

## Anesthesia recommendations for **Bullous Pemphigoid**

**Disease name:** Bullous Pemphigoid

**ICD 10:** L12.0

**ORPHAcode:** 703

**Synonyms:** Bullous pemphigoid (BP), Autoimmune subepidermal blistering disease, Chronic autoimmune blistering disorder

**Brief disease summary:** Bullous Pemphigoid (BP) is an acquired, chronic, autoimmune, subepidermal blistering disorder characterized by the formation of tense cutaneous bullae and, in some cases, mucosal involvement. It results from circulating autoantibodies directed against structural proteins of the basement membrane zone (BMZ), primarily BP180 (type XVII collagen) and BP230 [1]. The quoted incidence is 8.2% per million people, with predominant occurrence in individuals over 60 years of age [2]. Childhood BP is rare but described [3].

Mucous membrane pemphigoid (MMP), or cicatricial pemphigoid, is a variant predominantly affecting mucosal surfaces and resulting in scarring [4]. The condition is rare, with an estimated incidence of approximately 1 per 10 million. Commonly affected sites include the oropharynx, conjunctiva, larynx, esophagus, genitalia, and anus. Recurrent blistering may lead to strictures, dysphagia, visual impairment, and airway compromise [5]. The disease typically follows a relapsing-remitting course. Diagnosis is based on clinical features, histopathology, and immunofluorescence studies [6]. Fatal airway-predominant cases have been described despite aggressive immunosuppression [7].

Associations with other autoimmune blistering diseases (pemphigus, pemphigoid, epidermolysis bullosa acquisita, dermatitis herpetiformis, linear IgA disease), multiple autoimmune syndromes, and acquired hemophilia A have been reported [8,9].

More recently, cases temporally associated with SARS-CoV-2 vaccination have been described [10].

Oral and topical steroids are the standard first-line treatment. Two recent systematic reviews evaluated studies related to current and new treatments [2,11]. Because of multiorgan involvement, a multidisciplinary approach is needed involving dermatologists, ENT specialists and ophthalmologists in diagnosing and treating the disease [5].

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Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this recommendation.



Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

Translations may not always reflect the most recent updates of the English version.



**Find more information on the disease, its centers of reference and patient organizations on Orphanet: [www.orpha.net](http://www.orpha.net)**

## Emergency information

<b>A</b>	<b>AIRWAY / ANESTHETIC TECHNIQUE</b>	<p><u>Skin and mucous membrane fragility</u>: Risk of bleeding or airway obstruction due to oral or pharyngeal bullae.</p> <p><u>Airway manipulation</u>: Avoid adhesive tapes, tight masks, or rough laryngoscopy. Use smaller-sized, well-lubricated oral airways and tracheal tubes.</p> <p><u>Tracheal intubation</u>: Gentle laryngoscopy; use smaller-sized ETT; prefer oral intubation to nasal.</p> <p><u>Suction</u>: Prepare suction in case bullae rupture in mouth. Catheters should be well lubricated and used with low suction pressure.</p> <p><u>Anesthesia technique</u>: Regional anesthesia may be preferred if feasible to avoid airway manipulation. Check skin integrity at injection sites and avoid puncturing bullous or infected areas.</p> <p><u>Temperature management</u>: Avoid overheating and sweating, which may worsen skin breakdown.</p>
<b>B</b>	<b>BLOOD PRODUCTS (COAGULATION)</b>	<p>BP itself does not usually cause coagulopathy, but patients are often elderly and may be on systemic steroids, immunosuppressants (azathioprine, methotrexate, mycophenolate) → may cause cytopenias, delayed wound healing, or increased infection risk. No special blood product storage or coagulation preparations needed specifically for BP.</p>
<b>C</b>	<b>CIRCULATION</b>	<p>BP does not inherently affect cardiac structure. Patients tend to be older and may have age-related comorbidities (hypertension, coronary artery disease, heart failure).</p> <p>Cardiovascular effects of medications: High-dose steroids may contribute to fluid retention, hypertension, arrhythmias, or electrolyte disorders.</p> <p>Infection/sepsis risk if skin lesions are widespread or secondarily infected → consider hemodynamic instability in advanced cases.</p>
<b>D</b>	<b>DRUGS</b>	<p>Use NSAIDs cautiously as they may worsen skin integrity or renal function in elderly patients.</p> <p><u>Steroid therapy considerations</u>: Many BP patients are on chronic steroids → may require stress-dose hydrocortisone perioperatively for moderate-major surgeries.</p> <p><u>Immunosuppressants</u>: Watch for drug interactions (e.g., azathioprine with allopurinol).</p>

