vs. isoflurane in gastric surgery [14]). However, other factors should be considered, such as the effect of surgery (epidural anaesthesia as well as general anaesthesia may not protect patients from this immunosuppression during upper abdominal surgery [15]) or coexisting diseases (e.g., blood hypertension may act as a stimulus for inflammation and affect the inhibitory effect of different anaesthetic techniques to reduce postoperative stress response [13]).

Cancer recurrence rates

There is an increasing incidence of cancer diagnosis. Nearly two-thirds of these patients will undergo anaesthesia and surgery for intended cure or palliation as first-line treatment. Thus, the effects of anaesthesia on cancer recurrence could have wide-ranging impact on population health.

The perioperative period induces relative immunosuppression and creates a tumorigenic physiological environment. Cancer is a pathological condition influenced by several perioperative factors, including surgical stress and inflammatory responses, hypothermia, blood transfusions, tissue hypoxia, and the direct effects of anaesthetics and other perioperative drugs.

Surgical stress response involves the release of catecholamines, prostaglandins, and growth factors that activate pathways that may increase the metastatic ability of cancer cells.

Inflammatory response to surgery includes the liberation of interleukin-6 and prostaglandin E2, which may provoke the inhibition of NK cells activity,

Table I. Immunologic effects of volatile anaesthetics

Drug	Effect	Action	Research	Intervention
Volatile anaesthetics [16, 19, 29, 30]	R	NK cell activity	Human, in vitro	Breast cancer
	R	Hyposalivation. Altered nonimmunological oral mucous host defences with maintained immunoglobulin responses	Human, in vivo	Hysterectomy
	S	T-lymphocyte apoptosis	Human, in vitro	Cancer
	S	Angiogenesis through HIF-1 α activity	Human, in vitro	Cancer
	S	Tumor progression by triggering pro-inflammatory signaling	Human, in vitro	Cancer
	S	Metastasis, potentiating cancer cells and suppressing the immune function by different mechanisms: HIF-1 α up-regulation, increased angiogenesis, cell proliferation, and migration (increased ILGF ₁ and VEGF)	Human, in vitro	Cancer
	N	No differences (vs. intravenous anaesthesia) on the serum Hepatitis B Virus-DNA level in non-hepatobiliary minimally invasive surgery	Human, in vivo	Abdominal surgery
Nitrous oxide [20]	N	No effect on cancer progression	Human, in vivo	Colon cancer
Desflurane [31-34]		Mild immunosuppression Favorable preservation of IL-2/IL-4 and CD4(+)/CD8(+) T cell ratio in the perioperative period. Less adverse immune responses of leukocytes and NK cells than propofol anaesthesia.	Human, in vitro	Breast cancer
	A	Genotoxic and pro-inflammatory effect	Human, in vivo	
	R	Neutrophil recruitment and phagocytosis	Human, in vitro	Minor surgery
	A	Regulatory T cells (better transplant tolerance and graft function)	Human, in vivo	Kidney transplant
Enflurane [35]	I	Greater depression than halothane of leucocyte function	Human, in vivo	Hysterectomy
Halothane [36, 37]		Rare fulminant form of hepatitis	Human, animal, in vitro	
Isoflurane [33, 38-41]	A	Blood-brain barrier permeability	Human, in vivo	Cognitive dysfunction
	R	T lymphocyte activity and cytokine production	Human, in vivo	Lung cancer
	I	Phagocytic function	Human, in vitro	Tympanoplasty
	R	Interleukin-6 to interleukin-10 ratio after surgery (compared with propofol). Greater risk of infection	Human, in vivo	Alcoholic patients
	A	Signal transducer and activator of transcription (STAT) 5, protecting myocardium from ischemia/reperfusion injury through remote ischemic preconditioning	Human, in vivo	Coronary artery bypass grafting
Sevoflurane [3, 4, 34, 42, 43]		Mild immunosuppression. Greater lymphopenia than propofol in laparoscopic radical hysterectomy	Human, in vivo	Cervical cancer
	R	Pro-inflammatory cytokines production	Human, in vitro	Surgery
	R	Polymorphonuclear cells, reactive oxygen species and chemotaxis	Human, in vivo	
	R	Neutrophil recruitment and phagocytosis	Human, in vitro	
Xenon [44]	N	Xenon and sevoflurane anaesthesia did not have a pro-inflammatory effect and reduced phagocytosis and oxidative burst of granulocytes without affecting monocytes	Human, in vivo	Abdominal surgery,

Actions: reduce (R), augment (A), not effect (N), inhibit (I), stimulate (S).

