REVIEW ARTICLE

Awareness Under General Anesthesia

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SUMMARY

Background: Awareness while under general anesthesia, and the later recall of what happened during surgery, can be experienced by patients as horrific events that leave lasting mental trauma behind. Patients may have both auditory and tactile perception, potentially accompanied by feelings of helplessness, inability to move, pain, and panic ranging to an acute fear of death. For some patients, the experience of awareness under anesthesia has no sequelae; for others, however, it can lead to the development of post-traumatic stress disorder, consisting of complex psychopathological phenomena such as anxiety, insomnia, nightmares, irritability, and depression possibly leading to suicidality.

Methods: The literature on the subject was selectively reviewed.

Results: In the absence of risk factors awareness phenomena occur in one to two per 1000 operations under general anesthesia (0.1% to 0.2%) and are thus classed as an occasionally occurring critical event. In children, the risk of such phenomena occurring is 8 to 10 times higher. These phenomena are due to an inadequate depth of anesthesia with incomplete unconsciousness. They can be promoted by a number of risk factors that are either patient-related (ASA class III or above, medication abuse), surgery-related (Caesarean section, emergency procedures, surgery at night), or anesthesia-related (anesthesia without benzodiazepines, use of muscle relaxants).

Conclusion: Strategies for avoiding awareness phenomena under anesthesia include the training of staff to know about the problem and, specifically, the use of benzodiazepines, the avoidance of muscle relaxants if possible, and shielding the patient from excessive noise. EEG monitoring is effective but provides no guarantee against awareness. If awareness under anesthesia occurs despite these measures, the patient must be given expert, interdisciplinary treatment as soon after the event as possible in order to minimize its potential sequelae.

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The thought of being awake during their operation despite anesthesia is a worry often expressed by patients about to undergo surgery. These concerns are not entirely unfounded, for despite the most modern of anesthetic technology, awareness under anesthesia is a repeated occurrence. The frequency today has gone down sharply—almost to a tenth of what it was in the 1970s—but for patients without particular risks the rate is nevertheless still estimated at around 1 to 2 cases per 1000 anesthetizations (1–3). It may be assumed that not all anesthetized patients are specifically examined for awareness phenomena, and that therefore more cases occur than are recorded.

The aim of general anesthesia for surgical operations is to eliminate consciousness and pain and to prevent motor (muscle tension, defense movements), autonomic, and cardiovascular reflex responses (rise in blood pressure and heart rate). In most cases awareness occurrences are due to overly light anesthesia (e2). Awareness can occur with or without memory of events during the operation. The former is known as “recall” and represents an explicit memory achievement that can be asked about directly.

In contrast to this are more complex implicit awareness phenomena that lie hidden. Neuropsychological tests are needed to discover traces of perceived sensory stimuli that remain concealed in the subconscious (4).

Awareness and recall can be experienced as traumatizing horror scenarios, resulting in stories that can be picked up by magazines with a popular science orientation (e.g., “Patients Fully Conscious During Surgery” [“Patienten erleben Operation bei vollem Bewusstsein”; 28 July 2008, www.spiegel.de/wissenschaft/]). The suffering and sense of helplessness of those affected is clear from the organized self-help groups, networks, and internet platforms that have sprung up, offering problem orientation, prevention, and management of awareness and its possible sequelae.

The aim of this review is to evaluate awareness during general anesthesia in terms of its incidence, risk, and possible prevention and management strategies. It is based on a selective search of the international literature indexed on Medline on the subject of awareness and disorders caused by awareness, focusing on the past 15 years.

Awareness and its consequences

If consciousness is not adequately depressed, an explicit memory of events during general anesthesia

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BOX 1

Standardized interview to identify awareness occurrences*

- What is the last thing you remember happening before you went to sleep?
- What is the first thing you remember happening on waking?
- Can you remember anything that happened between these two points?
- Did you dream or have any other experiences whilst you were asleep?
- What was the worst thing about your operation?

* Modified from (5);
Interview carried out immediately following anesthesia (recovery room) and, ideally, again within the next few days.

TABLE 1

Perception during intraoperative awareness (3, 7)

	Prevalence (%)
Noises	85–100
Visual sensory impressions	27–46
Fear	78–92
Helplessness	46
Details of operation	64
Paralysis	60–89
Pain	41

may result. This can be explored during the postoperative round by means of structured interviews (5). If there is any suspicion that awareness has occurred, this must be addressed urgently in an interview immediately postoperatively (*Box 1*) and again after a few days. On average only about every third person affected reports the awareness experience immediately on coming round in the recovery room. By far the majority only refer to it very much later, up to 30 days after the event (1, 6, 7). This observation shows how important the postoperative round is altogether, but does also raise the question of when is the right time to investigate this issue.