		<p>Increased infection risk → prophylactic measures may need reinforcement.</p> <p><u>Premedication</u>: Consider anxiolytics but avoid overly sedating agents if airway mucosal involvement raises aspiration risk.</p> <p><u>Malignant hyperthermia</u> (MH): no increased risk.</p>
<b>E</b>	<b>EQUIPMENT</b>	<p><u>Monitoring equipment</u>: Non-adhesive ECG electrodes, soft wraps for NIBP cuffs.</p> <p>Padding for pressure points due to fragile skin.</p> <p><u>Transport</u>: Use draw sheets and low-shear surfaces for shifting patients; avoid friction, shearing forces.</p> <p><u>Positioning</u>: Careful padding and use of non-adhesive materials to avoid skin damage.</p>

### Additional disease information

Pathophysiology: BP results in circulating autoantibodies which activate complement and initiate an inflammatory cascade with recruitment of eosinophils and neutrophils, leading to dermo-epidermal separation and blister formation. Recent evidence points towards pathways independent of complement which may cause tissue damage [12]. Histopathology demonstrates a subepidermal blister with eosinophilic infiltrates, and direct immunofluorescence reveals linear IgG and/or C3 deposition along the BMZ. A rare and underrecognized manifestation is Pemphigoid of the Pulmonary System (POPS), involving the trachea and bronchi. POPS is characterized by blistering, erosive inflammation and progressive scarring that may cause irreversible airway stenosis and life-threatening obstruction. Unlike classic BP, POPS often presents in younger patients, frequently before 40 years of age. Symptoms may mimic asthma or COPD, leading to delayed diagnosis. Reported mortality approaches 45% due to respiratory failure [13].

Associations: BP has also been associated with neurological disease, particularly dementia, Parkinson disease and cerebrovascular disease, possibly due to immunologic cross-reactivity involving neuronal BP230 isoforms [14].

The association with malignancy remains controversial; some Asian studies report increased incidence, whereas Western data are inconsistent [15,16].

BP predominantly affects elderly patients who frequently have multiple other comorbidities. Frailty, reduced functional reserve, malnutrition, and secondary skin infections may further increase perioperative risk.

## Typical surgery and procedures

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The patient can present for various types of surgery, both elective and emergency. Surgery in these patients includes restoration of function where severe deformity is present, e.g., laryngeal and esophageal strictures and ophthalmological conditions. A patient may present as an emergency, e.g., for laparotomy (due to gastro-duodenal ulceration), or for Cesarean section, management of acute airway obstruction secondary to cicatricial laryngeal lesions, orthopedic procedures, or other routine elective procedures [17,18].

Once laryngeal stenosis occurs, repeated endoscopic laser excision of scar tissue may be needed to maintain an adequate airway [19].

## Type of anesthesia

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Patients with BP may present significant perioperative challenges due to skin fragility, chronic immunosuppressive therapy, and associated comorbidities. Mechanical trauma from adhesive tapes, monitoring devices, blood pressure cuffs, facemasks, airway instrumentation, patient positioning, or transfer may precipitate new blister formation and skin erosions (Koebner phenomenon) [21]. Careful padding and avoidance of excessive friction or adhesive use are therefore recommended.

Ketamine-based monitored anesthesia care with patient breathing spontaneously has been used in several BP patients. It provides rapid induction, preservation of airway reflexes and minimal trauma to the face and upper airway.

Despite concern about airway trauma, general anesthesia with tracheal intubation can be used if considered safer for the patient [20,21]. Tracheal intubation in a similar condition, epidermolysis bullosa dystrophica, has been described in 131 patients without intraoperative or postoperative airway obstruction [22].

Mucosal involvement, although less frequent than in pemphigus vulgaris, may affect the oral cavity, pharynx, larynx, or upper airway and can potentially complicate airway management. Airway instrumentation should be performed gently to minimize mucosal trauma and bleeding.

Whenever general anesthesia with a secured airway (endotracheal intubation or a supraglottic airway) is required, protective measures must be ensured, e.g., a tracheal tube should be secured with a soft cloth bandage rather than with adhesive tape. In patients with documented oral lesions, inserting a tracheal tube is a safer technique compared to a laryngeal mask airway because of the risk of bleeding from intraoral lesions [23].

Regional anesthesia can be used in these patients, but its safety is debated. There is no high-quality evidence that neuraxial anesthesia triggers BP flares; clinical judgment should guide decision-making. Nevertheless, regional techniques have been successfully employed, as they avoid general anesthesia and airway manipulation [24,25].

However, care should be taken to avoid skin trauma at puncture sites and during fixation of catheters or dressings. Use ultrasound guidance to reduce needle passes and minimize local tissue trauma. When securing an epidural or peripheral nerve block catheter, minimize skin contact and avoid large adhesive surfaces, rather, use suture fixation or a gauze wrap instead.

Neuraxial anesthesia has been routinely used for Cesarean delivery but avoid placing needles through active bullae [26,27]. Neuraxial opioids should be avoided as they are associated with pruritus, especially in cases involving morphine [21].