Table II. Immunologic effects of intravenous anaesthetics

Drug	Effect	Action	Research	Intervention
Benzodiazepines [16, 45-49]	N	T-lymphocyte apoptosis (midazolam)	Human, in vivo	Cancer recurrence
	I	Neutrophil function and activation of mast cells	Human, in vitro	
	R	Pro-inflammatory cytokine levels	Human and animal in vivo	
	S	M2 monocyte/macrophage phenotype	Animal in vitro	Rats
	I	Polymorphonuclear leukocytes phagocytosis and bactericidal activity (midazolam)	Human, in vitro	
	R	Significantly decreased chemotaxis, phagocytosis, and reactive oxygen species (ROS) (O ₂ ⁻ , H ₂ O ₂ , OH) production of neutrophils in a dose-dependent manner.	Human, in vitro	
Dexamethasone [50]	R	Major histocompatibility complex-II signaling, selecting P ligand signaling, and T cell recruitment	Human, in vivo	Severe COVID-19 patients
Dexmedetomidine [10, 51, 52]	A	Surgery outcomes improvement in heart transplant and cardiac surgery	Human, in vivo	Cardiac surgery
	R	Pro-inflammatory cytokine levels in experimental sepsis and neutrophil infiltration (prevented lung injury)	Animal, in vivo	Experimental sepsis and pulmonary injury
Droperidol [49]	I	Polymorphonuclear leukocytes phagocytosis and bactericidal activity	Human, in vitro	
Ketamine [16, 33, 45, 53-60]	I/N	NK cell activity	Human, in vitro	Cancer
	I	T lymphocyte function (induces T-lymphocyte apoptosis)	Human, in vivo	Cancer recurrence
	A	Th1/Th2 ratio, stimulating immune function	Human, in vitro	Healthy volunteers
	A	Anti-inflammatory cytokines	Animal, in vitro	Sepsis
	R	Pro-inflammatory cytokines in endotoxin induced shock	Animal, in vivo	Rats
	R	Macrophages nitric oxide production (inhibition NO synthetase)	Animal, in vitro	
	A	Phagocytic activity of macrophages	Human, in vitro	Tympanoplasty
	I	Maturation of bone marrow-derived dendritic cells	Human, in vitro	
	I	Neutrophil adhesion, degranulation, and antioxidant activity	Human, in vitro	
	I	Platelet aggregation	Human, in vitro	
	R	Significantly decreased chemotaxis, phagocytosis, and reactive oxygen species (ROS) (O ₂ ⁻ , H ₂ O ₂ , OH) production of neutrophils in a dose-dependent manner.	Human, in vitro	
Opioids [49, 56, 61-65]	R	NK cell activity. Fentanyl reduces NK-cells and CD8 ⁺ cytotoxic T-cells	Human, in vitro	Cancer
	R	Macrophage recruitment at the site of infection	Human, in vitro	
	I	Macrophage phagocytosis	Human, in vitro	
	A	Regulatory T cells (morphine)	Human, in vitro	
	R	Bactericidal function of neutrophils	Human, in vivo	
	R	T-cells Antigen presentation	Human and animal, in vitro	
	R	T-cells early pro-inflammatory response to opportunistic infections and altered differentiation to Th2 phenotype	Human and animal, in vitro	

Drug	Effect	Action	Research	Intervention
Opioids [49, 56, 61-65]	N	Polymorphonuclear phagocytosis and bactericidal activity (fentanyl and alfentanil)	Human, in vitro	
	S	Tumor neovascularization and expansion (morphine)	Human, in vivo	Cancer recurrence
	I	Immune responses and stimulate pathways that may support cancer cell proliferation	Human, in vivo	Cancer recurrence
	S	Gut microbiota dysbiosis in chronic opioid use	Human, in vivo	Opioid use
Propofol [33, 38, 40, 66-80]	R	T lymphocyte activity	Human, in vitro	
	A	Activation and differentiation of peripheral T-helper cells	Human, in vivo	Lung cancer surgery
	R	Neutrophilic oxidative stress	Human, in vitro	
	R	Serum cortisol response (vs. Isoflurane)	Human, in vivo	Hysterectomy
	R	Release of pro-inflammatory cytokines (anti-inflammatory effect) in endotoxemia-induced acute lung injury	Animal, in vivo	Rat
	A	Interleukin-6 to interleukin-10 ratio after surgery (compared with propofol).	Human, in vivo	Long-term alcoholics
	R	Oxidative damage to tissues during surgical procedures (neuroprotective effects)	Human, in vitro	
	R	Inducible nitric oxide synthetase	Animal, in vitro, in vivo	
	R	Pulmonary immune response (antiapoptotic and neuroprotective effects)	Human, in vitro	
	A	Respiratory burst neutrophil's function	Human, in vitro	Tympanoplasty
	I	Neutrophil superoxide and elastase release, chemotaxis	Human, in vitro	
	N	Phagocytic activity	Animal, in vitro	
	I	Macrophages chemotaxis, oxidative burst, and phagocytosis	Animal, in vitro	
	N	NK cell activity	Human, in vitro	Breast cancer
	R	Less inhibitory effect on T lymphocytes, on the differentiation of Th cells into Th1 cells, and better preserve Th1/Th2 ratio than inhalational sevoflurane in children	Human, in vitro	Bronchoscopy, severe mycoplasmal pneumonia
	N	Myocardium protection from ischemia-reperfusion injury	Human, in vivo	Cardiac surgery
	R	Negative consequences associated with perioperative immunosuppression	Human, in vivo	Breast cancer
	A	Antitumoral effects (immune-preserving effects, reductions in IL-6 and other inflammatory markers and directly regulating key ribonucleic acid pathways and signaling in cancer cells)	Human, in vivo	Cancer recurrence
	I	TIVA inhibit neuroinflammation by inhibiting the increase in serum levels of IL-17	Human, in vivo	Parkinson surgery
Thiopental [45, 49, 81-84]		Moderate immunosuppressive effects	Human, in vitro	
	S	Anti-inflammatory effects on neutrophil antibacterial functions	Human, in vitro	
	I	NK cell activity	Human, in vitro	
	R	T lymphocyte activity and lymphocyte apoptosis (protective effects)	Human, in vitro	
	R	Pro-inflammatory cytokines	Human, in vitro	
	I	Neutrophil polarization, chemotaxis, adherence, phagocytosis, oxidative burst and reactive oxygen species (ROS) (O ₂ ⁻ , H ₂ O ₂ , OH) production in a dose-dependent manner.	Human, in vitro	

Actions: reduce (R), augment (A), not effect (N), inhibit (I), stimulate (S).

