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Consensus Statement for the Management and Treatment of Port-Wine
Birthmarks in Sturge-Weber Syndrome

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IMPORTANCE Sturge-Weber syndrome (SWS) is a neurocutaneous syndrome involving the skin, brain,
and eyes. Consensus recommendations for management are lacking.

OBJECTIVE To consolidate the current literature with expert opinion to make recommendations that will
guide treatment and referral for patients with port-wine birthmarks (PWBs).

EVIDENCE REVIEW In this consensus statement, 12 nationally peer-recognized experts in dermatology
with experience treating patients with SWS were assembled. Key topics and questions were formulated
for each group and included risk stratification, optimum treatment strategies, and recommendations
regarding light-based therapies. A systematic PubMed search was performed of English-language
articles published between December 1, 2008, and December 1, 2018, as well as other pertinent studies
identified by the expert panel. Clinical practice guidelines were recommended.

FINDINGS Treatment of PWBs is indicated to minimize the psychosocial impact and diminish nodularity
and potentially tissue hypertrophy. Better outcomes may be attained if treatments are started at an
earlier age. In the US, pulsed dye laser is the standard for all PWBs regardless of the lesion size, location,
or color. When performed by experienced physicians, laser treatment can be safe for patients of all
ages. The choice of using general anesthesia in young patients is a complex decision that must be
considered on a case-by-case basis.

CONCLUSIONS AND RELEVANCE These recommendations are intended to help guide clinical practice
and decision-making for patients with SWS and those with isolated PWBs and may improve patient
outcomes.

There is a need for a consensus statement regarding an approach to managing Sturge-Weber
syndrome (SWS). In 2018, the Sturge-Weber Foundation published a comprehensive review of research
needs regarding the pathogenesis, clinical features, and treatment options for SWS.1 Our consensus
aims to provide clinical practice guidelines for the care of the major dermatologic feature of SWS: the
port-wine birthmark (PWB).

Sturge-Weber syndrome is a sporadic, congenital, neurocutaneous syndrome involving the skin,
brain, and eyes, with an estimated prevalence of 1 in 20 000 to 1 in 50 000 live births.2 It is caused by a
somatic mosaic mutation in the GNAQ gene located on chromosome 9q21, affecting neural crest cells
emanating from the forebrain region and resulting in vascular abnormalities of the cutaneous forehead,
cerebral cortex, and eye.3,4 Patients with SWS typically have at least 2 of the following 3 components:
facial PWB, vascular malformation in the brain, and vascular malformation in the eye. However, clinical
manifestations vary, and workup and treatment are guided by the extent of these manifestations.
The goals of this consensus statement are to review the literature and provide an approach to risk stratification and evaluation of PWBs, offer guidance on diagnostic workup for patients with suspected or newly diagnosed SWS, and assess current treatment options for PWBs in light of the patient’s age and condition severity. The treatment recommendations are currently applicable to all patients with a PWB.

Methods

Twelve national experts in dermatology were consulted to develop a consensus statement on the management and treatment of cutaneous manifestations of SWS as part of a larger consensus statement. The panel was created from a list of experts provided by the Sturge-Weber Foundation who had significant experience in treating patients with SWS and patients with PWBs who agreed to participate. Three key needs were identified: (1) risk stratification and evaluation of PWBs, (2) optimum treatment strategies for PWBs, and (3) specific recommendations regarding light-based therapies. The expert group was divided into 4 subgroups that formulated questions to address each topic. An extensive literature review was performed using PubMed for English-language articles published between December 1, 2008, and December 1, 2018, an arbitrarily selected date range, to explore articles within the past 10 years. Articles before 2008 or after 2018 were added by the expert panel based on importance. Search terms included Sturge-Weber syndrome plus the following: clinical presentation, pathogenesis, risk prediction, port-wine birthmark or port-winestain, diagnostic workup, triage, management, treatment, laser therapy, light-based therapy or treatment, photodynamic therapy, infantile hemangioma, and nevus simplex. A total of 112 articles were identified; 76 were relevant to dermatology. This number was narrowed to 41 articles based on abstract or full-text review and supplemented with 10 additional references identified by the expert panel. Publications were assigned to questions for each key topic and distributed to each subgroup to develop responses and key guidelines, which were consolidated into 10 key topics (Box). One of us (S.S.) drafted the manuscript and presented it to all 4 subgroups for electronic discussion and modification. The drafts were circulated to the full expert panel and edited multiple times until each participant gave final approval.

