Abstract: We present a case of the combination of a bilateral supraclavicular block and a caudal block in a two year old boy who needed amputations of four extremities after a pneumococcal sepsis. With the use of ultrasound guidance, reduction of local anaesthetic dose could be obtained in order not to reach the toxic dose of the local anaesthetic. Amputations of four extremities is not common practice. A good postoperative pain management is more than a challenge.

Key words: Anesthesia; regional; pediatric; supraclavicular; caudal.

Case report

Disease history

A two year old boy was admitted on the Pediatric Intensive Care Unit (PICU) with symptoms of neurological deterioration and fever. The fever started two days before admission. The morning of admission, the child awoke vomiting and lost conscience.

In his personal history he was known as a term born child after an uncompli cated pregnancy with a normal weight of 3370 gram. He had a normal development. He is known with sickle cell anaemia.

On admission his weight was 14.5 kilograms. He rapidly developed an ARDS and septic shock, and was diagnosed with a pneumococcal sepsis. His stay on the PICU was characterized with sickle cell crises, anaemia, transfusion reactions and pre-renal kidney insufficiency.

He developed necrosis of both hands and legs due to bad peripheral circulation as result of the full blown sepsis and high inotropic support. The degree of necrosis was difficult to determine at the beginning due to his coloured skin. During his stay he received high doses of morphine and ketamine as sedation and pain control. His pain medication was reduced using a detoxification program and he was discharged from the PICU after 19 days with only paracetamol as pain medication.

Due to parents’ decision there was no further treatment for the necrosis of hands and legs until the day of surgery four months after demission of the PICU.

Procedure

On the day of his second admission, prior to surgery, the patient needed no pain medication any more. The child received no premedication. General anaesthesia was induced by sevoflurane inhalation. Fentanyl and propofol were given prior to placing the laryngeal mask. The patient was placed in lateral decubitus with the knees drawn up to the chest in order to facilitate caudal anaesthesia. Following the landmarks (coccyx, sacral conua) the classical depression between the two bony prominences (hiatus sacralis) was easily found. After decontamination, the needle (Epican® Paed caudal 25G, B Braun) was inserted and the classic “plop” was felt. Aspiration of the needle did not give any blood or CSF. Confirmation of the good position of the needle was obtained by ultrasound guidance. During injection of the local anaesthetic (6 cc Ropivacaine 2 mg/ml), the advancement and location of the anaesthetic was followed through ultrasound (Philips®, HDX 11, linear probe 7-12 MHz 38 mm) (Fig. 3) as described by Roberts et al. in

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2005 (1). There were no additives added to the injected local anaesthetic.

After turning the patient back in supine position, the child was prepared for a bilateral supraclavicular brachial plexus block. Ultrasound guidance was used to determine the landmarks (artery subclavia, clavicle, brachial plexus, pleura and first rib). To obtain this view, the linear (linear 38-mm 7-12 MHz – HDX11 – Philips®) transducer was placed firmly over the supraclavicular fossa in the coronal oblique plane to obtain a good transverse view of the subclavian artery and brachial plexus. The head is slightly turned to the contra-lateral side. The needle (B Braun Stimuplex® D plus 35 mm) was advanced in plane (IP) from lateral to medial in the same plane as the transducer until the brachial plexus is reached. The needle was placed at optimal injection site, which has been described as being in the “corner pocket”, according to SOARES et al. (2). This point is bordered by the first rib inferiorly, the subclavian artery medially and the brachial plexus superiorly. The supraclavicular brachial plexus is seen as a group of hypo-echoic nodules frequently described as a “cluster of grapes” (3). Electrical stimulation (threshold stimulating current at 0,3 mA) was used to confirm the identification of brachial plexus with biceps and triceps twitches.

The procedure was performed bilateral and 2,5 cc Ropivacaine 5 mg/ml were injected each side. A good spread of local anaesthetic was visualized on ultrasound with a hydro-dissection of the fascial sheath and perineural tissues.

After the performance of the blocks, muscle relaxant (Atracurium) was administered to facilitate intubation. Anesthesia was maintained with sevoflurane and air/oxygen mixture (end-tidal sevoflurane of 2 Vol%). No additional monitoring of depth of anesthesia was used.

During surgery no additional opioids were needed. Postoperative intravenous paracetamol was added and patient’s parents and nurses judged the pain relief postoperative to be excellent (according to the Children’s Hospital Eastern Ontario Pain Scale (CHEOPS)). Motor and sensory blockade was difficult to access due to the age. Postoperative low dose intravenous morphine drip was added (10 mcg/kg/h) for another 12 hours. After 24 hours postoperatively only paracetamol was required for pain relief.

**DISCUSSION**

In paediatric loco-regional surgery of the upper extremity, the axillar block was the gold standard because of the easy trans-arterial procedure. The problem of an inconsistent block due to the lack of musculocutaneous nerve analgesia for tourniquet pain or skin analgesia below the elbow was less important because the loco-regional technique was often combined with general anaesthesia in the paediatric patient population.

Papers on paediatric supraclavicular blocks are still rare (4). Reasons for the sporadic use of the technique in children are the risk of pneumothorax, the lack of experience, technical difficulties (material), physiological difficulties (e.g. relatively large head) (5) and the fact that loco-regional anaesthesia is performed on anaesthetized or sedated patients (6).

A lot of pediatric loco-regional techniques are blind techniques, e.g. penile block, caudal block, ilioinguinal, iliohypogastric block. Thanks to ultrasound guidance pediatric regional blind blocks became “deblinded”. Ultrasound guidance found its way to pediatric brachial plexus blocks in the beginning of the 21st century (8). BROWN et al. published a review article in 1999 on the benefits of local and
regional anaesthesia in children (7). He stated that a loco-regional technique should be performed unless contraindicated. MARHOFER et al. reviewed different block regions of the pediatric ultrasound guided brachial plexus and more specific the infraclavicular region (9).

Later on more and more articles were published about the advantages of using ultrasound as guidance techniques in performing more challenging blocks. One of the advantages was a dose reduction of the local anaesthetic needed to block a region. Other advantages are for instance shorter onset times and longer block duration (10, 11). These advantages may be the reason for the recent successes in pediatric peripheral regional anesthesia and ultrasound guidance (7, 12). These benefits however are not yet proven for neuraxial techniques.

A reduction in dose per block makes it possible to perform more than one block at the time in one patient. The maximal dose for ropivacaine for locoregional techniques in children, is 3 mg/kg. In
the presented case the total amount of local anaesthetic did not override this maximal dose due to dose reduction enabled by the use of ultrasound guidance (13-16). An additional prolongation of duration of the supraclavicular block can also be obtained by using adjuvants as proven in literature (17) but was not used here. The use of adjuvants keeps on being a debatable subject (18).