Table III. Immunologic effects of local anaesthetics

Drug	Effect	Action	Research	Intervention
Local anaesthetics [16, 17, 85-90]	S	Anti-inflammatory effects on polymorphonuclear cells	Human, in vitro	
	R	Adherence, migration and accumulation of macrophages at the site of inflammation	Human, in vitro	
	R	Edema formation	Human, in vitro	
	S	Preservation of endothelial barrier integrity	Human, in vivo and in vitro	
	I, N	Cancer progression by decreasing the need for systemic opioids and volatile agents	Human, in vivo	
	I	Neutrophil and macrophage's function: adhesion, chemotaxis, phagocytosis, and production of superoxide anion and hydrogen peroxide (lidocaine, mepivacaine, procaine, prilocaine and tetracaine)	Human, in vitro	
Lidocaine [2, 4, 16, 85, 91]	S	NK cell activity	Human, in vitro	
	R	Pro-inflammatory cytokines	Human, in vitro	
	I	Adhesion, chemotaxis, phagocytosis, and the production of superoxide anion and hydrogen peroxide by neutrophils and macrophages	Human, in vitro	
	R	Cell injury induced by ischemic-reperfusion and inflammation	Human, in vitro	
	A	Anti-nociceptive and anti-inflammatory effects mediated by toll-like receptor, nuclear factor kappa- β , downstream cytokine effectors high mobility group box 1 and tumor necrosis factor- α	Human, in vivo and in vitro	
Bupivacaine [85, 87]	S	Tissue inflammation and release of inflammatory cytokines at the site of injection (more than lidocaine)	Human, in vitro	
Mepivacaine [90]	I	Immune profile similar to that of lidocaine, with mild anti-inflammatory effects Adhesion, chemotaxis, phagocytosis, and the production of superoxide anion and hydrogen peroxide by neutrophils and macrophages	Human, in vitro	
Prilocaine [90]	I	Adhesion, chemotaxis, phagocytosis, and the production of superoxide anion and hydrogen peroxide by neutrophils and macrophages	Human, in vitro	
Ropivacaine [85, 92]	S	Tissue inflammation (Less inflammatory effects than bupivacaine)	Human, in vitro	
	S	Caudal block anaesthesia with hydromorphone-ropivacaine had lesser impact on immune function compared to ropivacaine alone	Human, in vivo	Children hypospadias surgery

Actions: reduce (R), augment (A), not effect (N), inhibit (I), stimulate (S).

responsible for detecting and destroying circulating tumor cells.

Tissue hypoxia induces upregulating expression of the transcription Hypoxia-Inducible Factor 1-Alpha (HIF-1 α), which is important in the promotion of cellular pathways for angiogenesis, cell proliferation, and metastasis.

Traditionally, laboratory, animal, and retrospective

human data suggest that anaesthetic agents may affect cancer recurrence or improve cancer-related survival, but there is scarce evidence to support using a specific anaesthetic agent or technique to reduce the risk of cancer recurrence after surgery. There are few high-quality prospective clinical trials. These trials are difficult to design (considering population studied, number of patients, type of cancer...) and should continue over

time to evaluate recurrences and to isolate the effects of anaesthetics from all factors (including genomics or ambient exposition) that can affect cancer outcome.

It has been described that surgical inflammation, some anaesthetics, and inadvertent anaesthesia management suppress antitumor cells (CD4+ T helper 1-type cells, CD8+ cytotoxic T cells, and NK cells), and induce suppressive immune cells, which render cancer patients susceptible to tumor recurrence and metastasis after surgery. Accumulated basic and clinical data suggest that total intravenous anaesthesia with propofol, cyclooxygenase antagonists, and regional anaesthesia can decrease negative consequences associated with perioperative immunosuppression, possibly due to less surgical stress, perioperative immunosuppression, and angiogenesis when compared to general anaesthesia with volatile anaesthetics and opioids [16, 17].

Volatile anaesthesia, systemic morphine or synthetic opioids administration, unnecessary blood transfusions, intraoperative hypoxia, hypotension, hypothermia, and hyperglycemia should be avoided [16, 18]. These effects also depend on dose, duration, and time-of-use.

If we try to analyze these factors separately, we find that in the case of volatile anaesthetics, the published results are controversial. Some studies suggest the existence of proinflammatory effects, not confirmed in a following meta-analysis [19]. Laboratory studies concluded that volatile anaesthetics could enhance metastasis, potentiating cancer cells and suppressing immune function through different mechanisms, including the upregulation of HIF-1 α , increased angiogenesis, cell proliferation, and migration associated with rising levels of Insulin-Like Growth Factor 1 (ILGF₁) and Vascular Endothelial Growth Factor (VEGF).

There is little data about the effect of nitrous oxide that may not increase the risk of cancer recurrence after colorectal surgery [20].

Propofol has demonstrated anti-inflammatory, antioxidative and antitumoral effects (directly regulating key ribonucleic acid pathways and signaling in cancer cells) in laboratory studies and in different cancer cell lines in vitro. In animal models, propofol did not suppress NK cell activity or increase metastasis, whereas ketamine and thiopental did.

Regarding the anaesthesia technique, total intravenous anaesthesia (TIVA) vs. inhalation anaesthesia, the great majority of retrospective clinical studies showed no differences [21] or better overall survival

with TIVA. Studies comparing circulating tumor cells, fractions of postoperative immune cells or cancer regulatory factors have not been conclusive or present contradictory results.

Classically, it was described that perioperative regional anaesthetic and analgesic techniques may play a beneficial role in long-term oncological surgery outcomes due to attenuated surgical stress response by reducing catecholamine levels and minimizing immunosuppression [22]. However, the diversity and multifactorial complexity of patients and carcinogenic factors make it impossible to separate the effects of anaesthesia, surgery and other interference factors on cancer recurrence and metastasis [23].

Regional anaesthesia may prolong recurrence-free survival and overall survival after gastrointestinal cancer surgery, including gastric and esophageal cancer, by modulating the immune and inflammatory response. A fair number of articles proposed plausible reasons why regional anaesthesia may reduce cancer recurrences. However, the results from human studies are conflicting [24,25]: e.g., there was no clear evidence that change in single anaesthesia technology could directly affect the long-term prognosis of lung cancer patients [23].