Box. Key Topics for Dermatologic Management and Treatment in SWS

1. The characteristic skin manifestation of Sturge-Weber syndrome (SWS) is a port-wine birthmark (PWB), a congenital vascular malformation composed of malformed capillary-like vessels that is present at birth as a typically unilateral, bilateral, or centrally located, well-demarcated, pink to red patch on the face.
2. The best timing for evaluation of a facial PWB is at birth.
3. There are a number of factors that should be considered regarding treatment, including minimizing the psychosocial impact, diminishing nodularity and, potentially, tissue hypertrophy, and financial considerations for the family.
4. In the US, light-based devices are the standard of care for PWB treatments, and pulsed dye laser is considered first line.
5. Light-based devices are still first-line treatment for PWBs in patients with skin of color; however, higher rates of adverse effects may be seen than in lighter-skinned patients, mainly dyspigmentation and atrophic scarring. Moderate energy densities, less pulse overlap, and increased cooling are recommended in the treatment of patients with darker skin types to minimize risks.
6. There are a number of alternative therapies that have been investigated for PWBs that do not respond to traditional laser and light-based treatments.
7. The interval between laser treatments is dependent on a multitude of factors. No optimal interval has been established by scientific evaluation; thus, treatment interval must be tailored to each patient.
8. Greater rates of lightening and possible prevention of future darkening and hypertrophy may be attained if treatments are started at an earlier age. The main goal of treatment is to ensure healthy and adequate psychosocial development and minimize the stigma associated with PWBs.
9. Pulsed dye laser in young patients is a safe treatment option with a low incidence of permanent complications when performed by an experienced laser surgeon.
10. Laser treatments can be associated with significant discomfort. The choice of using general anesthesia is complex, and informed decision-making should be shared with the patients and their parents/guardians.

**Key Points**

**Question** What are clinical practice guidelines for treatment and management of port-wine birthmarks, including those associated with Sturge-Weber syndrome?

**Findings** In this consensus statement, 10 key recommendations for treatment of port-wine birthmarks were formulated. These recommendations address risk stratification, optimum treatment strategies, and recommendations regarding light-based therapies.

**Meaning** The recommendations provided in this statement may help guide clinical decision-making for these patients.

**Dermatologic Factors**

Key topic 1: The characteristic skin manifestation of SWS is a PWB, a congenital vascular malformation composed of malformed capillary-like vessels that is present at birth as a typically unilateral, bilateral, or centrally located, well-demarcated, pink to red patch on the face.

The best predictor for SWS is a facial PWB involving any part of the forehead, including the upper eyelid and the midline frontonasal prominence (Figure, A). The distribution appears to follow the patterns of embryologic vasculature, challenging the long-held belief of a trigeminal nerve cause. Not all patients with PWBs will develop SWS; however, certain distributions indicate an increased risk. Studies have reported a 7% to 28% risk for SWS in patients with a PWB in what was previously described as a V1 distribution. More recent research has reported that hemifacial, forehead, and median PWB locations are associated with increased SWS risk (Figure, B). Bilateral PWBs or those that extend from the forehead to include the cheek and skin overlying the mandibles have a higher risk of SWS, but the forehead location is the strongest independent predictor of SWS risk. Port-wine birthmarks in SWS most often involve the lateral forehead and are less commonly localized to the midline forehead, but there are exceptions, as even a small PWB of the midline forehead can be associated with severe neurologic disease. Facial PWBs persist throughout life and may become darker red or red-purple over time. Particularly when located over the midface, facial PWBs may develop progressive vascular ectasia/thickening, soft tissue hypertrophy, and proliferative nodules that are prone to bleeding, discomfort, and less commonly, infection. On histologic examination, most such nodules represent vascular ectasias, pyogenic granulomas, or arteriovenous malformations, although other epithelial and mesenchymal hamartomas have been described. Progression may result from both vascular ectasia and specific genetic alterations with PWBs that lead to soft tissue hypertrophy. Progressive changes are uncommon before puberty. Eczematous skin changes (eg, Meyerson phenomenon) have been observed within PWBs earlier in childhood, particularly in children with preexisting atopic dermatitis.

