FEATURE ARTICLE

CE 1.5 Contact Hours

Skin Cancer

Back to Basics: Basal Cell Carcinoma

Kyleen E. Davis

ABSTRACT: Basal cell carcinoma (BCC) is the most common form of skin cancer in the United States, with an estimated 4.3 million cases diagnosed each year. The major risk for BCC is primarily related to sun exposure; however, multiple modifiable and nonmodifiable risk factors contribute to the development of this condition. Although it rarely metastasizes, BCC can cause significant morbidity through local tissue destruction and infiltration into vital underlying organs. There are multiple treatment options for BCC, but Mohs micrographic surgery is considered to be the gold standard of therapy. For individuals with unresectable or metastatic BCC, new and emerging therapies involving inhibition of the Hedgehog signaling pathway have shown promising results. This article discusses the most current literature for dermatology nurses on the epidemiology, assessment, and treatment of BCC with the focus on early detection and management to lower morbidity and offer better patient outcomes.

Key words: Basal Cell Carcinoma, Dermoscopy, Mohs Micrographic Surgery, Nonmelanoma Skin Cancer, Photodynamic Therapy

Basal cell carcinoma (BCC) is the most common form of skin cancer, with an estimated 4.3 million cases diagnosed in the United States each year (PDQ Adult Treatment Editorial Board, 2018). Although it rarely metastasizes, BCC can cause significant local tissue destruction, resulting in disfigurement and infiltration into vital underlying structures if left untreated. Intermittent intense sun exposure—including blistering sunburns—radiation therapy, a positive family history of BCC, immunosuppression, and a fair complexion (Skin Types I or II) are risk factors for the development of BCC (Table 1; James, Berger, & Elston, 2011). In addition to environmental triggers, several genetic mutations are associated with BCC, although the exact mechanism of carcinogenesis is unclear (PDQ Adult Treatment Editorial Board, 2018).

PATHOGENESIS

BCCS are thought to arise from immature pluripotent cells associated with the hair follicle (James et al., 2011). Most genetic mutations associated with BCC involve the Hedgehog (Hh) signaling pathway, which controls for cell growth. The PTCH1 gene is most commonly affected in BCC, followed by sonic hedgehog and smoothened (James et al., 2011).

COMORBIDITIES

White patients with BCC are more likely to have a medical history of extracutaneous malignancy, rheumatoid arthritis, inflammatory bowel disease, and solid organ transplantation (Kimmel, Taft, & Keefer, 2016; Reinau, Surber, Jick, & Meier, 2014). In addition, patients who receive a diagnosis of BCC before the age of 60 years are found to have a higher rate of breast cancer, testicular cancer, and non-Hodgkin lymphoma (James et al., 2011). Melanoma also occurs at higher rates in this group. Other genetic syndromes associated with BCC include xeroderma pigmentosum, oculocutaneous albinism, and basal cell nevus syndrome—also known as Gorlin syndrome (Nolen, Beebe, King, Bryn, & Limaye, 2011).

CLINICAL FEATURES OF BCC

The main types of BCC are nodular, superficial, morpheaform, and fibroepithelial, with combinations of these types possible. Furthermore, different histopathologic patterns can be intertwined with clinical subtypes, forming variations such as cystic, micronodular, and basosquamous (Bolognia, Jorizzo, & Schaffer, 2012). BCCs can be further classified by the presence of pigment, although most BCCs are amelanotic. Pigmented BCCs comprise about 6% of all BCCs and are the most common type in the Latin American or Asian populations (Figure 1; James et al., 2011). With all BCC types, the location is mainly on the

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TABLE 1. Risk Factors Associated With Basal Cell Carcinoma

1. Modifiable risk factors
   - Intense sun exposure
     - History of blistering sunburns
     - Tanning bed use
   - Radiation therapy
   - Proximity to equator
   - Immunosuppression (organ transplant recipients, HIV disease)
   - Chemical carcinogens: ingestion of arsenic acid (medicine, pesticides), hydrocarbons, industrial oils, dyes, solvents (Dessinioti, Antoniou, Katsambas, & Stratigos, 2010)
2. Nonmodifiable risk factors
   - Gender (males at a higher risk)
   - Positive family history of BCC
   - Fitzpatrick Skin Types I and II
   - Higher nevus count on extremities (>10; Wei, Li, & Nan, 2019)
   - History of melanoma

Note. Adapted from James et al., 2011.

head and neck—a consequence of the role that ultraviolet exposure plays on its development. The remainder of cases occur on the trunk and extremities, with rare occurrences on the non-hair-bearing areas, such as the genital mucosa (Marzuka & Book, 2015).