This disparity of findings and its clinical importance motivated the performance of meta-analyses analyzing the impact of regional techniques effects on survival and cancer recurrence after oncologic surgery, although most of them encountered the same problems: heterogeneous studies and different results, which do not allow us reaching a definitive conclusion.

Therefore, several meta-analyses concluded that regional techniques might improve overall survival but not reduce cancer recurrence [26], whereas others did not find differences between the regional techniques and general anaesthesia groups in overall survival rate, time to cancer recurrence, and cancer-related mortality [22]. A recent meta-analysis of 15 randomized trials including approximately 6000 patients who underwent various types of cancer surgery, confirmed these results, concluding that perioperative regional anaesthesia did not reduce postoperative recurrence-free survival, overall survival, or time to tumor progression [27].

We must also consider that the heading of regional analgesia/anaesthesia includes different techniques that are very different from each other. This makes it difficult to draw evidence-based conclusions. However,

there are two analgesic regional techniques frequently used to improve oncologic surgery outcomes: the paravertebral block and epidural analgesia. There are no definitive data to support or refute the use of paravertebral blocks for the reduction of cancer recurrence, but this block is associated with lower levels of inflammation and a better immune response in comparison with general anaesthesia and opioid-based analgesia [24], and may have a beneficial effect on the overall survival of patients with lung cancer [28]. Concerning epidural analgesia, there is no evidence to recommend or refute its use to reduce cancer recurrence after gastroesophageal cancer surgery [24].

It is necessary to verify the hypothesis that regional analgesia/anaesthesia might improve recurrence-free survival and overall survival after oncologic surgery by conducting large multicenter randomized clinical trials. However, until conclusive data will be available, in patients or situations where there are no anaesthetic contraindications, it is reasonable to select those anaesthetic techniques described as beneficial in some studies.

Conclusion

In the first part of this review, we outlined the need to design strategies to minimize the immune alterations that are essential to prevent perioperative dysfunction.

There is no one-size-fits-all technique to preserve immune function during anaesthesia and the variability in existing studies complicates this issue. Therefore, we must change our attitude, moving away from the classic concept of anaesthesia directed exclusively at the surgical and immediate postoperative periods and adopting the concept of perioperative medicine, including long-term implications. We should enhance the patient's preoperative preparation, with physical

and treatment optimization through patient blood management and prehabilitation programs. During the intraoperative period, we must focus on maintaining homeostasis and mitigating excessive pro-inflammatory responses to surgery by selecting the best drugs, anaesthetic techniques, ventilation modes, fluid therapy, blood management, and pH, temperature, and glycemic control. Finally, we should apply all these techniques and postoperative care available in post-anaesthesia care units.

Several topics remain unanswered despite of progress made in clarifying how anaesthesia affects immune function. Future research should focus on understanding the mechanisms behind anaesthesia-induced immunomodulation, identifying immune biomarkers, and developing strategies to reduce adverse outcomes. Large-scale clinical trials are also crucial to assess how these immune changes affect surgical outcomes and long-term morbidity.

In conclusion, advancing our knowledge of anaesthesia's immunomodulatory effects is a keystone to improve patient safety and the effectiveness of perioperative management.

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Conflict of interest

None

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References

1. Ludwig N, Hilger A, Zarbock A, Rossaint J. Platelets at the Crossroads of Pro-Inflammatory and Resolution Pathways during Inflammation. *Cells*. 2022;11(12).
2. Yuki K, Shibamura-Fujiogi M. Surgical Site Infections and Perioperative Optimization of Host Immunity by Selection of Anesthetics. *Biomed Res Int*. 2021;2021:5576959.
3. Margraf A, Ludwig N, Zarbock A, Rossaint J. Systemic Inflammatory Response Syndrome After Surgery: Mechanisms and Protection. *Anesth Analg*. 2020;131(6):1693-707.
4. Boavista Barros Heil L, Leme Silva P, Ferreira Cruz F, Pelosi P, Rieken Macedo Rocco P. Immunomodulatory effects of anesthetic agents