On the question of the nature of unwanted sensory perceptions during anesthesia, the most frequently reported are perceptions of sound (voices, sounds, noise) (*Table 1*) (3, 6, 7). Since anesthetics influence the physiological hearing function only indirectly, i.e.,

by blocking cognitive signal processing, it seems plausible that when consciousness is incompletely depressed, acoustic signal transductions may reach the brain. Acoustic protection from the general noise level in the operating room (ear protectors, disciplined maintenance of silence in the operating room) or alternative acoustic protection by the playing of music (over headphones) would thus seem to be extremely important measures for awareness prevention (e3).

Opinions vary about the association between acoustic perception and possible suggestion during anesthesia (8). Speculations about therapeutic (positive) suggestion are based on earlier findings of lower complication rates, more rapid recovery, and earlier release from hospital when sound recordings containing positive material about the course of the operation or disease were played during the surgery (9). Subsequent studies succeeded in reproducing comparable results only to a limited extent in small case numbers (e4). The main explanations for this are that important influential factors were not taken adequately into account: for example, telling the patient (during the informed consent process) that acoustic material will be used during the operation can reinforce expectations in one direction or another.

In addition, the patient's underlying mood (e.g., anxiety, stress) and the structure of the acoustic material have a decisive influence. Individual words are more likely to get through to the patient than formulated sentences. Whether information triggers negative, positive or neutral associations also appears to be significant. The formulation in the acoustic offering "You won't feel any pain" is unfavorable because the word "pain", a word with negative associations, is more likely to get through to patient than the formulated sentence as a whole (8). Awareness is more often experienced as less disturbing when the patient is free from pain, whereas if the patient is experiencing intense pain at the time, it draws attention to itself very strongly (3, 7). Memories of being unable to move because of muscle paralyzing drugs are also described as extremely stressful, with feelings of panic and fear of dying (1, 2).

Awareness may be without consequences for the person affected, but it can lead to an acute stress reaction that may be followed by post-traumatic stress disorder (PTSD) (4), both of which have complex manifestations (*Table 2*). Psychopathologically, PTSD involves stress-reactive impaired information processing (7). Unfortunately, knowledge of PTSD is mainly based on single case reports, analyses of data relating to insurance lawsuits (10, e5), and studies of other PTSD patient groups after psychologically traumatic experiences such as torture, war, or abuse (eDSM IV 1994, eGuidelines 1999). Positive effects of psychotherapeutic interventions following the guidelines of the Association of Scientific Medical Societies in Germany (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften* [AWMF]; www.awmf.de) to treat PTSD (ICD-10: F 43.1) have been demonstrated in these patients groups (e6, e7).

Dealing with awareness-associated disorders often goes beyond the normal competence of anesthesiologists and requires referral to colleagues from other specialties. The main issues are early recognition, initiation of the diagnostic process for psychological trauma, and the involvement of psychiatrists, psychologists or psychotherapists in treatment (e5). In the first few weeks after the event, the prognosis for spontaneous –remission is relatively good. If symptoms persist for longer than 4 weeks, there is a risk that they will become chronic; reported rates for the development of persistent neuropsychological disturbances in awareness patients range from 10% or 20% up to 33% (3, 7, 11).

Incidence of awareness and risks

When no particular risk factors are present, awareness occurs with an incidence of 1 to 2 cases per 1000 anesthetics (0.1% to 0.2%) (Table 3) and thus are an occasional critical event. In Germany, an estimated 8 million anesthetics are carried out per year; this would give awareness occurrences in 8000 to 16 000 patients per year, which is a considerable number.

Factors promoting awareness are present as patient-associated risk factors in the form of comorbidities (ASA [American Society of Anesthesiologists] class III or above) and reduced cardiovascular reserve capacity. To protect the cardiovascular system in such cases, overly light anesthesia is often induced (2, 7). Patients with chronic pain conditions who frequently take analgesics or have a drug dependency also often receive inadequate opioid dosages. While some authors estimate that young patients and women have a higher risk of awareness (6, 7), others postulate that the risk of awareness in adults is independent of age and sex (2). Obesity can mean a higher risk of awareness because it makes it difficult to estimate the pharmacokinetics of the anesthetic (e8), although opinions vary on this point (7). Children are a risk group with much higher rates of awareness—eight- to 10-fold higher—(12, e9, e10). From the pharmacokinetic point of view, the reason for this is that the anesthetic is redistributed more rapidly, which results in reduced certainty of an adequate effective plasma concentration (13).