## **Necessary additional preoperative testing (beside standard care)**

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Patients receiving high-dose immunosuppression require targeted preoperative assessment beyond routine testing. A complete blood count is important for those on myelosuppressive agents such as corticosteroids, azathioprine, rituximab, or dupilumab. Serum electrolytes should be checked, with particular attention to potassium often depleted through skin losses and sodium, which may be deranged due to blister-related fluid loss or dehydration. Hepatic function tests are indicated for patients on immunosuppressive drugs. Serum protein levels, including albumin, should be measured in patients with mucosal or oral lesions who are at risk of malnutrition. Vaccination history should also be reviewed, and when possible, vaccines should be administered prior to rituximab therapy to optimize immune response.

For patients with airway or respiratory involvement, additional evaluation may be necessary. When upper airway involvement is suspected, further airway assessment (e.g., flexible laryngoscopy) and, where appropriate, pulmonary function testing including spirometry may assist anesthetic planning [28].

Medication-specific considerations also guide perioperative decision making. Rituximab causes prolonged B-cell depletion; therefore, elective procedures should ideally be timed either before initiation or after immune reconstitution, with increased vigilance for infection and impaired vaccine responses. Dupilumab and omalizumab are generally less immunosuppressive and have demonstrated acceptable perioperative safety, making routine withholding unnecessary, though decisions should remain individualized. Biologics with steroid-sparing effects may reduce steroid-related risk but can also mask infection, warranting a low threshold for clinical surveillance [3,29].

Finally, preoperative optimization should include multidisciplinary input from dermatology, ophthalmology, ENT, and anesthesia, treatment of any active skin infections, and ensuring adequate nutritional status, especially protein and albumin levels [6].

## **Particular preparation for airway management**

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Airway involvement in these patients can be significant and requires careful preoperative assessment. Tracheobronchial disease may present with cough and dyspnea, while vesicular eruptions and subsequent scarring can narrow or even occlude the upper airway, resulting in stridor [30].

Preexisting oropharyngeal bullae may limit mouth opening, and narrowing at the laryngeal inlet may contribute to difficult intubation. Airway manipulation carries a risk of hemorrhage, and instrumentation such as laryngoscopy or tracheal intubation can induce new bullae formation, further complicating airway management.

Airway management must be individualized, guided by mucosal involvement, degree of scarring, and anticipated difficulty. In select cases, awake fiberoptic intubation or even a planned surgical airway may be safer. Minimizing shear and friction during laryngoscopy is critical. Oral intubation is preferred over the nasal route, and oral airways should be avoided to prevent mucosal trauma. Prior to mask ventilation, applying 1% hydrocortisone cream and Vaseline-soaked gauze can reduce the risk of bullae formation from face mask contact [31].

When intubation is required, a smaller-than-usual endotracheal tube should be chosen, secured with a soft cloth bandage rather than adhesive tape [32]. Suction catheters should be well lubricated and used at low suction pressures.

Additional supportive strategies may assist in optimizing safety. Humidified High-Flow Nasal Oxygen (HFNO) can provide effective preoxygenation and apneic oxygenation in patients with facial lesions who cannot tolerate mask ventilation [8].

In rare cases of severe upper-airway stenosis, specialized ventilation techniques such as jet ventilation have been reported, though these require expert teams and carry inherent risks [33]. When upper-airway access is severely compromised by ulceration, adhesions, mucosal deformity, epiglottic involvement, or vocal-cord webbing, tracheostomy under local anesthesia may be necessary [34].

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### **Particular preparation for transfusion or administration of blood products**

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In BP, antibodies are targeted against BP180 [5] BP230 [35]. Plasmapheresis can be a useful adjunct in refractory or severe BP by removing pathogenic autoantibodies and inflammatory mediators [36]. However, it is not considered standard first-line therapy because the available evidence is limited and heterogeneous. For instance, a recent case report described a patient with recalcitrant BP who exhibited dramatic improvement after therapeutic plasma exchange (TPE) [37]. When planning transfusions in BP patients undergoing plasmapheresis, clinicians should account for volume shifts and the removal of plasma proteins (e.g., immunoglobulins), though there is no need for disease-specific modifications to blood products beyond standard protocols [35].

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### **Particular preparation for anticoagulation**

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Anticoagulation in patients with BP should follow standard clinical guidelines; however, given the increased risk of venous thromboembolism, individual risk assessment is essential and appropriate thromboprophylaxis should be instituted when indicated [38,39].

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### **Particular precautions for positioning, transportation and mobilization**

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To avoid friction and pressure-induced trauma, careful positioning should be done. It is preferable to let patients position themselves on the operating room table as it will reduce pressure and friction-induced trauma. Sheets should be free of creases. Gauze pieces soaked with hydrocortisone cream and Vaseline may be applied to pressure areas like heels and elbows [20].

