

Blue in dermatology

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ABSTRACT

Blue is one of the primary colors of pigments, and our eye perceives blue when observing light wavelengths are between approximately 450 and 495 nm. There are several blues seen in dermatology, and it would be imperative to know as a dermatologist how various blues present to arrive at a conclusive diagnosis and use it in multiple indications, follow-up, and for better therapeutic outcomes.

Key words : Blue; Blue nevus; Dermoscopy; Blue vitiligo; Blue skin diseases

INTRODUCTION

The word blue comes from Middle English blewe or bleu, from the Old French bleu, Old High German word blao (meaning shimmering, lustrous) [1]. The word azure in heraldry is used for blue [2]. Blue is among the three primary colors of pigments in painting and the RGB color and traditional color theory model. It lies in between violet and green in the visible light spectrum, and the eye perceives blue when observing light wavelengths between approximately 450 and 495 nm. In dermatology, we categorize the blues' in the following manner (Table.1).

1. Cutaneous lesions

a) Blueberry muffin baby

It is the term given to characteristic eruption in neonates, often present at birth, comprising widespread, erythematous, purple, circular, or oval macules, papules, and nodules reflecting dermal erythropoiesis seen in several congenital infections, notably rubella, cytomegalovirus, Coxsackie B2 infection, parvovirus B19, congenital syphilis, toxoplasmosis, Rh incompatibility, ABO blood group incompatibility, hereditary spherocytosis, and twin-twin transfusion syndrome, (Fig. 1); [3].

b) Blue ear sign

In relapsing polychondritis, auricular inflammation may lead to thinning of the cartilage resulting in a bluish hue to the ears. Recurrent bouts of inflammation cause realignment of collagen fibers' and structural thinning, thereby altering tissue transparency and allowing the coloration of underlying vascular tissue to become more prominent [4].

c) Blue nevus: (Blue nevus of Jadassohn-Tièche; Dermal melanocytoma; Nevus bleu; Blue neuronevus).

It represents benign tumors of dermal melanocytes. Common blue nevus presents blue to blue-black, firm papule, nodule, or plaque, often with an onset during childhood or adolescence. The Tyndall phenomenon is responsible for the blue coloration of nevi. Multiple blue nevi may be associated with the LAMB (lentiginos, atrial myxomas, mucocutaneous myxomas, and blue nevi) syndrome (Fig. 2); [5].

d) Blue rubber bleb nevus syndrome (BRBNS): Bean syndrome

It is an uncommon condition characterized by multiple venous malformations affecting the skin and internal viscera, gastrointestinal tract involvement being the most common. In BRBNS, three types of lesions are

How to cite this article: Jain SA, Rao MS, Mahesh AR. Blue in Dermatology. Our Dermatol Online. 2022;13(e):e6.

Submission: 16.08.2021; **Acceptance:** 23.01.2022

DOI:10.7241/ourd.2022e.6

described by Bean, which are often noted during the neonatal period or at birth, although they can present later. The first type is compressible, red-blue, nipple-like lesions. The second type is blue-black non-blanching macular lesions, and the third type is subcutaneous, vascular, soft tissue lesions [6]. The lesions clinically are characteristically blue/purple soft compressible nodules with a rubbery feel. They are dome-shaped, almost nipple-like “rubber blebs,” which may coalesce to form large masses [7].

e) Blue vitiligo

Depigmentation in vitiligo is due to the absence of melanocytes in the epidermis. The bluish tinge maybe is due to the deposition of drugs like psoralens and

zidovudine or as a post-inflammatory process [8]. Few authors believe that acutely massive, intense inflammatory infiltrate in the dermo-epidermal junction leading to basal cell degeneration and dropping off melanocytes into the dermis gives a bluish hue to the patches due to the Tyndall effect [9].

f) Mongolian blue spots

Mongolian blue spots are congenital macular areas of blue-grey pigmentation due to dermal melanocytosis of varying sizes and shapes located on the sacral region in normal infants. Extensive Mongolian spots have been associated with Hurler syndrome, GM1 gangliosidosis type I, mucopolipidosis II, and bilateral nevus of Ota [10].

g) Maculae ceruleae (Blue spots)

Maculae ceruleae means sky-blue (ceruleae) spots (maculae). It refers to the bluish macules occasionally seen on the bodies of persons infested with Pthirus

Table.1: Various categories of blues' in dermatology.