Awareness risks are also often mentioned for particular operations (intervention-related risks). Cesarean sections are especially associated with risk (14). In these cases awareness is the result of choosing too low a dosage for fear of inducing anesthetic overloading and respiratory depression in the fetus. Emergency operations and operations performed at night also appear in the statistics with higher awareness rates (6). Errors of management of anesthesia, such as technical errors by the anesthetist and/or behavioral errors due to overwork, can also be causes of awareness under anesthetic.

Finally, awareness has also been repeatedly associated with particular anesthetic drugs (drug-related risks). Particular attention has been drawn to muscle relaxants when consciousness has not been adequately depressed during surgery. Reports of negative

TABLE 2

Clinical symptoms of post-traumatic stress disorder (7)

Key symptoms	Examples
Reliving the trauma	Agonizing recall of the trauma, flashbacks, nightmares, exaggerated emotional or physical reaction on exposure to cues
Avoidance symptoms	Avoidance of activities, places, thoughts, feelings, and conversations related to the trauma
Emotional numbness	General lack of interest, detachment or estrangement from others, restricted range of affect
Hyperarousal	Sleep disturbances, irritability or outbursts of anger, difficulty concentrating, excessive alertness, exaggerated startle reaction

perceptions range from nightmare agony to feelings of helplessness and powerlessness, since the patients could not draw attention to themselves because their muscle function had been neutralized. In comparative studies muscle relaxants represent a risk factor with markedly higher awareness rates (almost twice as high: 0.18% versus 0.1%) (1, 2). However, muscle relaxants are often unavoidable during general anesthesia, as they are the only means by which movements and defensive tension can be prevented, thus allowing optimal conditions for surgery.

For years there has been debate about protection from awareness when total intravenous anesthesia (TIVA, e.g., with propofol) is used, as against inhalation anesthetics. Differences at the level of molecular mechanisms of effect or regional efficacy (cerebral cortex versus brainstem) are claimed for the anesthetics mentioned (15). Whether these differences allow differences in risks of awareness to be inferred has not yet been proved. At present, the studies seem more to indicate that awareness in the individual case is the result of under-dosage, and is thus subject more to quantitative than to qualitative criteria (6, 7).

According to the present state of knowledge, benzodiazepines, because of their amnesia-inducing effects, are very valuable in preventing awareness and recall, such that failure to give benzodiazepines significantly increases the risk of awareness phenomena (6, 7). However, the reverse does not hold: giving benzodiazepines does not provide absolutely reliable protection. Since awareness occurs unnoticed and unpredictably, ascertaining what the right moment might be to give benzodiazepines aimed at preventing awareness is virtually impossible. In addition, the amnesia-inducing effect of these substances is dose-dependent, and therefore cannot always be maintained at a steady level during long operations (16).

For many decades nitrous oxide (laughing gas) was valued in the clinical practice of inhalation anesthesia because of its analgesic potency and its induction of retrograde amnesia with extremely short induction and

TABLE 3

Incidence (%) of awareness under anesthesia with explicit memory (recall)

Author	Year	Incidence (%)	No. of cases
Sandin (19)	2000	0.18/0.1* ¹	18/11 785
Sebel (2)	2004	0.13	25/19 575
Myles (21)	2004	0.17–0.91	13/2463 2/1225 (EEG) 11/1238
Ekman (20)	2004	0.04	2/4945
Pollard (25)	2007	0.007	6/87 361
Avidan (22)	2008	0.21	4/1941 2/967 (EEG) 2/974 (MAC>0.7)
Errando (6)	2008	1.0/0.8* ²	39/3921
Samuelsson (3)	2008	0.14	10/6991
Paech (e12)	2008	0.26	2/763
Xu (e13)	2009	0.41	46/11 101

Awareness and recall are given as case and patient group numbers obtained in the studies cited by means of standardized interviews (5); EEG, electroencephalographic monitoring; MAC, minimal alveolar concentration, monitoring of end-tidal anesthetic gas concentration;

*¹reanalysis after exclusion of muscle relaxants;

*²reanalysis after exclusion of patients at risk for awareness (see Figure)

recovery times. Today, nitrous oxide is falling out of use, for environmental reasons. Contrary to initial fears, literature searches show that the presence or absence of nitrous oxide seems to have no influence on the incidence of awareness phenomena (7).