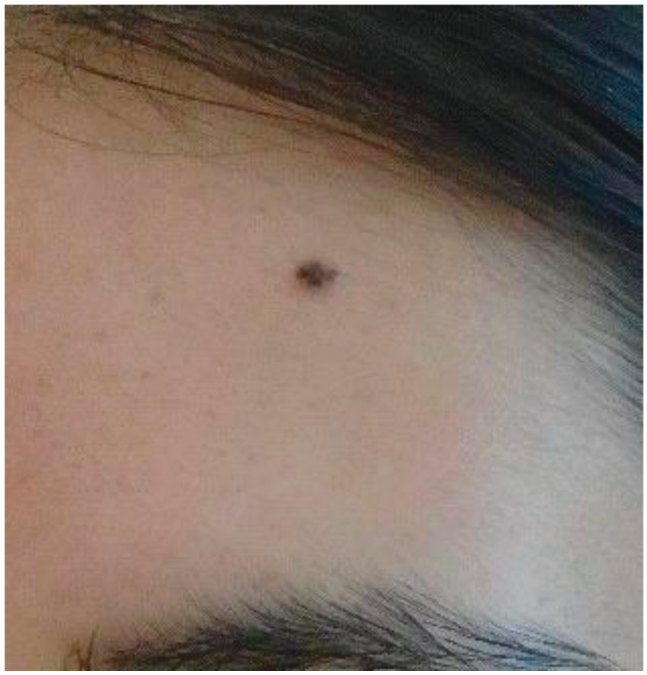


FIGURE 1. A pigmented basal cell carcinoma on the left upper forehead in an Asian female. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

TYPES OF BCC

Nodular BCC

Nodular BCC accounts for approximately 60%–80% of cases and most often presents on the skin of the head (Figure 2; James et al., 2011). This type of BCC generally begins as a small, dome-shaped, pink papule with a pearly or translucent appearance (Nolen et al., 2011). The edges of the lesion may have rolled borders, because of retraction of the stroma. As the nodular BCC continues to enlarge, the overlying upper layers of the epidermis become thinner, exposing blood vessels to easy trauma and bleeding, with subsequent ulceration.

Superficial BCC

Superficial BCC is another common form of BCC, comprising about 15% of total cases (James et al., 2011). The location of superficial BCC is most often the trunk (45%) but may also occur on the distal extremities, head, and neck. Superficial BCC typically manifests as a red, scaly, psoriasiform plaque that enlarges slowly over time and is often confused with a patch of eczema or psoriasis (Figure 3).

Morpheaform

Morpheaform BCC accounts for about 5%–10% of cases and typically presents as a white, shiny, scar-like plaque with ill-defined borders (Figure 4). In addition, atrophy is often present. This type of BCC is known for subtlety

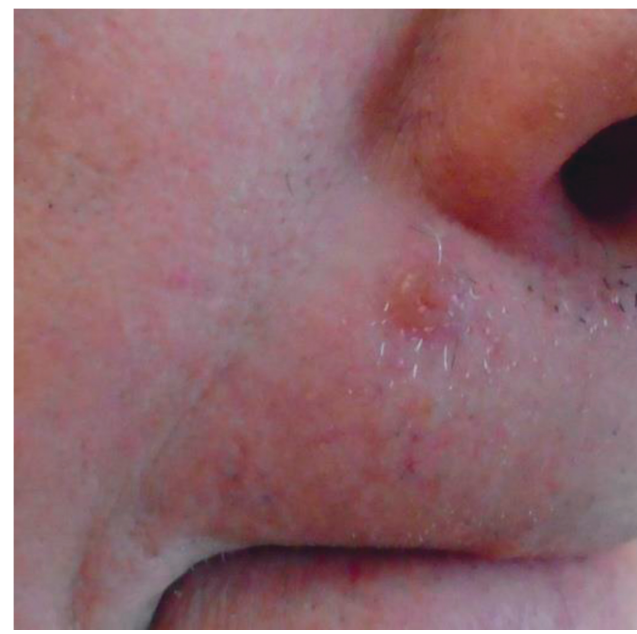


FIGURE 2. Nodular BCC of the right perinasal area. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