- in perioperative medicine. *Minerva Anesthesiol.* 2020;86(2):181-95.
5. Yuki K, Eckenhoﬀ RG. Mechanisms of the Immunological Effects of Volatile Anesthetics: A Review. *Anesth Analg.* 2016;123(2):326-35.
 6. Li MH, Xu ZZ, Huang SM, Li T, Li XY, Wang DX. Effect of combined epidural anaesthesia on tumor-infiltrating lymphocytes in lung adenocarcinoma: a prospective exploratory sub-analysis. *Acta Anaesthesiol Scand.* 2018;62(5):687-700.
 7. Chen WK, Ren L, Wei Y, Zhu DX, Miao CH, Xu JM. General anesthesia combined with epidural anesthesia ameliorates the effect of fast-track surgery by mitigating immunosuppression and facilitating intestinal functional recovery in colon cancer patients. *Int J Colorectal Dis.* 2015;30(4):475-81.
 8. Liang LQ, Jiao YQ, Guo SL. Effects of sevoflurane inhalation anesthesia on cognitive and immune function in elderly patients after abdominal operation. *Eur Rev Med Pharmacol Sci.* 2018;22(24):8932-8.
 9. Chutipongtanate A, Prukviwat S, Pongsakul N, Srisala S, Kamanee N, Arpornsuvaritkun N, et al. Effects of Desflurane and Sevoflurane anesthesia on regulatory T cells in patients undergoing living donor kidney transplantation: a randomized intervention trial. *BMC Anesthesiol.* 2020;20(1):215.
 10. Yuki K. The immunomodulatory mechanism of dexmedetomidine. *Int Immunopharmacol.* 2021;97:107709.
 11. Jafarzadeh A, Hadavi M, Hassanshahi G, Rezaeian M, Vazirinejad R. General Anesthetics on Immune System Cytokines: A Narrative Review Article. *Anesth Pain Med.* 2020;10(4):e103033.
 12. Mejia-Terrazas GE, Ruiz-Suarez M, Vadillo-Ortega F, Franco YBRE, Lopez-Munoz E. Effect of interscalene nerve block on the inflammatory response in shoulder surgery: a randomized trial. *J Shoulder Elbow Surg.* 2019;28(9):e291-e303.
 13. Chen Y, Jiang S, Wu Y. Effect of 2 different anesthesia methods on stress response in neurosurgical patients with hypertension or normal: A prospective clinical trial. *Medicine (Baltimore).* 2016;95(35):e4769.
 14. Wu Y, Zhang L, Yin G, Liu Y, Chen L. Stress Response to Propofol versus Isoflurane Anesthesia in Patients Undergoing Gastric Surgery. *J Coll Physicians Surg Pak.* 2019;29(3):201-4.
 15. Kawasaki T, Ogata M, Kawasaki C, Okamoto K, Sata T. Effects of epidural anaesthesia on surgical stress-induced immunosuppression during upper abdominal surgery. *Br J Anaesth.* 2007;98(2):196-203.
 16. Kim R. Effects of surgery and anesthetic choice on immunosuppression and cancer recurrence. *J Transl Med.* 2018;16(1):8.
 17. Fodale V, D'Arrigo MG, Triolo S, Mondello S, La Torre D. Anesthetic techniques and cancer recurrence after surgery. *ScientificWorldJournal.* 2014;2014:328513.
 18. Kurosawa S. Anesthesia in patients with cancer disorders. *Curr Opin Anaesthesiol.* 2012;25(3):376-84.
 19. O'Bryan LJ, Atkins KJ, Lipszyc A, Scott DA, Silbert BS, Evered LA. Inflammatory Biomarker Levels After Propofol or Sevoflurane Anesthesia: A Meta-analysis. *Anesth Analg.* 2022;134(1):69-81.
 20. Fleischmann E, Marschalek C, Schlemitz K, Dalton JE, Gruenberger T, Herbst F, et al. Nitrous oxide may not increase the risk of cancer recurrence after colorectal surgery: a follow-up of a randomized controlled trial. *BMC Anesthesiol.* 2009;9:1.
 21. Kim NY, Jang WS, Choi YD, Hong JH, Noh S, Yoo YC. Comparison of Biochemical Recurrence After Robot-assisted Laparoscopic Radical Prostatectomy with Volatile and Total Intravenous Anesthesia. *Int J Med Sci.* 2020;17(4):449-56.
 22. Bartlett E, Urman RD, Urits I, Kaye AD, Viswanath O. Impact on cancer recurrence rates: Is regional anesthesia superior to general anesthesia? *J Clin Anesth.* 2022;79:110082.
 23. Wang J, Liu L, Song Y, Jiao J, Zhong Y. Current Understanding on Perioperative Management in Lung Cancer: Implications for Anesthetic Considerations. *Drug Des Devel Ther.* 2021;15:835-42.
 24. Perez-Gonzalez O, Cuellar-Guzman LF, Navarrete-Pacheco M, Ortiz-Martinez JJ, Williams WH, Cata JP. Impact of Regional Anesthesia on Gastroesophageal Cancer Surgery Outcomes: A Systematic Review of the Literature. *Anesth Analg.* 2018;127(3):753-8.
 25. Cata JP, Hernandez M, Lewis VO, Kurz A. Can regional anesthesia and analgesia prolong cancer survival after orthopaedic oncologic surgery? *Clin Orthop Relat Res.* 2014;472(5):1434-41.
 26. Sun Y, Li T, Gan TJ. The Effects of Perioperative Regional Anesthesia and Analgesia on Cancer Recurrence and Survival After Oncology Surgery: A Systematic Review and Meta-Analysis. *Reg Anesth Pain Med.* 2015;40(5):589-98.
 27. Li T, Meng X, Wang D, Wang Q, Ma J, Dai Z. Regional anesthesia did not improve postoperative long-term survival of tumor patients: a systematic review and meta-analysis of randomized controlled trials. *World J Surg Oncol.* 2023;21(1):68.
 28. Lee EK, Ahn HJ, Zo JJ, Kim K, Jung DM, Park JH. Paravertebral Block Does Not Reduce Cancer Recurrence, but Is Related to Higher Overall Survival in Lung Cancer Surgery: A Retrospective Cohort Study. *Anesth Analg.* 2017;125(4):1322-8.
 29. Quan J, Chen X, Tang X, Liu X, Li J, Yi B, et al. Effects of General Anesthesia on Changes of Serum Hepatitis B Virus-DNA Levels in Infected Patients Underwent Non-Hepatobiliary Minimally Invasive Surgery: A Pilot Observational Study. *Infect Drug Resist.* 2022;15:6631-40.
 30. Buckley A, McQuaid S, Johnson P, Buggy DJ. Effect of anaesthetic technique on the natural killer cell anti-tumour activity of serum from women undergoing breast cancer surgery: a pilot study. *Br J Anaesth.* 2014;113 Suppl 1:i56-62.
 31. Arruda NM, Braz LG, Nogueira FR, Souza KM, Aun AG, Figueiredo DBS, et al. Inflammation and DNA damage induction in surgical patients maintained with desflurane anesthesia. *Mutat Res Genet Toxicol Environ Mutagen.* 2019;846:403073.
 32. Woo JH, Baik HJ, Kim CH, Chung RK, Kim DY, Lee GY, et al. Effect of Propofol and Desflurane on Immune Cell Populations in Breast Cancer Patients: A Randomized Trial. *J Korean Med Sci.* 2015;30(10):1503-8.