A well known complication of brachial plexus blocks is diaphragm paralysis. When an interscalene block is used, there is a 100% incidence of diaphragmatic paresis accompanied by a 25% reduction in forced vital capacity (FRC) (19). When a supraclavicular block is used, only 50% of patients have diaphragmatic paresis and there is no reduction in FRC (20). A study by Renes et al. however showed no diaphragm paresis using lower dosages of local anaesthetic (20 mL supraclavicular) (21) and a lower incidence of diaphragm paresis using 10 mL for the interscalene approach (22) in adult patients. This was one of the reasons that the supraclavicular region was chosen above the interscalene approach. The advantage of a supraclavicular approach in comparison with the axillary approach is that a smaller amount of local anaesthetic is needed to block the plexus and also that the incidence of diaphragm paralysis is lower with almost no alterations of FRC. This can be important if a bilateral plexus block is desirable.

To perform these blocks we used a linear 7-12 MHz 38 mm probe. Better is to use a smaller size of probe but this was on that moment not available in our department.

**Conclusion**

We presented a case of a two year old boy who needed amputations of four extremities after a pneumococcal sepsis. We combined a bilateral supraclavicular block and a caudal block using ultrasound guidance.

This case report shows that the use of ultrasound guidance can be beneficial in difficult situations. The use of ultrasound as guidance technique for peripheral nerve block can reduce the total dose of local anaesthetic. This is especially interesting when more than one block needs to be performed, like in this case, in order to avoid toxic dose levels.

For neuraxial blocks with ultrasound guidance however, like the caudal block used in this case, no dose reduction could yet be proven in literature in favour to the classical neuraxial techniques.

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**References**


Lipomatous hypertrophy of the interatrial septum: The typical echographic aspect is worth being known

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Abstract: A 65-year-old man was scheduled for an on-pump coronary artery bypass graft procedure because of a three-vessels coronary artery disease. A right atrial mass appended to the interatrial septum was discovered during intraoperative transoesophageal echocardiography. Therefore, the right atrium was opened. Gross examination revealed a fatty lesion of the interatrial septum. A biopsy was performed before the atrium was closed. A histological diagnosis of lipomatous hypertrophy of the interatrial septum was made. Lipomatous hypertrophy of the interatrial septum is a mass of adipocytes infiltrating the interatrial septum. The aspect of "dumbbell" produced by the sparing of the Fossa Ovalis is typical. The lesion is benign and remains asymptomatic most of the time although it can be responsible for cardiac arrhythmias or circulatory obstruction. The typical echographic aspect should be known to avoid unnecessary surgical resection.

CASE REPORT

A 65-year-old man was scheduled for an on-pump coronary artery bypass graft surgery. The patient had started to complain about chest pain on exertion for a few weeks. A coronary angiogram revealed the presence of a three vessels coronary artery disease. The ventriculography showed a normal left ventricular systolic function.

A transoesophageal echocardiogram (TEE) was performed after the induction of anaesthesia and revealed a 5 cm x 3.5 cm mass at the posterior part of the interatrial septum (Fig. 1). The mass appeared slightly speckled but homogeneous and had well-defined borders. There was no extension outside the right atrium and the tricuspid blood flow was unaffected. Although all these characteristics suggest a benign condition, none of the anaesthetists and surgeons who saw the images were able to identify the lesion with some certainty.

It was therefore decided to open the right atrium for further evaluation. The lesion appeared to be fatty and to arise from the upper interatrial septum, bulging into the right atrium. A biopsy was performed and histological analysis confirmed the diagnosis of lipomatous tissue. The right atrium was closed and four coronary artery bypass grafts were performed. Separation from the cardiopulmonary bypass was uneventful. The patient was extubated six hours after the end of surgery. He was discharged from hospital on post-operative day 10.

DISCUSSION

This case reemphasizes the role of intraoperative TEE in adult cardiac surgery patients. This is in accordance with the guidelines over the use of perioperative TEE recently updated by the American Society of Anesthesiology (1). During coronary artery bypass graft surgery, TEE can help to detect new or unsuspected cardiac pathologies, to subsequently adjust both the anesthetic and surgical plans, and to assess the results of surgery. In this case, TEE allowed diagnosing an unsuspected lesion.

The differential diagnosis of cardiac mass has recently been reviewed elsewhere (2). In the presence of a cardiac mass, a few basic characteristics are helpful to distinguish between benign tumors, malignant tumors, tumorlike lesions and thrombi. Smooth and well-defined borders, absence of irregularities or myocardial infiltration, involvement of
no more than one cardiac chamber and lack of calcification or area of necrosis are all suggestive of a benign lesion. In contrast, large lobular lesions with ill-defined borders and large area of necrosis or calcification as well as myocardial infiltration or extension to other cardiac chambers rather suggest malignity. Thrombi can be difficult to distinguish from tumors but their most common location is the left atrial appendage and they usually appear in patients having a prothrombotic condition such as atrial fibrillation, obstruction to flow, hypercoagulable state (3).

In our patient, the four-chambers view revealed the presence of a right atrial mass that we were unable to identify. The most commonly seen atrial tumor is the myxoma. However, 75% of the myxomas occur in the left atrium. Moreover, myxomas usually arise from the interatrial septum near the fossa ovalis and are frequently anchored via a stalk-like pedicle. These characteristics made the diagnosis of myxoma unlikely in our patient. The other benign cardiac tumors that can occur throughout the heart are lipomas. They are usually subendocardial and appear fixed and slightly echodense.

However, in our patient, careful examination of the four-chambers view and moving the imaging plane to 149° showed that the lower part of the interatrial septum was enlarged too, although to a lesser extend (Fig. 1). The process spared the Fossa Ovalis. This resulted in a dumbbell-shaped interatrial septum. Such an echographic aspect is typical of a condition called lipomatous hypertrophy of the interatrial septum that we should have recognized to avoid an unnecessary opening of the right atrium.

Lipomatous hypertrophy has been described for the first time in 1964 (4). It corresponds to an infiltration of the interatrial septum by proliferating mature adipocytes. Macroscopically, it appears as a well-circumscribed but non-encapsulated adipose tissue. Typically, the lesion predominates in the upper part of the interatrial septum and spares the Fossa Ovalis as it was the case in our patient. This explains the characteristic “dumbbell” shape usually reported (5).

Lipomatous hypertrophy of the interatrial septum is a benign condition. Its etiology remains unclear. Risk factors include advanced age, female gender and obesity. There are no definitively established diagnosis criteria but the diagnosis is usually considered when the thickness of the interatrial septum exceeds 2 cm. The incidence of the lipomatous hypertrophy of the interatrial septum was initially thought to be low (1% of the population). However, the condition is increasingly recognized as a consequence of a steadily increasing access to imaging techniques such as computed tomography, magnetic resonance imaging and echocardiography. It is most of the time asymptomatic and discovered incidentally on an examination performed for another purpose. Rarely, the hypertrophic septum can cause arrhythmia or obstruction to flow. Surgery has to be considered only in these exceptional symptomatic cases (6).