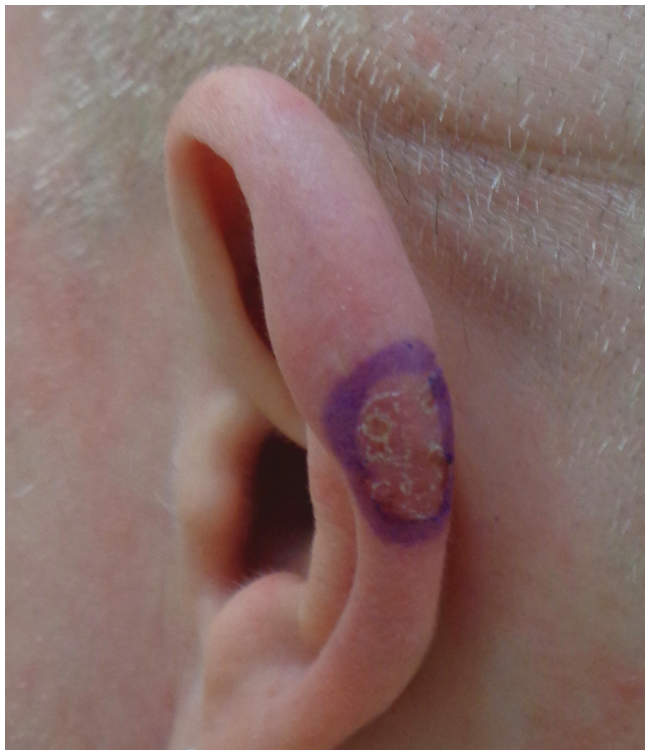


FIGURE 3. Superficial BCC of the left mid-helix. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

in its presentation, often being mistaken for a scar, which may delay diagnosis (Marzuka & Book, 2015). This delay can result in significant local tissue destruction, because the biologic behavior of morpheaform BCC also tends to be more aggressive than other forms.

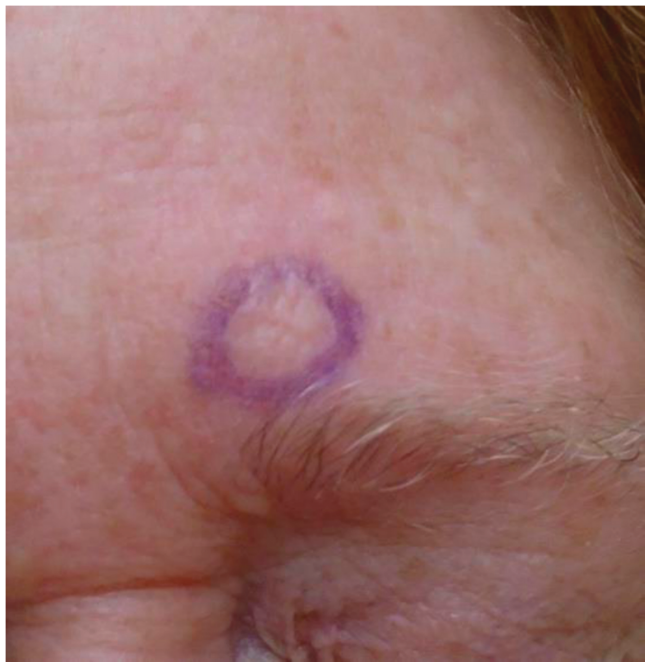


FIGURE 4. Morpheaform BCC of the left forehead. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

Fibroepithelioma of Pinkus

Fibroepithelioma is a rare variant of BCC that typically presents as a pink or skin-colored sessile papule or plaque on the lumbosacral area, groin, or thigh (Figure 5). The pedunculated appearance of these BCCs may cause them