Optimization of anesthesia depth only possible to a limited extent

General anesthesia consists of the working together of four different components (blockades) (17) (Figure):

- Mental block (hypnosis, blocking of perception, consciousness, and memory)
- Sensory block (analgesia, blocking of pain perception)
- Motor block (blocking of muscular tension and stimulus-triggered motor responses)
- Reflex block (blocking of autonomic nervous and cardiovascular reactivity, prevention of blood pressure spikes and/or cardiac arrhythmias).

Exactly how the components memory function, loss of consciousness, pain perception, and sensory and autonomic blockade work together and determine the overall level of anesthesia, however, is not understood in detail (10). A dilemma exists, because there is no generally accepted unit of measurement for general anesthesia, and there are no reference values. In clinical practice, the dosage of anesthetics is chosen on the

basis of experience from pharmacological studies and surrogate parameters such as blood pressure and heart rate.

However, blood pressure and heart rate are as little suited to acting as a guide to adequate depression of consciousness as are lacrimation, sweating, or motor reactions. The functional condition of the real target organ, the brain, can only be judged indirectly and hence inadequately. Only in a very few cases of awareness have the patients shown clinical signs of insufficient depth of anesthesia (7). The phenomenon of absence of physiological reactions (e.g., increased blood pressure, tachycardia, sweating) is often promoted by antihypertensive drugs (beta blockers). An analysis of compensation claims after awareness occurrences in the USA shows the limited value of surrogate markers usually used to estimate the quality of anesthesia. A rise in blood pressure was seen in only 15% of cases, increased heart rate in only 7%, and motor movements in only 2% (18).

Against this background, for years the attempt has been pursued to image dose-dependent effects of anesthetic on the functional condition of the brain, the target organ, using electroencephalography (EEG). Commercially available EEG systems today allow computer-aided analysis of complex electrical signals in the brain, and by an automatic index calculation offers the advantage of individual estimation of the depth of sedation or anesthesia (19). However, EEG monitoring—like all measurement values—must always be interpreted in the context of the other clinical signs of anesthesia depth (blood pressure, pulse, sweat secretion, movement).

To what extent EEG when used in a targeted way can help to prevent awareness is a matter of debate. One study in which 4945 anesthetized patients with EEG monitoring were compared to a historical control group without EEG monitoring showed a five-fold reduction of the risk of awareness (20). Another study of 2500 patients even postulated an 82% risk reduction with EEG monitoring (21). Contrasting with these, however, was the demonstration that systematic maintenance of suitably high anesthetic gas concentrations (0.7 to 1.3 MAC) were at least as effective against awareness as EEG monitoring (22). In addition, it has not yet been demonstrated that anesthetic EEG monitoring allows sufficiently accurate distinctions when judging the important border zones between loss and recovery of consciousness (perception) (19). Finally, many studies do not include enough patients to allow proper statistical proof. Assuming a current incidence of 0.1% to 0.2%, effective prevention of awareness by EEG monitoring would dictate an impracticable prospective study design with at least 20 000 to 50 000 patients to fulfill statistical requirements (23).

Awareness occurrences can be caused by technical errors by the anesthetist. Monitoring of effective concentrations has proved valuable as a way to identify such treatment errors. For inhalation anesthesia techniques, this is done according to anesthesiological

FIGURE

Ideal depth of anesthesia presented as a structure made up of anesthesia components (17). The depth of anesthesia is subject to an antagonism (left) between the dose-dependent anesthetic effect and the surgical pain stimulus. An overly light anesthesia is associated with an increased risk (right) of awareness events (awareness, recall), which can induce a stress disorder (PTSD) as a complication of inadequate anesthesia. Risks for awareness and recall (right) may be patient-related, intervention-related, or anesthesia-related.

standards by measuring the gas concentrations in the ventilation system and can be used as an alarm system (24). Threshold value monitoring of inhalation anesthetics has, as described above, shown a comparable reduction of awareness risks to EEG monitoring (22). For intravenous anesthesia techniques, on the other hand, in practice a lack of effective concentration monitoring has to be accepted. Effective concentration (plasma concentration) monitoring cannot be measured directly in the patient, but can only be calculated by surrogate markers, ideally using special computer-aided pump systems based on pharmacokinetic models. Simultaneous EEG monitoring gives a rough picture of the depth of narcosis and thus protects the patient better from technical errors.