S.No.	
I	Cutaneous lesions:
a)	Blueberry muffin baby
b)	Blue ear sign
c)	Blue nevus
d)	Blue rubber bleb nevus syndrome (BRBNS)
e)	Blue vitiligo
f)	Mongolian blue spots
g)	Maculae ceruleae (Blue spots)
h)	Blue sclera
i)	Blue neck syndrome
j)	Blue Scrotum Sign of Bryant
k)	Blue ball sign
l)	Blue-grey stippling (Hermans Spot) and Punctuate blue-white lesions (kopliks spots)
m)	Acute idiopathic blue finger
n)	Blue man syndrome
o)	Sea blue histiocytosis syndrome
p)	Blue hands
q)	Blue toe syndrome
II	Nails
	Blue chromonychia
III	Glands
	Blue pseudochromhidrosis
IV	Procedural
a)	Blue light
b)	Blue peel
c)	Blue-green and Blue white fluorescence – Woods lamp
d)	Blue toning PTP laser technology
e)	Blue color in dermoscopy
f)	Blue Stains
	1. Toluidine blue
	2. Methylene blue
	3. Alcian blue
	4. Trypan blue
	5. Evans blue
	6. Luxol fast blue
	7. Lactophenol cotton blue
	8. Chicago blue stain
V	Miscellaneous
a)	Blue kit
b)	Blue color blister pack – MDT PB
c)	Blue Cheese – EAC



Figure 1: Blueberry muffin baby – left thigh.



Figure 2: Blue nevus.

pubis (the pubic or crab louse); [11]. Though rare maculae ceruleae, secondary to pediculosis capitis bite, have been reported [12].

h) Blue sclera

It is seen in patients with Ehlers-Danlos syndrome – characterized by increased skin elasticity, fragility, and vulnerability of the vessels, weakness of the joint ligament apparatus. It is also seen in Pseudoxanthoma elasticum, Osteogenesis imperfecta [13], Marfan's syndrome, and Alkaptonuria.

i) Blue neck syndrome

In Northern Kerala, it's a common condition, and the affected skin has a dull, dry matt surface with a characteristic bluish-black color, with a distinctive pigmentation of the skin folds and the surface clearly visible as nonpigmented grooves. KOH mounts of skin scrapings from the neck, when examined under a microscope, show nematode larvae [14].

j) Blue Scrotum Sign of Bryant

JH Bryant described scrotal ecchymosis associated with a ruptured abdominal aortic aneurysm (AAA); [15]. Non-traumatic discoloration beneath the intact scrotal or penile epithelium can occur due to blood's extravasation in the retroperitoneum. After AAA rupture, ecchymosis typically appears within three to six days.

K) Blue ball sign:

In lymphogranuloma venereum, it's a sign of impending rupture where underlying abscess with edema and livid color of the overlying skin over bubo is seen.

l) Blue-grey stippling (Hermans spot) and Punctuate blue-white lesions (Kopliks spot)

In measles, blue-grey stippling may appear on tonsils (Hermans spot). The punctuate blue-white lesions surrounded by erythematous areola on buccal mucosa against the second molar (Kopliks spots) are pathognomonic and appear on 2-4 days of fever. Similar spots may be seen at conjunctivae at the medial canthi [16].

m) Acute idiopathic blue finger: Achenbach's syndrome, also known as paroxysmal finger hematoma:

It is characterized by the presence of acute bluish discoloration of fingers, accompanied by pain [17]. It is a benign condition and has a self-limiting course. Spontaneous subcutaneous bruising is believed to be the underlying mechanism [18].

n) Blue man syndrome

It occurs due to excessive exposure to chemical compounds of the element silver or silver dust and due to the adverse effects of the amiodarone drug [19].

o) Sea blue histiocytosis syndrome

It is an uncommon systemic histiocytosis that Silverstein first coined in 1970. It is generally observed with lipid storage diseases and in various hematological conditions, but the syndrome's exact pathogenesis is still not well established [20,21]. It is characterized by organomegaly, most commonly with hepatosplenomegaly and numerous histiocytes in the bone marrow. These histiocytes contain numerous cytoplasmic granules that stain deep blue with the May-Grunwald Giemsa stain [22].

p) Blue hands

It occurs due to either lack of oxygen in the blood or freezing temperatures. It is a symptom of cyanosis.

q) Blue toe syndrome

It is also known as Trash Foot, or Purple Toe Syndrome [23] "Blue toe syndrome" (BTS) refers to the acute onset of painful purple digits in the absence of evident trauma, cold-associated injury, or disorders that induce generalized cyanosis [24].