Key topic 2: The best timing for evaluation of a facial PWB is at birth.
Identification of an at-risk facial PWB, especially those involving the forehead, should prompt an eye examination for congenital glaucoma and neurology referral. In cases in which the diagnosis is uncertain, referral to an experienced specialist is appropriate (eAppendix in the Supplement). Differential diagnoses include segmental infantile hemangioma that may warrant a PHACE (posterior fossa anomalies, hemangioma, arterial anomalies, cardiac anomalies, and eye anomalies) workup or other capillary malformations, such as nevus simplex. Early diagnosis of a PWB affords the option of maximizing early laser treatments, which may be performed without the need for general anesthesia and may improve treatment outcome.3

**Determination of the Optimum Treatment**

Key topic 3: There are a number of factors that should be considered regarding treatment, including minimizing the psychosocial impact, diminishing nodularity and, potentially, tissue hypertrophy, and financial considerations for the family.

Patients and parents seek treatment for several reasons, including lesion appearance that affects quality of life, confidence, and self-esteem, among other psychosocial issues.15 Laser treatments may prevent or treat the proliferative nodules that can develop over time.16 There is no clear evidence that laser treatment definitively prevents tissue hypertrophy. However, superficial overgrowth may be minimized if adequate vessel removal is achieved. Because laser light is unable to reach deep vessels, PWBs may develop hypertrophy despite treatment.

Key topic 4: In the US, light-based devices are the standard of care for PWB treatment, and pulsed dye laser (PDL) is considered first line.

Pulsed dye laser has the longest history of efficacy and safety for treatment of PWBs, and many studies support this device as the standard.6,17 For infants, PDL is considered the standard of care in the US. Experienced surgeons can safely perform laser surgery in patients of all ages.

Several other wavelength lasers (532, 755, and 1064 nm) and intense pulsed light have been used for PWB treatment. These techniques can be used for all PWBs but are especially useful for those that have demonstrated PDL resistance. The longer wavelengths (755 and 1064 nm) may help target larger or deeper vessels, such as those in patients with nodular and hypertrophic lesions.6,18 These
devices also target hemoglobin but have a higher risk of damage to nontargeted tissue than PDL. To our knowledge, there have been few or no randomized clinical trials with these alternative devices, and children have not been included in most of the reports. However, small studies have shown promising results for recalcitrant PWBs.\textsuperscript{19,20} The Alexandrite laser is the most commonly used alternative when PDL is inadequate.\textsuperscript{21} Long-pulsed Nd:YAG may also be considered but has a particularly narrow margin of safety.\textsuperscript{6}

A variety of fractionated ablative devices designed for facial rejuvenation have also been used for PWB treatment. Many of these devices use infrared laser pulses (carbon dioxide, erbium:YAG, and erbium:glass), while others use bipolar radiofrequency ablation to coagulate skin and blood vessels. In small studies combined with PDL, efficacy has been demonstrated with these devices for recalcitrant PWBs.\textsuperscript{22,23}