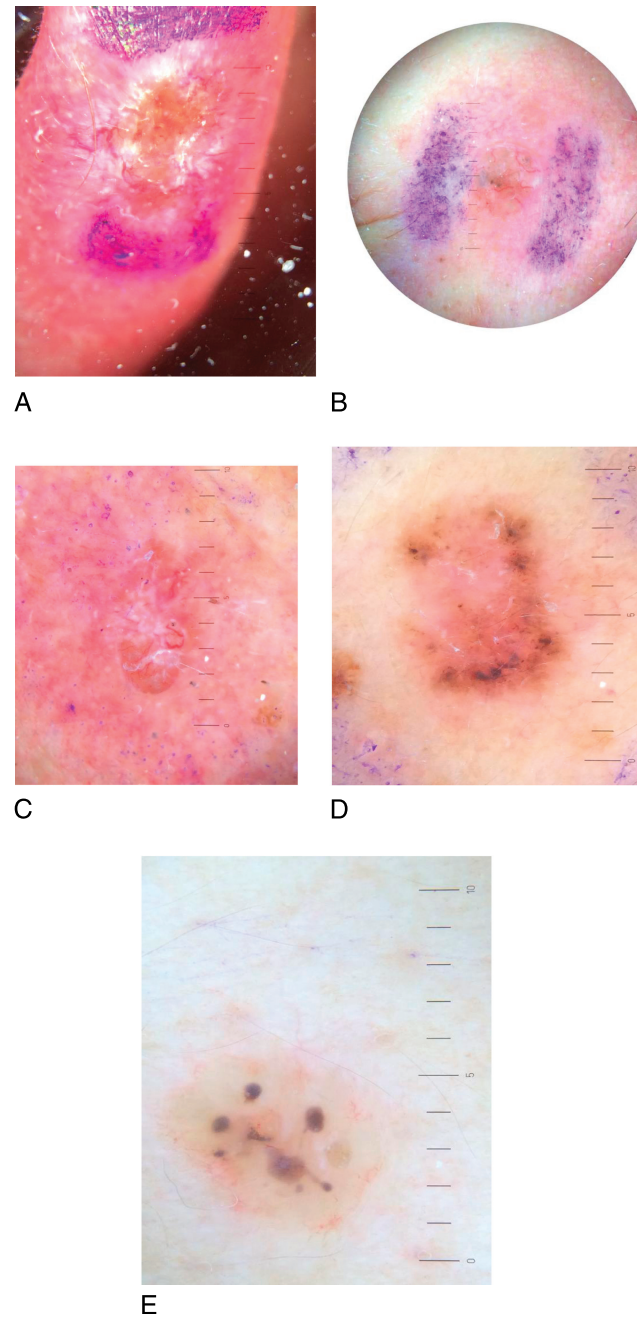


FIGURE 5. Dermoscopy of BCC. A, Ulceration and arborizing vessels. B, Arborizing vessels, blue-gray ovoid nests. C, Arborizing vessels. D, Leaf-like structures. E, Spoke-wheel areas. Photos courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

to be overlooked for large skin tags or intradermal nevi (Bolognia et al., 2012; James et al., 2011).

DERMOSCOPY OF BCC

Dermoscopy is an important tool in the assessment of BCC. A retrospective study examining 609 BCCs investigated the variability in dermoscopy of the presenting lesion. The most common pattern was found to be arborizing—orbranching—blood vessels, occurring in 57.1% of BCCs (Altamura et al., 2010). A second pattern of blue-gray ovoid nests was apparent in 47.5% of BCC lesions, whereas multiple blue-gray globules were observed in approximately 26.1% of lesions (Altamura et al., 2010). In addition, 15.9% of BCCs showed leaf-like structures, 9% showed spoke-wheel areas, and 39.2% had associated ulceration (Altamura et al., 2010). As expected with BCC, there was no pigment network (Bolognia et al., 2012).

HISTOPATHOLOGY OF BCC

Slow-growing BCCs, such as nodular and superficial types, exhibit lobules that extend into the papillary or reticular dermis, with cleft retraction, peripheral palisading, and stromal mucin often being prominent (Stanoszek, Wang, & Harms, 2017). Aggressively growing BCCs—such as micronodular, infiltrative, and morpheaform—share features of increased cell necrosis, mitotic activity, and stromal proliferation. These variants show higher rates of recurrence and, very rarely, metastasize (Stanoszek et al., 2017).