Recommendations for clinical practice

Anesthesiological prevention strategies can help to prevent and to minimize the risk of awareness occurrences (Box 2). In addition, in one study continuous personnel training together with close monitoring and the implementation of quality criteria have led to exceptionally low awareness rates (Table 3) (25). Furthermore, monitoring of anesthetic gas concentrations and EEG and consistent discipline in the operating room with acoustic protection for the anesthetized patient can prevent awareness. This means that avoiding loud noises and conversations and/or giving the patient earphones with or without music (13) are key parts of awareness prevention. An essential practical point for behavior in the operating room is not to allow any negative suggestive influence to act on the anesthetized patient through a negative choice of words, e.g., “pain,

cancer, inoperable, pointless.” Gray areas in the threshold zones of perception can at present not be monitored adequately (8, 19, e11).

Summary

Modern anesthesia techniques ensure an adequate depth of narcosis with appropriate blockade of the senses (touch, hearing), so that as a rule there need be no fear of awareness and its sequelae. A successful problem-oriented approach to undesired awareness occurrences consists of the following preventive measures:

- Training of personnel
- Elimination of technical errors in the administration of anesthesia
- Maintaining quiet in the operating room, or giving the patient acoustic protection
- Premedication with benzodiazepines.

Awareness or recall phenomena, with an incidence currently reported at 0.1% to 0.2%, can in some cases lead to long-term neuropsychological disorders, in the form of acute stress reaction or, more seriously, post-traumatic stress disorder. To fail to take a patient’s subjective complaints seriously, or to ignore them altogether, is to commit a treatment error. With early expert treatment, the prognosis for awareness-associated disorders is good; persistent symptoms, by contrast, will tend to become chronic. A basic knowledge of the awareness problem, together with a clear understanding of competent procedure (Box 3), is a requirement in all medical fields in which consciousness is partially or completely depressed for diagnostic or operative interventions.

BOX 2

Strategies to prevent awareness under anesthesia

- Training for the anesthesia personnel (training of vigilance; scientific discussion of the awareness problem)
- Patient information during the premedication interview
- Preoperative risk assessment for awareness (patient evaluation)
- Adequate premedication, benzodiazepines
- No unnecessary use of muscle relaxants
- Provide extra monitoring (EEG) for risk patients
- Avoid technical errors in the administration of anesthesia
- Acoustic protection for the patient; quiet or silence in the operating room; avoid negative comments (negative suggestions)
- Provide music via headphones
- Postoperative evaluation of the patient (standardized interview).
- Have a plan ready to deal with awareness, and work through it deliberately in a targeted manner: e.g., if it is suspected that the patient is aware, in this situation speak to the patient calmly

BOX 3

How to manage patients who have experienced awareness

- Take complaints about awareness seriously and discuss them with the patient
- Advise the patient to contact the anesthetist involved
- Give a general description of the symptoms of disorders associated with awareness (post-traumatic stress disorder, PTSD):
 - Anxiety states
 - Sleeplessness
 - Nightmares
 - Irritability
 - Depression, to the extent of suicidal thoughts
- Explain the seriousness of PTSD
- Explain that early treatment of PTSD gives quite a good prognosis, but that persistent symptoms run the risk of becoming chronic
- Offer professional help: psychologist, psychiatrist, psychotherapist
- Possibly contact the relevant medical societies for information on regional support

Conflict of interest statement

PD Dr. Rundshagen has received lecture fees from Abbott GmbH. Professor Bischoff declares that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

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KEY MESSAGES

- Awareness during anesthesia with recall occurs in adults at a rate of 1 to 2 cases per 1000 anesthetizations.
- Particular risks may relate to
 - The patients (ASA classification $\geq$ III, medication misuse)
 - The intervention, or the circumstances of the intervention (cesarean section, emergency surgery, surgery out of hours)
 - The anesthesia (not using benzodiazepines, using muscle relaxants).
- Children are a separate risk group in which rates of awareness are 8- to 10-fold higher.
- Awareness may be without sequelae, or it may result in post-traumatic stress disorder as a complication of anesthesia.
- Vigilance, training of personnel, careful attention to risk factors, and expert treatment where awareness has occurred can reduce the incidence and any negative sequelae of awareness during anesthesia.

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