To summarize, we report a case of incidentally discovered lipomatous hypertrophy of the interatrial septum during a routine TEE examination. This condition typically appears as an enlarged and dumbbell-shaped interatrial septum. Since it is benign and should not be treated except for rare symptomatic cases, its aspect is worth being known by anyone practicing TEE to avoid unnecessary and potentially hazardous exams and treatment.
References


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Linking sleep and general anesthesia mechanisms: this is no walkover

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Abstract: This review aims at defining the link between physiological sleep and general anesthesia. Despite common behavioral and electrophysiological characteristics between both states, current literature suggests that the transition process between waking and sleep or anesthesia-induced alteration of consciousness is not driven by the same sequence of events. On the one hand, sleep originates in sub-cortical structures with subsequent repercussions on thalamo-cortical interactions and cortical activity. On the other hand, anesthesia seems to primarily affect the cortex with subsequent repercussions on the activity of sub-cortical networks. This discrepancy has yet to be confirmed by further functional brain imaging and electrophysiological experiments. The relationship between the observed functional modifications of brain activity during anesthesia and the known biochemical targets of hypnotic anesthetic agents also remains to be determined.

Key words: Sleep; general anesthesia; consciousness; mechanisms.

INTRODUCTION

When referring to induction of general anesthesia, vernacular language often uses the expression of “putting someone to sleep”. This is related to the behavioral characteristics commonly thought to be part of both states, including altered consciousness, reduced movements, and closing of the eyes (1). Besides behavioral similarities, sleep and anesthesia share common electroencephalographic modifications including slow wave activity (2). Hence, temptation of merging sleep and anesthesia mechanisms into a hodgepodge is high. In order to understand how hypnotic anesthetic agents produce an alteration of consciousness, three main types of experimental paradigms have been used. In vitro electrophysiological studies on neurons and brain tissues have allowed identifying their biochemical targets, mainly in terms of neurotransmitter systems, and ionic channels. Animal models, and the study of mutants, have confirmed the involvement of specific neurotransmitter systems, and shed light on the influence of hypnotic agents on sub-cortical arousal systems. Finally, electrophysiological and imaging studies in humans have evidenced their selectivity on specific functional regions and networks in the brain. The current challenge consists in making the link between all those mechanistic elements, compare them to the known mechanisms of sleep, synthesize the similarities and differences, and try to determine if the initiation of the cascade leading to the alteration of consciousness during sleep and anesthesia is located at the same place in the brain and involves the same brain mechanisms.

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This will be the aim of the present review. After comparing the behavioral and electrophysiological characteristics of sleep and anesthesia, the systems sustaining arousal and the emergence of consciousness will be described. The known mechanisms of physiological sleep will then be summarized. This will allow placing hypnotic anesthetic agents within those systems and mechanisms by envisaging their multiple biochemical targets, their action on sleep and arousal pathways, and, finally, their functional effect on the brain.

**Behavioral and electroencephalographic characteristics of sleep and general anesthesia**

The behavioral resemblance between sleep and general anesthesia does not outlive detailed analysis. According to Franks and Zecharia, sleep can be defined as “a naturally occurring, periodic state of rest during which consciousness of one’s environment and responses to external stimuli are largely suspended” (1). However, resting attitude, altered environmental awareness, and suppression of responses to external stimuli are not the only behavioral elements that must be part of the description of sleep, and of other altered consciousness states. A more precise description should include the presence or absence of wakefulness, spontaneous or evoked purposeful movements, muscle tone, awareness of the environment, response to command, self perception, mental imagery, and reversibility upon external stimulation (Table 1).

Physiological sleep is not a unitary entity. One must discriminate the so called rapid-eye-movement (REM) sleep from the slow wave sleep (or non-REM sleep). During non-REM sleep, of course, wakefulness is absent, and the eyes are closed. Muscle tone is normal, and spontaneous movements occur. This state is associated with various degrees of consciousness alteration, whose reversibility by external stimulation depends on sleep depth. Awareness of the environment and ability to respond to command fall off. There is no awareness of self and mental imagery, despite possible occurrence of dream. REM sleep is more frequently associated with dreaming, and hence mental imagery, with virtual self perception. Due to muscle atonia, no movements occur, except for specific movements of the eyes. Awareness of the environment is altered, as well as response to command. REM sleep is easily reversed by external stimulation. Surface electroencephalographic

<table>
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<th>Table 1</th>
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<tr>
<td>Behavioral and surface electroencephalogram (EEG) characteristics of sleep and general anesthesia. n-REM = non-rapid-eye-movement ; REM = rapid-eye-movement ; Inhib. neurotrans. = agents that promote inhibitory neurotransmission such as barbiturates, propofol, benzodiazepines, etomidate, and halogenated vapors ; α2 agonists = α2-adrenergic agonists ;</td>
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<tr>
<td>St.-dep. = stage-dependent ; Des. fast = desynchronized fast activity</td>
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<td><strong>Sleep</strong></td>
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<td>Wakefulness</td>
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<td>Movements</td>
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<td>Purposeful</td>
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<td>Muscle tone</td>
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<td>Response to command</td>
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<td>Self perception</td>
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<td>Reversibility</td>
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<td>EEG features</td>
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(EEG) modifications during non-REM sleep include waxing and waning oscillations of 12-15 Hz frequency lasting for at least a half second (spindle oscillations) and K-complexes (high voltage negative peak immediately followed by a slower positive complex) at sleep onset, and widespread increased power in lower frequencies (delta waves or slow oscillations, 0.5-4 Hz) at deeper stages. Slow oscillations originate in frontal regions and propagate to posterior regions of the cortex following a reproducible track (3). REM sleep displays EEG patterns that are close, but not identical, to those observed during the wake state, including low voltage desynchronized fast activity, and increased power in the theta range (4-10 Hz) (4, 5).

During general anesthesia, alteration of consciousness is achieved using anesthetic agents with hypnotic properties. All of them do not alter the above-cited behavioral elements in the same way. In that respect, different classes must be distinguished. Agents that mainly enhance inhibitory neurotransmission such as barbiturates, propofol, benzodiazepines, etomidate, and halogenated vapors suppress wakefulness, awareness of the environment and response to command, as well as self awareness. They also lessen muscle tone, and movements. When maintained at sufficiently high concentrations, reversibility by external stimulation is difficult. Hence, those agents produce a state that is rather close to deep non-REM sleep, with the exceptions of reduced muscle tone and movements, and less easy reversibility. However, dreaming has been reported during propofol and desflurane anesthesia (6), particularly during emergence from anesthesia. In case of dreaming, electroencephalographic activity is similar to that observed during REM sleep. Otherwise, surface EEG alterations achieved with those agents depend on the administered dose. When increasing doses, beta activation first occurs (low amplitude 13-30 Hz waves), followed by a progressive slowing towards delta activity, near burst suppression (bursts followed by periods of flat signal), and, eventually, isoelectricity (7). Spindles can be observed (6), and slow wave activity appears similar to slow waves of non-REM sleep with subtle differences (2).