33. Erol A, Reisli R, Reisli I, Kara R, Otelcioglu S. Effects of desflurane, sevoflurane and propofol on phagocytosis and respiratory burst activity of human polymorphonuclear leucocytes in bronchoalveolar lavage. *Eur J Anaesthesiol.* 2009;26(2):150-4.
34. Yuki K, Hou L, Shibamura-Fujiogi M, Koutsogiannaki S, Soriano SG. Mechanistic consideration of the effect of perioperative volatile anesthetics on phagocytes. *Clin Immunol.* 2021;222:108635.
35. Khan FA, Kamal RS, Mithani CH, Khurshid M. Effect of general anaesthesia and surgery on neutrophil function. *Anaesthesia.* 1995;50(9):769-75.
36. Ray DC, Drummond GB. Halothane hepatitis. *Br J Anaesth.* 1991;67(1):84-99.
37. Walton B. Immunological aspects of halothane hepatitis. Possible relevance of biotransformation. *Acta Anaesthesiol Belg.* 1975;23 Suppl:155-9.
38. Von Dossow V, Baur S, Sander M, Tonnesen H, Marks C, Paschen C, et al. Propofol increased the interleukin-6 to interleukin-10 ratio more than isoflurane after surgery in long-term alcoholic patients. *J Int Med Res.* 2007;35(3):395-405.
39. Kottenberg E, Musiolik J, Thielmann M, Jakob H, Peters J, Heusch G. Interference of propofol with signal transducer and activator of transcription 5 activation and cardioprotection by remote ischemic preconditioning during coronary artery bypass grafting. *J Thorac Cardiovasc Surg.* 2014;147(1):376-82.
40. Ren XF, Li WZ, Meng FY, Lin CF. Differential effects of propofol and isoflurane on the activation of T-helper cells in lung cancer patients. *Anaesthesia.* 2010;65(5):478-82.
41. Liu L, Shang L, Jin D, Wu X, Long B. General anesthesia bullies the gut: a toxic relationship with dysbiosis and cognitive dysfunction. *Psychopharmacology (Berl).* 2022;239(3):709-28.
42. Rodriguez-Gonzalez R, Baluja A, Veiras Del Rio S, Rodriguez A, Rodriguez J, Taboada M, et al. Effects of sevoflurane postconditioning on cell death, inflammation and TLR expression in human endothelial cells exposed to LPS. *J Transl Med.* 2013;11:87.
43. Liu S, Gu X, Zhu L, Wu G, Zhou H, Song Y, et al. Effects of propofol and sevoflurane on perioperative immune response in patients undergoing laparoscopic radical hysterectomy for cervical cancer. *Medicine (Baltimore).* 2016;95(49):e5479.
44. Fahlenkamp AV, Coburn M, Rossaint R, Stoppe C, Haase H. Comparison of the effects of xenon and sevoflurane anaesthesia on leucocyte function in surgical patients: a randomized trial. *Br J Anaesth.* 2014;112(2):272-80.
45. Nishina K, Akamatsu H, Mikawa K, Shiga M, Maekawa N, Obara H, et al. The inhibitory effects of thiopental, midazolam, and ketamine on human neutrophil functions. *Anesth Analg.* 1998;86(1):159-65.
46. Li J, Tan H, Zhou X, Zhang C, Jin H, Tian Y, et al. The Protection of Midazolam Against Immune Mediated Liver Injury Induced by Lipopolysaccharide and Galactosamine in Mice. *Front Pharmacol.* 2018;9:1528.
47. Helmy SA, Al-Attayah RJ. The immunomodulatory effects of prolonged intravenous infusion of propofol versus midazolam in critically ill surgical patients. *Anaesthesia.* 2001;56(1):4-8.
48. Tsao CM, Wu CC, Liaw WJ, Ho ST. Effects of midazolam on organ dysfunction in rats with endotoxemia induced by lipopolysaccharide. *Acta Anaesthesiol Taiwan.* 2009;47(1):10-6.
49. Krumholz W, Endrass J, Hempelmann G. Inhibition of phagocytosis and killing of bacteria by anaesthetic agents in vitro. *Br J Anaesth.* 1995;75(1):66-70.
50. Neyton LPA, Patel RK, Sarma A, Consortium UC, Willmore A, Haller SC, et al. Distinct pulmonary and systemic effects of dexamethasone in severe COVID-19. *Nat Commun.* 2024;15(1):5483.
51. Geze S, Cekic B, Imamoglu M, Yoruk MF, Yulug E, Alver A, et al. Use of dexmedetomidine to prevent pulmonary injury after pneumoperitoneum in ventilated rats. *Surg Laparosc Endosc Percutan Tech.* 2012;22(5):447-53.
52. Cavalcanti V, Santos CL, Samary CS, Araujo MN, Heil LB, Morales MM, et al. Effects of short-term propofol and dexmedetomidine on pulmonary morphofunction and biological markers in experimental mild acute lung injury. *Respir Physiol Neurobiol.* 2014;203:45-50.
53. Nakagawa T, Hirakata H, Sato M, Nakamura K, Hatano Y, Nakamura T, et al. Ketamine suppresses platelet aggregation possibly by suppressed inositol triphosphate formation and subsequent suppression of cytosolic calcium increase. *Anesthesiology.* 2002;96(5):1147-52.
54. Mazar J, Rogachev B, Shaked G, Ziv NY, Czeiger D, Chaimovitz C, et al. Involvement of adenosine in the antiinflammatory action of ketamine. *Anesthesiology.* 2005;102(6):1174-81.
55. Gao M, Jin W, Qian Y, Ji L, Feng G, Sun J. Effect of N-methyl-D-aspartate receptor antagonist on T helper cell differentiation induced by phorbol-myristate-acetate and ionomycin. *Cytokine.* 2011;56(2):458-65.
56. Forget P, Collet V, Lavand'homme P, De Kock M. Does analgesia and condition influence immunity after surgery? Effects of fentanyl, ketamine and clonidine on natural killer activity at different ages. *Eur J Anaesthesiol.* 2010;27(3):233-40.
57. Taniguchi T, Shibata K, Yamamoto K. Ketamine inhibits endotoxin-induced shock in rats. *Anesthesiology.* 2001;95(4):928-32.
58. Mills CD. Molecular basis of "suppressor" macrophages. Arginine metabolism via the nitric oxide synthetase pathway. *J Immunol.* 1991;146(8):2719-23.
59. Ohta N, Ohashi Y, Fujino Y. Ketamine inhibits maturation of bone marrow-derived dendritic cells and priming of the Th1-type immune response. *Anesth Analg.* 2009;109(3):793-800.
60. Weigand MA, Schmidt H, Zhao Q, Plaschke K, Martin E, Bardenheuer HJ. Ketamine modulates the stimulated adhesion molecule expression on human neutrophils in vitro. *Anesth Analg.* 2000;90(1):206-12.
61. Roy S, Balasubramanian S, Sumandeep S, Charboneau R, Wang J, Melnyk D, et al. Morphine directs T cells toward T(H2) differentiation.