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### **Interactions of chronic disease and anesthesia medications**

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BP onset has no direct interaction with anesthetic drugs but may be associated with the following adjuvant drugs that are likely to be used during the perioperative period. These are furosemide, ibuprofen, ACE inhibitors, metronidazole, spironolactone and some antibiotics (e.g., ampicillin, cephalosporins) [40]. BP is associated with an increased risk of myocardial infarction, cerebrovascular events, peripheral vascular disease, pulmonary embolism, and cardiovascular mortality. Appropriate prevention strategies should be considered [41].

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## Anesthetic procedure

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Many patients receive prolonged systemic corticosteroid therapy and/or steroid-sparing immunosuppressive agents such as azathioprine, mycophenolate mofetil, methotrexate, rituximab, or doxycycline. These therapies may predispose patients to impaired wound healing, infection, adrenal suppression, osteoporosis, diabetes mellitus, hypertension, and electrolyte disturbances [16], all of which may influence perioperative management.

Additional anesthetic considerations in BP include the need for a preoperative corticosteroid loading dose in patients receiving chronic steroid therapy, given the risk of adrenal suppression. Because the skin is extremely fragile, taping should be avoided, including for eye protection, and alternative non-adhesive methods should be used. Peripheral venous access may be difficult due to widespread lesions. In such cases, central venous cannulation may be required, and the catheter should ideally be secured with skin stitches rather than adhesive dressings. Local infiltration anesthesia is generally contraindicated because it can trigger skin sloughing or new bullae formation. For neuraxial anesthesia, needle insertion should be performed only through unaffected skin whenever possible.

During difficult intubation, it is preferable to avoid muscle relaxants, and if available, a mixture of oxygen with a low-density gas such as helium (e.g., 20% O<sub>2</sub> / 80% helium) may help reduce airflow turbulence. In spontaneously breathing patients, a clear polyethylene head hood can be useful to minimize contact trauma while allowing oxygen delivery. Standard anesthetic agents such as opioids, thiopental sodium, and propofol may be used safely, as no BP-specific complications have been reported.

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## Particular or additional monitoring

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Care should be taken to avoid pressure and friction during the placement of monitoring devices.

The electrode gel reduces electrical impedance at the skin-electrode interface, thereby improving ECG signal quality. The biocompatible adhesive provides gentle adhesion and allows atraumatic removal [42].

Intravenous lines and arterial cannulas should be fixed with sutures and gauze bandages. Taping should be avoided. Blood pressure cuffs should be well padded. Some authors prefer direct measurement of blood pressure in preference to non-invasive blood pressure.

Avoid unnecessary suctioning tubes and temperature probe insertion in nasal and oral cavities.

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## Possible complications

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Rough handling of patients with BP can lead to the formation of new bullae and bleeding from exposed raw areas. Mechanical contact of the tracheal tube balloon may cause bullae formation within the trachea [43]. Additionally, the use of high-pressure jet ventilation in patients with narrowed laryngeal orifices can result in subcutaneous emphysema [33].

Traumatized skin in BP patients often develops lesions in previously unaffected areas, a phenomenon known as the Koebner phenomenon [21]. Postoperative delayed wound healing is common, making close coordination with the dermatology team essential to ensure timely resumption of immunosuppressive therapy.

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### **Postoperative care**

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Avoid blind pharyngeal suctioning at the end of the procedure.

Extubation should be gentle and the patient should be observed for postoperative stridor, new bullae formation and any difficulty in breathing.

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### **Disease-related acute problems and effect on anesthesia and recovery**

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Emergency situations may occur if cicatricial pemphigoid involves the oral cavity, epiglottis and vocal cords. Patients may present with stridor and dyspnea due to narrowing of the laryngeal inlet. Obstruction is more obvious during inspiration, as the walls of the glottis are drawn together due to negative intratracheal pressure. Tracheostomy may be needed in advance in some cases.

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### **Ambulatory anesthesia**

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Ambulatory anesthesia should only be done in patients with BP if mucous membranes are not involved in the disease process.

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### **Obstetrical anesthesia**

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Pregnancy can trigger or exacerbate autoimmune blistering disease, particularly Pemphigoid gestationis, a pregnancy-associated variant of BP [44]. Disease activity may worsen during the first and second trimesters, while some improvement may occur in the third trimester, possibly due to increased endogenous corticosteroid production. There is a risk of sepsis or skin infection at sites of local anesthetic injection; therefore, neuraxial techniques should be performed through areas free of active lesions, which is considered safe for lumbar puncture.

Case reports have been published which show that single-shot spinal anesthesia is safe for Cesarean section. However, general anesthesia is not contraindicated if the oral mucosa is not involved with the disease [26,27].

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