When discussing the option of laser treatment with families, several factors should be addressed, the first of which is pain control. Topical anesthetics; epidermal cooling methods; injection of local anesthetics; nerve blocks; intramuscular pain medication, such as meperidine; or general anesthesia can minimize discomfort.\textsuperscript{16} Multiple factors are involved in choosing the optimal method of pain control for a patient, including but not limited to patient age and state of health, PWB location and extent, availability of methods dependent on practice, surgeon experience, and parent/child preference. Second, adverse effects should be discussed; these are detailed in key topic 10. Third, the family will be faced with financial obligations. Costs may include such factors as professional fees of the laser surgeon, anesthesia fees, and facility fees. The fourth factors are clinical outcomes. Realistic expectations should be set with families as complete PWB clearance is rarely achieved.\textsuperscript{24} Pulsed dye laser can achieve 50% to 90% clearance, and most patients will have more than 50% lightening.\textsuperscript{6} Most patients require 8 to 10 treatments or more for optimal results; however, touch-up treatments are frequently needed even after an initial successful series of lightening. Despite considering the following factors, response is difficult to predict.

Several factors have an effect on treatment response. Patients with lighter skin types have a better treatment response.\textsuperscript{25} Port-wine birthmarks on the face and neck respond better than those on the extremities,\textsuperscript{17} and PWBs on the lateral face respond better than those in the central face.\textsuperscript{22,26} Proximal extremity lesions respond better than distal extremity lesions.\textsuperscript{17} The eyelids and neck are at higher risk for blistering and scarring, and this possibility should be considered when selecting laser parameters. Based on our experiences, individuals with PWBs associated with SWS may be more resistant to laser. Pink, red, and reticular lesions may respond better than those that are purple and geographic shaped.\textsuperscript{17,25} Not unexpectedly, PWBs with overgrowth will show a lesser response than those that are flat, smooth, and not associated with contour change.\textsuperscript{6,17}

Fifth, psychosocial consequences should be discussed. It is important that the short- and long-term well-being of the patient from a psychosocial perspective is considered and, above all else, the patient’s safety.

Key topic 5: Light-based devices are still first-line treatment for PWBs in patients with skin of color; however, higher rates of adverse effects may be seen than in lighter-skinned patients, mainly dyspigmentation and atrophic scarring. Moderate energy densities, less pulse overlap, and increased cooling are recommended in the treatment of patients with darker skin types to minimize risks.

Port-wine birthmarks occur in patients with all skin types, and this is probably the greatest factor influencing treatment. While limited clinical studies exist for certain races/ethnicities, specifically East Asian and Indian patients, and in certain skin types, particularly Fitzpatrick skin types V and VI, a few studies provide insight for pigmented skin. In one study, PDL was used successfully in Indian patients without permanent adverse effects, although the lightening achieved was modest.\textsuperscript{27} This study included 74 flat, nonhypertrophic PWBs with a mean of 7.3 treatment sessions and 24 hypertrophic
PWBs with a mean of 8.5 treatment sessions. The mean lightening achieved was 54% in nonhypertrophic lesions and 40% in hypertrophic lesions.\textsuperscript{27} In East Asian populations, PDL has also been used safely and successfully. While the percentage of improvement varies, reported results are slightly better than those in the aforementioned Indian study with fewer treatment sessions. In 239 Korean patients, 51.9\% showed a good to excellent response, defined as greater than 51\% clearance, after a mean of 4.29 sessions.\textsuperscript{28} In a study of 848 Chinese patients, a 69.9\% response was achieved after a mean of 6.2 sessions.\textsuperscript{29} This study also underscored the importance of patient age in treatment response, with a 93.9\% response rate reported in children treated during the first year of life and only a 25\% response rate in adults treated when they were older than 50 years.

While patients with darker skin types can experience improvement in their PWBs, they are also at higher risk of persistent dyspigmentation, atrophy, and scarring.\textsuperscript{17,21} In general, moderate fluences, less pulse overlap, and increased cooling are recommended in treating patients with skin of color, and patients should be counseled that transient hyperpigmentation is common.\textsuperscript{27}

Key topic 6: There are a number of alternative therapies that have been investigated for PWBs that do not respond to traditional laser and light-based treatments.