Ketamine is certainly the most representative among the hypnotic agents that mainly act through an inhibition of excitatory neurotransmission. Nitrous oxide can also be considered as part of that class. These agents have long been qualified as “dissociative” (8), insofar as they produce unconsciousness while preserving wakefulness, a state close to the recently renamed vegetative state, or Unresponsive Wakefulness Syndrome (UWS) (9). During ketamine administration, spontaneous reptilian non purposeful movements are commonly present. Subjects lose awareness of their environment and response to command. Intense dreamlike experience often occurs, with inadequate self perception. Reversibility upon external stimulation is not obtainable at high doses. Regarding surface EEG, ketamine produces an increase in high amplitude rhythmic theta activity, reduced alpha activity (8-13 Hz), and polymorphic delta activity with scattered beta activity (10).

Alpha₂-adrenergic agonists and inert gases also have hypnotic properties but do not belong to the above-mentioned classes. The decreased alertness and the state of tranquility induced by α₂-adrenergic agonists such as dexmedetomidine or clonidine are easily reversed by external vocal or tactile stimulation. With increasing concentration of such agents, subjects long keep the ability to respond to verbal command, and several cognitive brain functions are preserved, although memory and motor skill impairment has been reported (11, 12). Hence, α₂-adrenergic agonists are remarkable in that they alter wakefulness while preserving several aspects of awareness. The associated EEG changes are characterized by an increased energy in the lower frequency band (delta and theta activity) and in the spindle frequency range (12-15 Hz) (1, 13). Therefore, α₂-adrenergic agonist sedation is behaviorally and electrophysiologically very close to non-REM sleep. Xenon is currently the only inert gas used in clinical practice. Although having different biochemical targets, its behavioral effects mimic those of halogenated vapors (14), as well as their effects on the electroencephalogram (10).

In light of the above descriptions, sleep and anesthesia-induced behavioral and electroencephalogram modifications are heterogeneous. Hence, it is necessary to describe the mechanisms known to sustain arousal and awareness, before deeply inventoring the mechanisms of each state and find the link between them.

Arousal pathways

Cortical arousal and wakefulness during normal waking is sustained by a complex network of interconnected nuclei, with reciprocal projections to the cortex. Those neural pathways can be divided into three categories, depending on the location of their nuclei of origin, namely the pons, the midbrain, and the hypothalamus-basal forebrain.

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A detailed description of each nucleus and its projections can be found in the excellent review by Franks (15).

Pontine nuclei are cholinergic, noradrenergic, serotonergic, or glutamatergic. Cholinergic pontine nuclei project onto pontine, thalamic, mesencephalic reticular formation, and basal forebrain arousal nuclei, as well as onto regions of the prefrontal cortex. The locus coeruleus is the pontine source of noradrenergic neurons. It has a direct arousal effect on the cortex, and indirect effects through thalamic innervations and the inhibition of sleep-promoting pathways in the basal forebrain and preoptic areas. Pontine serotonergic neurons originate in the dorsal raphe and project onto the cortex, thalamus, and basal forebrain, while pontine glutamatergic neurons emerge from the oral pontine nucleus and project onto the thalamus and the cortex.

Arousal nuclei of the midbrain are glutamatergic and dopaminergic. Glutamatergic neurons project onto thalamic, basal forebrain, and pontine arousal nuclei, as well as onto the locus coeruleus. Dopaminergic neurons innervate the thalamus, the basal forebrain, and the cortex.

In the hypothalamus, orexinergic and histaminergic nuclei project diffusely to the cortex, thalamus, and other arousal nuclei. The cholinergic sources of the basal forebrain spread onto the cortex, the limbic system, and specific thalamic arousal nuclei.

From this schematic summary of the complex arousal network, it appears that acetylcholine, noradrenaline, serotonin, histamine, orexin, glutamate and dopamine are the main neurotransmitters of wakefulness, and that all of them can have direct arousal effects on the cortex. They endorse cortical

### Table 2

Schematic summary of arousal systems. + = arousal promoting effect; − = inhibition; LC = locus coeruleus

<table>
<thead>
<tr>
<th>Location of nuclei</th>
<th>Neurotransmitter</th>
<th>Projections</th>
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<tbody>
<tr>
<td>Pons</td>
<td>Acetylcholine</td>
<td>+ Prefrontal cortex</td>
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<td></td>
<td></td>
<td>+ Arousal nuclei</td>
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<tr>
<td>Noradrenaline (LC)</td>
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<td>+ Cortex</td>
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<td></td>
<td></td>
<td>+ Arousal nuclei</td>
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<tr>
<td></td>
<td></td>
<td>− Sleep promoting pathways</td>
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<tr>
<td>Glutamate</td>
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<td>+ Cortex</td>
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<tr>
<td>Serotonin</td>
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<td>+ Cortex</td>
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<td></td>
<td></td>
<td>+ Arousal nuclei</td>
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<tr>
<td>Midbrain</td>
<td>Glutamate</td>
<td>+ Arousal nuclei</td>
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<tr>
<td></td>
<td></td>
<td>Pons, Thalamus, Basal forebrain, LC</td>
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<tr>
<td></td>
<td>Dopamine</td>
<td>+ Cortex</td>
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<td></td>
<td></td>
<td>+ Arousal nuclei</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>Orexin</td>
<td>+ Diffuse</td>
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<td></td>
<td></td>
<td>Arousal nuclei</td>
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<tr>
<td></td>
<td>Histamin</td>
<td>+ Diffuse</td>
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<td></td>
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<td>Arousal nuclei</td>
</tr>
<tr>
<td>Basal forebrain</td>
<td>Acetylcholine</td>
<td>+ Cortex</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+ Limbic system</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+ Thalamus</td>
</tr>
</tbody>
</table>
arousal, which is a prerequisite for the emergence of consciousness and its several components.