DIFFERENTIAL DIAGNOSIS OF BCC

Clinical mimics of BCC are numerous (Table 2). Nodular BCC may be confused with sebaceous hyperplasia, with the latter being recognized by its rim of yellow papules and a central dell. Dermal nevi can also appear clinically similar to nodular BCCs; however, clinicians can utilize dermoscopy to aid in distinguishing between these two lesions, with dermal nevi showing a pigment network and comma-shaped blood vessels compared with the arborizing vessels of BCC (Togawa, 2017). Other benign lesions to consider in the differential diagnosis of BCC are seborrheic keratosis, which can appear similar to nodular BCC, and eczema or psoriasis, which can mimic superficial BCC. Malignant or premalignant neoplasms that simulate BCC include squamous cell carcinoma, amelanotic melanoma, Paget's disease, and actinic keratosis. Ulcerated BCC on the shins is frequently misdiagnosed as a stasis ulcer (James et al., 2011).

TREATMENT OF BCC

The selection of a treatment method for BCC must take into account four factors: tumor size, location, histology, and history (recurrent vs. primary; James et al., 2011). Other considerations include preference of the patient and perineural invasion, as evidenced by the presence of pain.

Surgery

Surgical removal of BCC is considered first-line therapy, with the gold standard being Mohs micrographic surgery. Mohs is a type of surgical technique that involves progressive radial sectioning of malignant tissue with examination of resected margins in real time (Figure 6; PDQ Adult Treatment Editorial Board, 2018). This is continued until adequate uninvolved margins have been achieved. With this technique, the narrowest margins are taken to avoid tumor recurrence while maximally preserving healthy tissue, which is critical in high-risk anatomical locations, such as the face, neck, hands, and scalp. In addition to preserving cosmesis in patients with BCC, Mohs surgery results in cure rates up to 99%. Alternatively, traditional surgical excision has shown cure rates up to 90%–95%, as long as the BCC is small (less than 2 cm in diameter) and nonaggressive and adequate 4-mm margins are achieved (Luz, Ferron, & Cardoso, 2015).

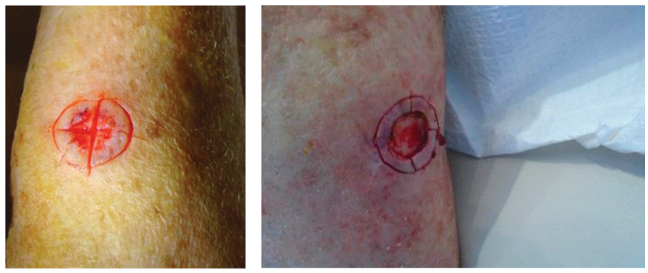
Curettage With Electrodesiccation

With electrodessication and curettage, a sharp curette is used to scrape the tumor down to its base, followed by electrodessication of the lesion base (PDQ Adult Treatment Editorial Board, 2018). The relapse rate is between 1% and 15% in small tumors but increases to 50% in tumors

TABLE 2. Differential Diagnosis of Basal Cell Carcinoma

Benign	Malignant or premalignant
• Dermal nevi	• Squamous cell carcinoma
• Sebaceous hyperplasia	• Actinic keratosis
• Eczema	• Paget's disease
• Psoriasis	• Melanoma
• Seborrheic keratosis	• Merkel cell carcinoma
• Molluscum contagiosum	• Microcystic adnexal carcinoma
• Dermatofibroma	• Dermatofibroma sarcoma protuberans

Note. Adapted from Singh, Lin, Hocker, Tan, & Burgin, 2019.



A B

FIGURE 6. Mohs micrographic surgery. A, 1st stage Mohs micrographic surgery on the lower extremity. B, 2nd stage Mohs micrographic surgery on the lower extremity. Photos courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

above 3 cm because of difficulty in determining tumor depth with this technique (Peikert, 2011).