- Surgery. 2001;130(2):304-9.
62. Roy S, Ninkovic J, Banerjee S, Charboneau RG, Das S, Dutta R, et al. Opioid drug abuse and modulation of immune function: consequences in the susceptibility to opportunistic infections. *J Neuroimmune Pharmacol*. 2011;6(4):442-65.
 63. Ninkovic J, Roy S. Role of the mu-opioid receptor in opioid modulation of immune function. *Amino Acids*. 2013;45(1):9-24.
 64. Gong L, Dong C, Ouyang W, Qin Q. Regulatory T cells: a possible promising approach to cancer recurrence induced by morphine. *Med Hypotheses*. 2013;80(3):308-10.
 65. Edinoff AN, Derise OC, Sheppard AJ, Miriyala S, Virgen CG, Kaye AJ, et al. The Influence of Analgesic Modalities on Postoperative Cancer Recurrence. *Anesth Pain Med*. 2022;12(1):e123463.
 66. Chen CY, Tsai YF, Huang WJ, Chang SH, Hwang TL. Propofol inhibits endogenous formyl peptide-induced neutrophil activation and alleviates lung injury. *Free Radic Biol Med*. 2018;129:372-82.
 67. Fan W, Zhu X, Wu L, Wu Z, Li D, Huang F, et al. Propofol: an anesthetic possessing neuroprotective effects. *Eur Rev Med Pharmacol Sci*. 2015;19(8):1520-9.
 68. Gokcinar D, Ergin V, Cumaoglu A, Menevse A, Aricioglu A. Effects of ketamine, propofol, and ketofol on proinflammatory cytokines and markers of oxidative stress in a rat model of endotoxemia-induced acute lung injury. *Acta Biochim Pol*. 2013;60(3):451-6.
 69. Takao Y, Mikawa K, Nishina K, Obara H. Attenuation of acute lung injury with propofol in endotoxemia. *Anesth Analg*. 2005;100(3):810-6.
 70. Hsing CH, Lin MC, Choi PC, Huang WC, Kai JI, Tsai CC, et al. Anesthetic propofol reduces endotoxemic inflammation by inhibiting reactive oxygen species-regulated Akt/IKKbeta/NF-kappaB signaling. *PLoS One*. 2011;6(3):e17598.
 71. Wang T, Wei XY, Liu B, Wang LJ, Jiang LH. Effects of propofol on lipopolysaccharide-induced expression and release of HMGB1 in macrophages. *Braz J Med Biol Res*. 2015;48(4):286-91.
 72. Pirttikangas CO, Salo M, Mansikka M, Gronroos J, Pulkki K, Peltola O. The influence of anaesthetic technique upon the immune response to hysterectomy. A comparison of propofol infusion and isoflurane. *Anaesthesia*. 1995;50(12):1056-61.
 73. Hwang WJ, Joo MA, Joo J. Effects of anesthetic method on inflammatory response in patients with Parkinson's disease: a randomized controlled study. *BMC Anesthesiol*. 2020;20(1):187.
 74. Lim JA, Oh CS, Yoon TG, Lee JY, Lee SH, Yoo YB, et al. The effect of propofol and sevoflurane on cancer cell, natural killer cell, and cytotoxic T lymphocyte function in patients undergoing breast cancer surgery: an in vitro analysis. *BMC Cancer*. 2018;18(1):159.
 75. Yu H, Chen L, Yue CJ, Xu H, Cheng J, Cornett EM, et al. Effects of propofol and sevoflurane on T-cell immune function and Th cell differentiation in children with SMPP undergoing fiberoptic bronchoscopy. *Ann Med*. 2022;54(1):2574-80.
 76. Yi S, Tao X, Wang Y, Cao Q, Zhou Z, Wang S. Effects of propofol on macrophage activation and function in diseases. *Front Pharmacol*. 2022;13:964771.
 77. Huh J, Hwang W. The Role of Anesthetic Management in Lung Cancer Recurrence and Metastasis: A Comprehensive Review. *J Clin Med*. 2024;13(22).
 78. Chen X, Lu P, Chen L, Yang SJ, Shen HY, Yu DD, et al. Perioperative propofol-paravertebral anesthesia decreases the metastasis and progression of breast cancer. *Tumour Biol*. 2015;36(11):8259-66.
 79. Kato R, Foex P. Myocardial protection by anesthetic agents against ischemia-reperfusion injury: an update for anesthesiologists. *Can J Anaesth*. 2002;49(8):777-91.
 80. Yamamoto W, Hamada T, Suzuki J, Matsuoka Y, Omori-Miyake M, Kuwahara M, et al. Suppressive effect of the anesthetic propofol on the T cell function and T cell-dependent immune responses. *Sci Rep*. 2024;14(1):19337.
 81. Roesslein M, Schibilsky D, Muller L, Goebel U, Schwer C, Humar M, et al. Thiopental protects human T lymphocytes from apoptosis in vitro via the expression of heat shock protein 70. *J Pharmacol Exp Ther*. 2008;325(1):217-25.
 82. Loop T, Liu Z, Humar M, Hoetzel A, Benzing A, Pahl HL, et al. Thiopental inhibits the activation of nuclear factor kappaB. *Anesthesiology*. 2002;96(5):1202-13.
 83. Loop T, Humar M, Pischke S, Hoetzel A, Schmidt R, Pahl HL, et al. Thiopental inhibits tumor necrosis factor alpha-induced activation of nuclear factor kappaB through suppression of kappaB kinase activity. *Anesthesiology*. 2003;99(2):360-7.
 84. O'Donnell NG, McSharry CP, Wilkinson PC, Asbury AJ. Comparison of the inhibitory effect of propofol, thiopentone and midazolam on neutrophil polarization in vitro in the presence or absence of human serum albumin. *Br J Anaesth*. 1992;69(1):70-4.
 85. de Klaver MJ, Weingart GS, Obrig TG, Rich GF. Local anesthetic-induced protection against lipopolysaccharide-induced injury in endothelial cells: the role of mitochondrial adenosine triphosphate-sensitive potassium channels. *Anesth Analg*. 2006;102(4):1108-13.
 86. Rodgers A, Walker N, Schug S, McKee A, Kehlet H, van Zundert A, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ*. 2000;321(7275):1493.
 87. Sinclair R, Eriksson AS, Gretzer C, Cassuto J, Thomsen P. Inhibitory effects of amide local anaesthetics on stimulus-induced human leukocyte metabolic activation, LTB4 release and IL-1 secretion in vitro. *Acta Anaesthesiol Scand*. 1993;37(2):159-65.
 88. Cassuto J, Sinclair R, Bonderovic M. Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. *Acta Anaesthesiol Scand*. 2006;50(3):265-82.
 89. Efremov SM, Kozireva VS, Moroz GB, Abubakirov MN, Shkoda OS, Shilova AN, et al. The immunosuppressive effects of volatile versus intravenous anesthesia combined with epidural analgesia on kidney cancer: a pilot randomized controlled trial. *Korean J Anesthesiol*. 2020;73(6):525-33.