**EMERGENCE OF CONSCIOUSNESS**

The conscious experience originates in the cerebral cortex. Two main theories are currently proposed to explain the emergence of mental content. The first one is the global workspace theory (16, 17). According to this theory, specialized functional brain networks made of hierarchically organized interconnected brain regions synchronize their activity to generate perceptual and mnemonic information. Interconnections between brain regions dynamically change according to circumstances. The generated information is pooled into a global workspace, and regulating systems allow one cognitive element or the other to separate from background information and emerge into the conscious field. The second theory is the information integration theory of consciousness (18), which has received more support from experimental evidence than the first one. In this theory, information would be generated by stereotypical patterns of brain responses, and integration of information would emerge from connectivity inside large scale cerebral networks. Some of those networks are qualified as resting state networks, or ‘intrinsic connectivity networks’ (19), because they elicit functional connectivity in a lying down individual with eyes closed, no external stimulation, and doing nothing else but thinking. Among the resting state networks, the medial frontoparietal default mode network (DMN) is involved in the awareness of self (20), and the dorsolateral frontoparietal executive control network (ECN) is involved in the awareness of the environment (21) (Fig. 1). Resting state auditory and visual networks have also been described (22). DMN and ECN have anti-correlated activities, that is alternate activation approximately every 20 seconds (21, 23). Conscious perception of external stimulation would only be possible during ECN activation. Peripheral sensory information would first reach the sensory networks through the thalamus and under the control of sub-cortical thalamo-regulatory systems involving the putamen (24). It would then pass through several hierarchically organized levels of integration, including cross-modal interaction. Other components of consciousness would be sustained by specific networks, such as the one for associative learning (25), emotions (26), or pain and its emotional components (27).

**CHANGES ASSOCIATED WITH SLEEP**

Inhibitory nuclei that are active during sleep are mainly γ-amino-butyric acid (GABAergic) and galaninergic. They are located in the preoptic area and basal forebrain. Their firing rate increases immediately prior to sleep. Among them, the ventro-lateral preoptic nucleus (VLPO) appears to play a key role (28). In the waking subject, the noradrenergic locus coeruleus tonically inhibits the VLPO. At sleep onset, this inhibition disappears, and the VLPO releases the inhibitory neurotransmitter GABA at several sites, including the histaminergic tuberomammillary nucleus (TMN), and all the noradrenergic, serotonergic, cholinergic, and orexinergic arousal nuclei described above. The widespread inhibition of arousal pathways switches tightly interconnected thalamic and cortical neurons from a tonic firing to a hyperpolarized and burst firing mode (1). As a consequence, thalamic oscillations occur, leading to the emergence of sleep spindles in the EEG. Diffuse synchronization of thalamic and cortical activity also occurs, resulting in the outbreak of slow delta waves. Functional brain imaging has revealed that global brain activity decreases during non-REM sleep, with marked relative decreases in selected brain regions including brain-stem, thalamus, basal ganglia, and basal forebrain, as well as in the prefrontal cortex, anterior cingulate cortex, and precuneus (5). However, specific sub-cortical and cortical regions involved in the generation of spindles and slow waves increase their relative activity (5). Functional connectivity within the DMN is impaired during deep non-REM sleep (29), but not during light non-REM sleep (30). Perception and interpretation of external information, although still possible, is altered. It seems that, beside a possible guardian role of the prefrontal cortex in assessing saliency of incoming information and triggering an awakening response if necessary, there exists a sleep-induced deactivation of primary sensory areas (5).

The initiation of REM sleep depends on complex feed-back interactions between cholinergic REM sleep promoting neurons located in the tegmentum, and serotonergic, noradrenergic, and GABAergic REM sleep inhibiting neurons located in the dorsal raphe, locus coeruleus, and reticular formation (31). These interactions would lead to cyclic occurrences of REM sleep behavioral and EEG patterns, including muscle atonia, rapid-eye movements, and EEG disynchronization. Regarding global brain activity, no significant difference from wakefulness can be found, although
several brain regions increase their relative activity (e.g. tegmentum, thalamus, basal forebrain, amygdala, hippocampus, anterior cingulate cortex, and temporoparietal areas), while others decrease it (dorsolateral prefrontal cortex, posterior cingulate, precuneus, and inferior parietal cortex) (5). In contrast to non-REM sleep, few are known about external information processing during REM sleep.

BIOCHEMICAL TARGETS OF HYPNOTIC ANESTHETIC AGENTS

Having summarized the physiology of waking and sleep, we can now discuss the possible targets of hypnotic anesthetic agents within those systems. The first level to be explored is the molecular level. In vitro electrophysiological recordings and the study of mutants have allowed identifying a large number of neurotransmitter receptors, ion channels, and other functional neuronal proteins that are sensitive to the action of hypnotic anesthetic agents. Among them, only a few have received enough experimental support to be linked to the clinical effect of anesthetic agents (15) (Table 3).

The first one is the type A GABA receptor, which can be synaptic or extra-synaptic, and is widely distributed across the brain. GABA is a major inhibitory neurotransmitter. Agents such as

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Table 3

Principal biochemical targets of the hypnotic effect of anesthetic agents. Summarized from (15) and (14). + = activation; − = inhibition; 0 = no effect; GABA = γ-aminobutyric acid; GABA_A = GABA receptor type A; NMDA = N-methyl-D-aspartate; NMDA_R = NMDA receptor; 2P_K_channels = two-pore potassium channels; n and m AChR = neuronal nicotinic and muscarinic acetylcholine receptor; Glycine_R = glycine receptor; HCN = hyperpolarization-activated cation channel; Na_channels = voltage-gated presynaptic sodium channels; Vapors = halogenated vapors; N,O = nitrous oxide

<table>
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<th>Agonist/Effect</th>
<th>Propofol</th>
<th>Benzodiazepines</th>
<th>Barbiturates</th>
<th>Etomidate</th>
<th>Vapors</th>
<th>Xenon</th>
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<td>+</td>
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<td>−</td>
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<td>Na_channels</td>
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<td>−</td>
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<td>−</td>
<td>−</td>
<td>−</td>
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</tbody>
</table>
propofol, halogenated vapors, etomidate, benzodiaze- 
peines, and barbiturates have been demonstrated to 
promote GABAergic, and hence inhibitory neuro-
transmission (14).

Some types of potassium channels, the two-

type potassium channels (TREK, TASK, and 
TRESK channels), can be activated by hypnotic 
anesethic agents, with a net result of hyperpolariza-
tion and neuronal inhibition. This is the case for 
halogenated vapors, nitrous oxide, ketamine and 
xenon (32). Those potassium channels are widely 
distributed across the brain, and are either pre-
synaptic or postsynaptic. They are considered to be 
responsible for the background modulation of 
unoral excitability.

Another major target of hypnotic anesthetic 
agents is the N-methyl-D-aspartate (NMDA) gluta-
mate receptor subtype, whose inhibition causes 
excitation of the slow components of synaptic 
transmission (15). NMDA receptors are inhibited 
by halogenated vapors, nitrous oxide, xenon, and 
ketamine. This inhibition is mainly responsible for 
their anti-noxious effect at the level of the dorsal 
horn of the spinal cord, and can probably not 
count alone for their hypnotic effect. The other 
hypnotic agents, such as propofol, are not or only 
weak inhibitors of NMDA receptors (33).