Alternatives to laser or intense pulsed light therapy can be divided into 4 groups: (1) adjuvant medications, (2) photodynamic therapy, (3) surgery, and (4) corrective cover-up. There are currently no adjunctive medical therapies that have demonstrated consistent impressive efficacy for PWBs.\textsuperscript{30,31} Several small studies have reported some benefit for PDL plus topical imiquimod vs PDL alone.\textsuperscript{30} Similarly, a few small studies and case reports demonstrated some benefit of topical rapamycin as an adjunct with PDL\textsuperscript{22,33} but no consistent benefit over PDL alone. Photodynamic therapy involves the intravenous administration of a photosensitizer (various forms of porphyrin) followed by exposure to a light source, producing intravascular singlet oxygen molecules that destroy local tissue. Although photodynamic therapy is not currently performed in the US, studies from China have shown promising results.\textsuperscript{34-36} Approximately 20\% of patients experience hyperpigmentation and scarring. However, melanin does not influence the efficacy of photodynamic therapy, so this treatment can be performed in patients of all skin types, although patients with darker skin types will still be more susceptible to pigmentary change post treatment.\textsuperscript{6,17} Surgery can be used to selectively debulk thick PWBs or lip hypertrophy, remove larger nodules, or completely remove small lesions in which the resulting surgical scar is acceptable to the patient. A variety of corrective cover-up products and concealers are available for dermatologic conditions and can be used in patients with PWBs.

**Laser and Light-Based Therapies**

Key topic 7: The interval between laser treatments is dependent on a multitude of factors. No optimal interval has been established by scientific evaluation; thus, treatment interval must be tailored to each patient.

The interval between laser sessions depends on age, skin type, PWB location, pain tolerance, and presence of hypertrophy, nodules, or blebs. The interval is also influenced by resolution of prior purpura and/or hyperpigmentation, convenience, financial limitations, and potential restriction of activities after treatments. Only a few small studies in infants have analyzed the interval between PDL treatment sessions ranging from 2 weeks to 3 months.\textsuperscript{37,38} These studies do not provide a clear recommendation on shorter vs longer intervals, although a subset of patients appears to benefit from shorter intervals. These studies have demonstrated the safety of PDL when performed at short intervals.

In older children, adolescents, and adults, it is uncertain whether there is an optimal timing interval between treatments. A small pilot study in adults suggested that 2-week treatment intervals resulted in greater lightening compared with 6-week intervals.\textsuperscript{39} Other studies have failed to show this benefit.\textsuperscript{40} While shown to be safe, shorter treatment intervals may result in a higher incidence of
undesirable effects, especially in patients with darker skin who often benefit from longer intervals to avoid postinflammatory hyperpigmentation. It is also important to allow purpura to heal before treating again because the increased chromophore can heighten the risk of adverse effects.

Key topic 8: Greater rates of lightening and possible prevention of future darkening and hypertrophy may be attained if treatments are started at an earlier age. The main goal of treatment is to ensure healthy and adequate psychosocial development and minimize the stigma associated with PWBs. Based on expert observations and limited studies, treatment of PWBs at an earlier age, particularly in the first year of life, results in better outcomes. Factors associated with improved prognosis in young children include proportionately smaller PWBs, more superficial and smaller blood vessels, and less melanin as a competing chromophore for PDL. Liu et al found greater efficacy when treatments were started before age 6 years. Other studies have reported better responses in infants younger than 1 year, particularly with smaller PWBs (<20 cm). However, these studies are limited by their retrospective design and relatively short follow-up periods. Larger case-control studies are needed to support this observation.

Current laser technology is less successful in reverting progressive PWB changes of darkening, hypertrophy, and nodularity. Thus, performing laser treatment in early childhood may prevent or minimize these changes. Limited retrospective studies support the concept that early treatment inhibits progression; however, longitudinal studies are needed. It has been shown that patients aged 7 to 16 years with facial differences, including PWBs, experience impaired health-related quality of life. The negative impact in the child’s psychosocial development and quality of life is one of the main reasons to pursue early treatment. This impact may be diminished when lightening of the PWB is attained at an earlier age.

Key topic 9: Pulsed dye laser in young patients is a safe treatment option with a low incidence of permanent complications when performed by an experienced laser surgeon.