Photodynamic Therapy

Photodynamic therapy utilizes a topical photosensitizing agent that is applied to the tumor and followed by exposure to a specific wavelength of light. Light activation induces an oxidation reaction in the tumor, resulting in local cell destruction (PDQ Adult Treatment Editorial Board, 2018). High initial clearance rates have been reported with photodynamic therapy; however, recurrence rates up to 50% may occur with long-term follow-up (PDQ Adult Treatment Editorial Board, 2018; Figure 7).

Medications

Topical imiquimod and 5-fluorouracil have been used successfully in the treatment of low-risk nonmelanoma skin cancers, such as BCCs. Imiquimod is a toll-like receptor 7 agonist, which induces cytokines and promotes Th1-type immunity. It is Food and Drug Administration-approved for superficial BCC with directions to apply topically to the affected area five times a week for 6 weeks. Cure rates up to 82% have been reported in superficial BCC, making topical imiquimod a reasonably effective treatment for this specific histologic growth pattern, but less so for other types. Imiquimod should not be used on the face, hands, or feet and should be limited to a tumor size of 2 cm. Labeling for topical 5-flurouracil in the treatment of superficial BCC indicates that it should be applied to the tumor site twice daily for 3–6 weeks.

Cryosurgery

Cryosurgery is infrequently used in the treatment of BCC but may be suitable for patients for whom surgery is inappropriate. It must be limited to cases with small, well-defined primary tumors (PDQ Adult Treatment Editorial Board, 2018). Complications may include hypertrophic scarring and postinflammatory pigment changes, which can conceal a recurrent carcinoma (Bolognia et al., 2012). Recurrence rates with this treatment method are approximately 9% over a 5-year period (Bernardeau et al., 2000; Kuflik, 2004).

Radiation

Radiation is occasionally used to treat BCC for which surgery is contraindicated. Although radiation has the advantage of being a noninvasive procedure and results in cure rates in excess of 90%, it carries the disadvantages of poor margin control, prolonged course of therapy, possible scarring, and increased risk for future skin cancers, such as squamous cell carcinoma, at the irradiated site (Lebwohl et al., 2018).

Laser

Pulsed dye laser can be used to treat BCC; however, treatment is not yet standardized (Lebwohl et al., 2018). Most research trials have utilized four treatments at a high fluence, with success rates ranging from 65% to 90% over a 2-year period (Konnikov, Avram, Jarell, & Tannous, 2011; Lebwohl et al., 2018). A small study also showed efficacy with the carbon dioxide laser in the treatment of small, low-risk BCCs in patients with Gorlin syndrome (Nouri, Chang, Trent, & Jimenez, 2002).

FIGURE 7. Photodynamic therapy. Photo courtesy of Maral Skelsey, MD, Dermatologic Surgery Center of Washington. Used with permission.

Hh Pathway Inhibitors

For patients with locally advanced or metastatic BCC, vismodegib and sonidegib are examples of an emerging therapy that works by inhibiting the Hh signaling pathway (Cirrone & Harris, 2012). These medications are also being utilized in clinical settings for patients with unresectable BCC tumors, in individuals with multiple BCCs—for example, Gorlin syndrome—and preoperatively to decrease tumor size (Singh et al., 2019). A recent meta-analysis showed 64.7% and 31.3% response rates for partial and complete clearance of locally advanced BCC, respectively. For BCCs that became metastatic, there was a 33% partial response and a 3.9% complete clearance rate with these medications (Jacobsen, Aldahan, Hughes, Shah, & Strasswimmer, 2016).

FOLLOW-UP

Monitoring for recurrence is important in the management of patients with a history of BCC. For these patients, thorough skin checks should be performed at least annually, with a close inspection of previously treated BCC locations (Johnson et al., 2017). The highest rates of recurrence occur within 5 years of treatment; however, some tumors have been known to recur after a longer period. In addition to monitoring for recurrence, patients should be checked for new BCCs, as patients with a previous BCC have a 44% increased risk of developing a subsequent BCC (Marcil & Stern, 2000).

In summary, BCC is a common dermatologic disease that will be frequently encountered by dermatology nurses. Therefore, it is crucial for these clinicians to be knowledgeable in the assessment and management of these cancers. Early detection and treatment results in lower morbidity and better patient outcomes. ■

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