Central cholinergic neurotransmission plays an 
important role in cortical arousal (34), and sever-
al hypnotic agents including propofol, barbiturates, 
halogenated vapors, xenon, nitrous oxide and keta-
mine have been shown to alter nicotinic and/or 
muscarinic transmission. The glycine receptor is 
another potential target, mainly for halogenated 
volatile anesthetics. It is frequently associated with 
GABA, receptors, and mediates neuronal inhibition 
(14, 15). Hyperpolarization-activated cation (HCN) 
channels are important regulators of neuronal 
excitability and rhythmicity (35), particularly in 
thalamocortical neurons where they contribute to 
modulate thalamocortical oscillations (15). Propofol, and, to a lesser extent, halogenated vapors 
inhibit those channels. Finally, presynaptic voltage-
gated sodium channels are sensitive to the effect of 
halogenated volatile anesthetic agents, and their 
inhibition can delay glutamatergic neurotransmis-
sion (36).

Given the extraordinary multiplicity of bio-
chemical targets, and their large distribution across 
the brain, there must be subtle agent- and dose-
dependent differential tuning of the effect of 
hypnotic agents on each of them to end up with the 
pharmacodynamic consequences of anesthesia. 
Two options are available to understand this fine 
tuning, either look at the effect of hypnotic agents 
on specific sleep/arousal and consciousness net-
works using animal models, or examine the func-
tioning brain using functional brain imaging or 
electrophysiological techniques.

ANESTHETIC AGENT TARGETS WITHIN AROUSAL AND SLEEP 
SYSTEMS

The behavioral and electrophysiological 
similarities between sleep and anesthesia have long 
prompted scientists to search for an anesthesia-
operated consciousness switch within sleep/arousal 
networks (37). Indeed, there could be an enhance-
ment of sleep promoting pathways activity, an 
inhibition of arousal systems, an alteration of 
thalamo-cortical interactions, or a combination of 
these mechanisms. Mutant rodents for specific 
receptors, stereotaxic lesions of selected nuclei, 
quantification of c-Fos protein (a marker of 
nunoral activity) expression, and brain slice or in 
vivo electrophysiological recordings in animals, in 
the presence of specific agonists or antagonists, 
have been used to evidence the effect of hypnotic 
agents on those systems. Most of these studies are 
direct arguments of such effects, and translation 
to the in vivo human brain is not easy (37). In 
addition, the involved mechanisms could be 
different during induction of and emergence from 
anesthesia (38, 39). Among the arousal pathways, 
cholinergic, noradrenergic, serotonergic (15), 
orexinergic (40) and histaminergic (41, 42) systems 
have mostly been incriminated. The inhibition of 
arousal systems could be the result of a GABAergic 
neurotransmission enhancement within sleep path-
ways (28, 40). Regarding the cholinergic systems, 
the administration of centrally acting cholinesterase 
inhibitors can reverse propofol (34) and sevoflu-
rane-induced (43) loss of consciousness in humans. 
In that case, a brain activity pattern similar to the 
wake state is restored (44). However, it could be 
that these effects only result from a sufficiently 
powerful activation of cholinergic arousal, inde-
dependently from the basal mechanisms of anesthe-
sia-induced alteration of consciousness (15). The 
strongest arguments for the involvement of sleep 
pathways during a pharmacologically-induced 
alteration of consciousness are probably those 
which use the α2-adrenergic agonists clonidine 
and dexmedetomidine (13, 45) that inhibit the locus 
coeruleus.
FUNCTIONAL EFFECTS OF ANESTHESIA

At this stage of our review, further understanding of the mechanisms of anesthesia-induced alteration of consciousness can only come from whole brain functional observations, using techniques that have enough spatial and temporal resolution. Among them, positron emission tomography (PET), functional magnetic resonance imaging (fMRI), functional near infrared spectroscopy (fNIRS) and sophisticated electroencephalographic studies, combined with transcranial magnetic stimulation (TMS), have allowed substantial progress (46).

The first functional studies of the brain under anesthesia demonstrated that agents such as propofol (47, 48), halogenated vapors (49), barbiturates (50), benzodiazepines (51), xenon (52), and α₁-adrenergic agonists (13) dose-dependently reduce the activity of specific brain regions, including the thalamus, cuneus-precuneus, posterior cingulate cortex, and the fronto-parietal association cortices. The obtained images are similar to those observed during non-REM sleep, coma, generalized seizure, and UWS (53, 54). Most of these regions are part of the intrinsic connectivity networks DMN and ECN (23). Ketamine is an exception, as it offers a very different pattern of brain functional changes. Indeed, it produces activations in the anterior cingulate, thalamus, putamen, and frontal cortex (55, 56).

Considering these observations, anesthesia has obviously specific cortical effects. It could be proposed that, similarly to physiological sleep, anesthesia-induced modifications of cortical activity would be the result of its above-described subcortical effects. But the inverse is also possible, that is a primary effect on the cortex, with subsequent repercussions on cortico-sub-cortical interactions and activity in the sub-cortical structures. Accumulating evidence suggests that this second hypothesis is probably the right one.

Indeed, cortical effects of anesthetic agents occur at lower doses than sub-cortical effects (57-59), and higher order processing cortical areas are more sensitive than lower-order ones (60, 61). It seems that hypnotic agents, at least those promoting GABAergic neurotransmission, disrupt large-scale cortical connectivity and the ability of the brain to integrate information (62-64), while certain dynamic principles of the underlying networks are maintained (65). Connectivity and anticorrelation of DMN and ECN (66-68), and of other higher-order networks (69), is reduced by low concentrations of these agents. At those low concentrations, connectivity is preserved or even increased in lower-order sensory and motor networks (70), and thalamic activation by external stimuli still occurs (24). At concentrations producing loss of responsiveness, connectivity of DMN and ECN disappears, as well as their anticorrelation. In contrast, DMN and ECN become anticorrelated with thalamic activity (66), and connectivity in lower-order sensory networks is maintained with cross-modal interaction alterations.

CONCLUSIONS

Progress has recently been made in the understanding of the mechanisms of sleep and anesthesia-induced alteration of consciousness, and of consciousness itself. Anesthesia and sleep share common behavioral, EEG, and functional features. However, detailed analysis reveals that they probably originate from different backgrounds. Sleep is undoubtedly initiated in subcortical structures, while accumulating scientific data suggest an initial cortical origin for anesthesia, at least during the induction phase, with subsequent subcortical consequences. A simple reverse sequence of events during emergence from anesthesia is probably not what actually happens. These hypotheses remain to be confirmed, and verified for all classes of hypnotic anesthetic agents. The link with known biochemical targets also remains to be determined, as well as the exact sequential alterations of cortico-subcortical interactions. The currently available functional imaging and electrophysiological techniques have not yielded all their secrets yet, and further new elements can certainly be expected in the very near future.