The risks associated with laser treatment of PWBs can be categorized in 2 groups: risks inherent to the procedure and risks associated with the method of analgesia. The latter is discussed with the next key topic. The risks associated with PDL are focused on here because it is the most widely used and safest treatment option in infants and toddlers, particularly when compared with longer-wavelength vascular lasers. The safety and tolerance of PDL was also improved with the addition of cooling technology. Immediate treatment effects include erythema and purpura, which has traditionally been considered the desired clinical end point. The risk of complications has been reported to be less than 10%, and most complications are temporary. Swelling may occur, which in most patients is mild except in the periorbital or lip area. Dyspigmentation may occur in response to direct epidermal and melanocyte damage and is most common in patients with darker skin types, tanned skin, and recent sun exposure. Sun protection is advised before and after treatments. Temporary blistering may occur. Erosions, ulcerations, and secondary infection are rare when appropriate laser settings are used and adequate postprocedure skin care is followed. Permanent scarring, both atrophic and hypertrophic, is one of the most serious potential complications of PDL but has an estimated incidence below 1%. In addition, PDL treatment over hair-bearing areas may cause hair loss, which is typically temporary but can be permanent in an estimated 1.5% to 2.6% of cases.

The most serious potential complication resulting directly from PDL is ocular damage, especially when the periorbital area is treated. Appropriate use of corneoscleral eye shields is mandatory when treating the skin within the orbital rim. Laser-specific eye shields may be used when treating outside the orbital rim. Special care must be taken when PDL is performed without sedation, as young patients may move in response to the discomfort. Securing the patient’s position and ensuring eye protection is crucial when treating infants and toddlers. Parents, nursing staff, and the laser surgeon must also wear adequate protective eyewear.
Key topic 10: Laser treatments can be associated with significant discomfort. The choice of using general anesthesia is complex, and informed decision-making should be shared with the patients and their parents/guardians.

An important factor to consider when treating younger patients is the pain and discomfort associated with laser treatments. While treatment of small and moderate-size lesions is fast and generally well tolerated, patients with larger PWBs may experience significant discomfort, in which case topical anesthesia or sedation may be considered. Topical anesthetics, including lidocaine preparations, can be used safely, but there is a risk of methemoglobinemia, especially in infants. Published guidelines regarding topical anesthesia should be followed if this option is chosen.

General anesthesia requires careful consideration given the potential risks and higher cost. General anesthesia carries a risk of cardiorespiratory complications, which is highest in the neonatal period and decreases with age. It is common practice to wait until the infant is at least age 6 months to use general anesthesia for elective procedures, but procedures before this age can be performed without general anesthesia. Anesthesia should be administered by clinicians specialized in pediatric care to reduce the risk of perioperative morbidity. The risk of neurotoxicity with potential long-term negative effects on neurologic development has gained recent attention. The US Food and Drug Administration advises caution in patients younger than 3 years requiring repeated use of general anesthesia and sedation during surgeries or procedures, which is relevant to the management of PWBs as multiple treatments early in life are often performed. The warning was based predominantly on preclinical data, and ongoing trials may help to further clarify this risk. Until more information is available, the decision to use general anesthesia or sedation must be carefully considered.

When general anesthesia or sedation is not used, young infants have an advantage over toddlers. Pulsed dye laser treatment without general anesthesia is more safely and efficiently performed in infants since the area of involvement is proportionally smaller and the patient’s position and eye protection can be secured more easily. Nevertheless, the potential impact of painful procedures must be carefully weighed. Noxious stimuli early in life may lead to short-term and possibly long-term effects in behavior, particularly toward medical care. Parental stress and satisfaction must also be considered when making this decision.

Conclusions
This consensus statement provides expert consensus on identification and risk stratification, optimal treatment strategies, and recommendations for light-based therapies for patients with PWBs. These recommendations are intended to help guide clinical practice and decision-making for patients with SWS and those with isolated PWBs and may improve patient outcomes.

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