90. Azuma Y, Ohura K. Immunological modulation by lidocaine-epinephrine and prilocaine-felypressin on the functions related to natural immunity in neutrophils and macrophages. *Curr Drug Targets Immune Endocr Metabol Disord.* 2004;4(1):29-36.
91. Karnina R, Arif SK, Hatta M, Bukhari A. Molecular mechanisms of lidocaine. *Ann Med Surg (Lond).* 2021;69:102733.
92. Cai Y, Yang M, Liu X, Zhang L, Wang J, Sun Y. Effect of hydromorphone combined with ropivacaine caudal block on immune function after hypospadias surgery in children. *BMC Anesthesiol.* 2025;25(1):172.

Continuing education questionnaire:

1.- Regarding the modulation of the inflammatory response, indicate the incorrect answer:

- a. It can be triggered by infectious, non-infectious or surgical stimuli.
- b. It is a controlled reaction, through known pathophysiological mechanisms.
- c. Anaesthesia can modulate the inflammatory response.
- d. Surgery could exert a more important stimulus on the immune system than anaesthesia.
- e. Immunomodulation is especially important in transplant anaesthesia.

Answer:

b. The modulation of the immune response can sometimes appear in an uncontrolled manner, causing tissue damage. The reasons that induce this response are unknown.

2.- Indicate the correct answer regarding the effect of regional anaesthesia in tumor surgery:

- a. Regional anaesthesia improves survival.
- b. Regional anaesthesia does not improve survival.
- c. Regional anaesthesia does not improve tumor recurrence rates.
- d. Regional anaesthesia does not improve tumor progression time.
- e. All of the above are correct.

Answer:

e. All of the above are correct. The effect of regional anaesthesia on the outcome of oncologic surgery is controversial. There are different meta-analyses that come to different conclusions, from that regional anaesthesia can improve survival but not the rate of tumor recurrence, to that it has no effect on survival, recurrence rate, or time to tumor progression. For this reason, more randomized multicenter studies are needed.

3.- The effects of anaesthesia on the intestinal microbiota have been correlated with the following, except for:

- a. Postoperative and chronic pain.
- b. Neuropathic pain.
- c. Headache.
- d. Opioid intolerance.
- e. Delirium.

Answer:

d. Dysbiosis of the intestinal microbiota is accompanied by all of the above, in addition to inflammatory pain, postoperative neurological alterations, and increased tolerance to opioids

4.- Halogenated anaesthetics cause all of the following effects on the immune system except:

- a. Moderate immunosuppression.
- b. Angiogenesis.
- c. Decreased recruitment and phagocytosis of neutrophils (sevoflurane).
- d. Myocardial protection from ischemia-reperfusion injury (isoflurane).
- e. Improved tolerance and function of renal transplantation (desflurane).

Answer:

a. Halogenated anaesthetics cause mild immunosuppression.

5.- Indicate the incorrect statement:

- a. Midazolam inhibits the bactericidal activity and phagocytosis of polymorphonuclear leukocytes.
- b. Droperidol inhibits the bactericidal activity and phagocytosis of polymorphonuclear leukocytes.
- c. Fentanyl inhibits the bactericidal activity and phagocytosis of polymorphonuclear leukocytes.
- d. Propofol does not alter the function of NK (natural killer) cells.
- e. Ketamine does not alter the function of NK (natural killer) cells.

Answer:

c. Fentanyl and alfentanil do not alter the bactericidal activity and phagocytosis of polymorphonuclear leukocytes. The rest of the statements are true. In the case of ketamine, there are articles that indicate that it does not alter the function of NK cells, while others indicate that it can inhibit their function. This is another example of the diversity of results and the need for multicenter clinical trials that allow us to more adequately assess the effects of anaesthesia on the immune system.