References

into the physiology of human sleep, SLEEP, 33, 1589-603, 2010.


34. Lewis A. S., Chetkovich D. M., HCN channels in behavior and neurological disease: too hyper or not active enough?, MOL. CELL. NEUROC., 46, 357-67, 2011.


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61. Ramani R., Qia M., Constable R. T., Sevoflurane 0.25 MAC preferentially affects higher order association areas: a functional magnetic resonance imaging study in volunteers, ANESTH. ANALG., 105, 648-55, 2007.


64. Alkire M. T., Loss of effective connectivity during general anesthesia, INT. ANAESTHESIOLOGY CLIN., 46, 55-73, 2008.


Prizes for BEST POSTERS (500 Euros each)

SARB Award

Three prizes of 500 Euros each will be presented at the Annual Meeting for the following categories of poster:

1. the best clinical investigation poster,
2. the best anesthesia related basic science or laboratory investigation poster,
3. the best clinical investigation poster or laboratory investigation poster presented by a resident in anesthesia.

Posters may already have been presented at other scientific meetings during the 12 months preceding the ultimate date of submission, September 15th of each year.

The winning posters will be selected on the basis of originality of content as well as their innovative and scientific merit in the field of anesthesiology and related sciences.

An abstract of the poster (along with proof of acceptance by another meeting, if applicable) must be submitted to the secretary of the SARB, Anesthesia Research, UZ. KULeuven, Herestraat 49, B-3000 Leuven no later than September 15th of each year.

Abstracts must respect the format required for the SARB Research Meeting.

The abstracts will be submitted for evaluation to the members of the scientific committee.

The authors of the winning best posters will be notified prior to the Annual Meeting.

The applicant needs to be member of the SARB.

Prizes for BEST PUBLICATIONS (1000 Euros each)

SARB Award

The applicant must be a member of the Society for Anesthesia and Resuscitation of Belgium. Articles reporting clinical or laboratory investigations in the field of anesthesiology and related sciences are eligible if they have been published in a peer-reviewed journal during the 12 months preceding the ultimate date of submission, September 15th of each year. A prize of 1000 Euros will be awarded for the best clinical article. A further prize of 1000 Euros will also be awarded to the best anesthesia related basic science or laboratory investigation article.

The application will contain a copy of the full paper and must be submitted to the secretary of the SARB, Anesthesia Research, UZ KULeuven, Herestraat 49, B-3000 Leuven no later than September 15th of each year. The winning authors will be notified prior to the following Annual Meeting of the SARB.
The Society for Anesthesia and Resuscitation of Belgium
SARB RESEARCH GRANTS

1. The Society for Anesthesia and Resuscitation of Belgium is pleased to announce the SARB Research Grant.

2. The purpose is to support anesthesia research in Belgium with individual research grants derived from contributions made by philanthropists and industry to the Society for Anesthesia and Resuscitation of Belgium.

3. The applicant seeking such support must be a member of the Society for Anesthesia and Resuscitation of Belgium at the time of application and during the tenure of a research grant. A recipient of any previous research grant is ineligible to apply for another grant for a period of four years from start date of the previous grant. Active members of the Research Advisory Committee are ineligible to apply as a principal investigator during their term.

4. The research for which financial support is solicited must be relevant to the practice or theory of anesthesia. The project must be carried out in Belgium.

5. Each selected applicant will receive a research grant. An annual maximum of 20,000 € will be provided by the Society to one, two or maximum three grants (3 × 7,000 €; 2 × 10,000 €; 1 × 20,000 €; 1 × 15,000 € + 1 × 5,000 €). Half of each amount will be paid at the start of the project when the intended recipient of the grant has to presented and defended his application at the first or second Research Meeting of the year following the grant allocation. The remaining half will be paid when the following conditions are fulfilled: proof of acceptance for publication of the results of the research in an international Anesthesia journal, the presentation of the results on a Research Meeting of the SARB and the publication of a review of at least 12,000 words on the subject in the Acta Anesthesiologica Belgica. The applicant must follow the flow chart. The treasurer is responsible for the follow-up. This (financial) control of all grants is presented by the treasurer at the annual meeting (General Assembly) of the SARB.

6. The results can be published in any international Anesthesia Journal. This article, however, will not be allowed to be submitted for the competition for the best publication or major sponsor award.

7. Applications are invited from researchers who may be at any stage of career development, but must hold a position at the department of Anesthesiology of a Belgian university medical school or medical institution recognized for training specialists in anesthesia.

8. The term of the research grant will normally be three years starting the year after the award and is not renewable.

9. Each research grant is to be used to defray the costs of research up to its total value. Any commitments or expenditures incurred by a researcher in excess of the allocated research grant are the responsibility of the researcher alone and will not be reimbursed.

10. The employment of technicians and research assistants under such a research grant must conform to the institutional classification and requirements for such personnel. The SARB cannot be held responsible for covering the salaries and insurance of such personnel.

11. The use of and care for animals in any project supported by a research grant must be in accordance with the international guidelines on animal research. The involvement and recruitment of human subjects must conform to current guidelines, such as the Code of Ethical Conduct for Research Involving Humans, and the Declaration of Helsinki. A document indicating institutional review and approval of animal and/or human experimentation must be submitted prior to disbursement of any grant (the GCP guidelines).

12. The completed application form, and the completed application checklist (together constituting an application package), must reach the SARB secretariat. It is the responsibility of the applicant to ensure that all sections of the application form are completed in a clear and concise manner, all materials are provided, and that the application package reaches the SARB secretariat. Documentation of institutional approval for human and/or animal experimentation, where applicable, must be submitted with the application package. Applications that fail to fulfill these conditions will either not be considered or be withdrawn.

13. Receipt of the application will be acknowledged by e-mail.

14. The application for each grant will be judged by a SARB Research Advisory Committee on the basis of scientific merit, significance, feasibility and financial planning. The individual grants will be awarded to the project. It is recognized that full support of some projects will not be possible.
15. The research grant grants will be announced at the following annual meeting of the Society for Anesthesia and Resuscitation of Belgium.

16. Financial statements and a flow chart will be requested from the investigator holder of the grant. Any uncommitted balance following the term of the grant will revert to the Society for Anesthesia and Resuscitation of Belgium.

17. The recipient of a SARB research grant will be required to notify the SARB office if, for any reason, he/she is unable to complete the project for which the grant was awarded. Any uncommitted balance will have to be refunded to the SARB.

18. It is a requirement of this research program that all papers and abstracts resulting from the research initiative include an acknowledgement of support from the Research Grant Program of the Society for Anesthesia and Resuscitation of Belgium.

19. The completed application package should be sent to: The Department of Anesthesiology/Anesthesia-Clinical Research, University Hospitals KULeuven, SARB Secretary, Herestraat 49, 3000 Leuven, Belgium.
   Tel. +32 16 34.86.52,
   Fax +32 16 34.86.62.
   Or by e-mail: BVAR.SBAR@uzleuven.be

B. Application checklist

This checklist must be completed and submitted as part of the application package.

Applicant: ............................................................................................................................................................

Institution: ..........................................................................................................................................................

Title of Research: ..............................................................................................................................................

Please check each of the following:
[ ] All sections of the application form are complete.
[ ] The detailed research proposal section is limited to 5 additional pages.
[ ] The certification section is signed and dated by both the principal applicant and the department head.
[ ] The application form, together with this checklist, are included in the application package, can be scanned and sent by e-mail or sent by postal mail.
[ ] Financial planning.

Please check the following where appropriate:
[ ] Institutional approval for human experimentation is included in the application package.
[ ] Institutional approval for animal experimentation is included in the application package.

Applicant’s signature ................................................................. Date: .................................................................
C. Application form

This form is to be used to apply for the Society for Anesthesia and Resuscitation of Belgium (SARB) Research Grants Competition. Four copies of this form, together with the application checklist, are required for a complete application. Please ensure all additional typewritten pages are double spaced, with 2 cm. margins, using a minimum font size of 12-point Helvetica or Times Roman.

1. Applicant name:  
Degree:  
Position and dept.:  
Institution:  
Mailing address:  
Telephone Number:  
Fax number:  
E-mail:  
Current SARB membership:  
[ ] Associate  
[ ] Correspondent  
[ ] Titular

2. Co-applicant(s): (If necessary, add an additional page and label as Page 2A)
Name and degree:  
Position and dept.:  
Institution:  
Name and degree:  
Position and dept.:  
Institution:  
Name and degree:  
Position and dept.:  
Institution:  
Name and degree:  
Position and dept.:  
Institution:  

3. Title of research:  

4. Experimentation requiring institutional approval: (Check if appropriate)
[ ] Human Experimentation  
[ ] Animal Experimentation
(Document(s) indicating institutional review and approval must be submitted)

5. Institution to which grant should be paid:
Name of Institution:  
Mailing address:  
Bank account number:  

6. Certification:
We, the undersigned, certify that the information contained in this application is complete and correct to the best of our knowledge and that we approve and support the proposal described herein. If a grant is awarded pursuant to this application, we agree to abide by all statements and regulations governing SARB Research Grants as specified in the document SARB Research Grants Competition.

-------------------------------------------------------------
Applicant’s Name  Signature  Date

-------------------------------------------------------------
Department Head’s name  Signature  Date

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7. Information about applicant (Do not submit a curriculum vitae)
   Current professional status : (Check one only)
   a. Specialist in independent practice [ ]
   b. Specialist with academic (university-related) appointment [ ]
   c. Fellow [ ]

If you answered c above, state final date of training period: ______________________________

Education:
Degree(s) University or Institution Year(s)

Appointment and academic positions:
If professional status is a or b above, indicate hospital appointment(s) held, including the current one. If c, indicate training position(s) and anticipated appointment(s) during the term of the research grant, if granted.

Dates:
From: To: Institution Department Position

Research experience:
Dates:
From: To: Institution Department Supervisor

Publications:
Indicate total number of scientific publications to date: Abstracts ___________. Full manuscripts ___________.

List all full manuscripts published in past five years. (Use another page if necessary, labelled 4A).
8. Detailed research proposal:
   Provide:
   (i) title of research
   (ii) hypothesis
   (iii) background
   (iv) specific objectives
   (v) methods (including data analysis and potential pitfalls)
   (vi) significance

   A maximum of 5 double-spaced typewritten pages with 2 cm. margins, exclusive of references and figures, using a minimum font size of 12-pt Helvetica or Times Roman, may be added to this page. Label these additional pages as Pages 6A-E.

9. Time commitment for research:
   It is anticipated that the applicant will spend ................ hours per week on this project. Co-applicant(s) will spend ................ hours per week.

10. Research project dates:
    It is anticipated that the proposed project will commence on ................ and be completed by ..........................................................


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The purpose of the Research Meetings is to offer a forum to anesthesiologists and trainees in Anesthesia to present their clinical results as well as their basic experimental investigation. These projects are not only performed to gain the certificate of qualification in the anaesthesiology.

If the scientific project is performed to gain the certificate of qualification in Anesthesia the following guidelines are the standard.

The scientific lecture should be sent by e-mail and to the Secretariat of the Society for Anesthesia and Resuscitation of Belgium (c/o. Research Anesthesie, Universitaire Ziekenhuizen der K.U.Leuven, Herestraat 49, 3000 Leuven) as an abstract (DIN A4). An abstract form is available on the Website of the Society for Anesthesia and Resuscitation of Belgium (http://www.sarb.be), your abstract has to fit on one page.

The abstract form should be accompanied by a fulfilled cover letter for abstract submission. Membership to the Society for Anesthesia and Resuscitation of Belgium (150 EUR. for residents) is required. The accompanying letter should be signed. This letter is also available on the Website.

The abstract will be reviewed by a review committee of the Society for Anesthesia and Resuscitation of Belgium. The abstract will be accepted or refused. The decision will be communicated two weeks before the Research Meeting. This communication will also include the deadline for submitting the presentation in case of acceptance.

The final version of this abstract should be submitted to the secretary of the Society for Anaesthesia and Resuscitation of Belgium and also by e-mail to BVAR.SBAR@uzleuven.be.

The presentation must be given in the English language and include necessarily following parts:

- **INTRODUCTION**: include background information, the problems and / or the purpose of your lecture.
- **METHODS**: specify the used patient population, the treatment or method of anesthesiology, the method of statistic analysis.
- **RESULTS**: the results should be done in full text, also mentioning a table or diagram in case of significant differences.
- **CONCLUSION**: The advanced thesis should endorse the founded results and suggest other connections.
- **REFERENCES**: The conclusion should be followed by 3 KEY-REFERENCES referring the text.

The performance and the discussion should be in English. The time allowed for the oral presentation will be 15 minutes (10 to 12 minutes for presentation and 3 to 5 minutes for discussion or questions).

The Secretary-General proposes to submit the presentations by Power Point only to the following e-mail address (BVAR.SBAR@uzleuven.be). The secretariat will transfer them on a CD or USB memory stick.

Not more than one slide a minute. Do not make too busy slides and choose a colour combination legible text, diagram or table.

Use a pointer to highlight the data you are commenting on.

After the performance and provided that all formalities are fulfilled a proof will be delivered to complete the file to request a homologation on anesthesiology.

All information and forms are available in both national languages.

In any case the abstract and the comments of the Board should be made in ENGLISH.
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