2. Nails

Blue chromonychia

Blue discoloration of nails is most commonly drug-induced. Minocycline causes bluish discoloration due to the dermal deposition of iron chelates of the nail bed with sparing of lunulae in association with cutaneous and mucosal discoloration [25]. Antimalarials probably due to the deposition of melanin and hemosiderin cause blue brown discoloration [26]. Chemotherapeutics like cyclophosphamide, doxorubicin, and bleomycin cocktail therapy cause blue chromonychia due to matrix melanocyte activation. A similar discoloration is also reported with the use of azidothymidine for AIDS [27]. Besides drugs, other causes of blue nails include exposure to silver salts either occupationally or as medications, Wilson's disease (causing Azure lunula), glomus tumor of a nail, digital arterio-venous malformation, hereditary acrolabial telangiectasia, and advanced AIDS infection [27].

3. Glands

Blue pseudochromhidrosis

It has been reported in patients occupationally exposed to copper salts [28] and also noted with antiepilepsy drug topiramate [29].

4. Procedural

a) Blue light

Blue light therapy is non-invasive and is used to treat inflammatory acne. Narrowband blue light (415nm) has a bactericidal effect on *Propionibacterium acnes* [30]. It also leads to skin damage and accelerated aging.

b) Blue peel

The Blue peel is an in-office chemical peel that exfoliates surface layers of skin to treat acne, fine lines and wrinkles, scars, hyperpigmentation, and uneven tone texture. The peel's active ingredient is trichloroacetic acid (TCA).

c) Blue-green and Blue white fluorescence

In Woods lamp, dermatophytes of the *Microsporum* genus (Blue-green) and *T. schoenleinii* (Dull-blue) causing tinea capitis fluorescence, and the chemical responsible for the fluorescence is pteridine [31]. In depigmented or hypopigmented lesions, there is no or less melanin in the epidermis. Hence, there is a window through which the light-induced dermal collagen autofluorescence can be seen. Due to the abrupt cut-off in lesional skin visible emission, the margins of depigmented or hypopigmented spots appear under Wood's light sharper. The lesions due to auto-fluorescence appear bright blue-white [32].

d) Blue toning photoacoustic twin pulse (PTP) laser technology

PTP gives two times of Q energy (Toning Energy) for a pulse. Blue toning is a unique energy dispersion of 5:5, 6:4, 7:3, and 8:2. Blue toning gives 30 Qs in only one second. (15 Hz x 2 Qs). 1st Q and 2nd Q energy ratio is 6:4 for the best toning results for each skin type and user preferences.

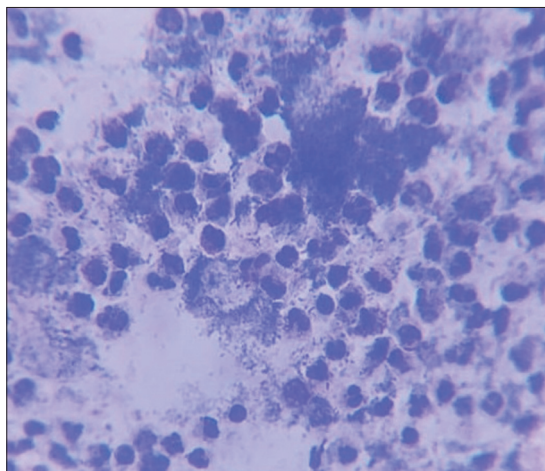


Figure 3: Methylene blue stain.

e) Blue color in dermoscopy

The blue color in lesions that are not vascular in origins are mostly related to a dermal localization of melanin arranged as either extracellular melanin granules or as clusters of cells (e.g., melanocytic nests in a nevus or aggregates of basaloid neoplastic cells in basal cell carcinoma) or located within cells arranged as solitary units (e.g., melanophages). Thus, blue color can be found in a wide range of nonmelanocytic and melanocytic lesions under dermoscopy [33].

f) Blue Stains

1. Toluidine blue

It is a basic thiazine metachromatic dye with a high affinity for acidic tissue components [34]. It stains polysaccharides purple and nucleic acid blue and also increases the sharpness of histology slide images. This stain is incredibly helpful in evaluating patients with pathological conditions involving mast cells, including cancers and allergic inflammatory diseases.

2. Methylene blue

It is a handy, colorful compound used as a dye to help them see life under the microscope. Stain in bacteriology; reagent for several chemicals; as a mixed indicator; as redox colorimetric agent. Targeting agent for melanoma (Fig. 3); [35].

3. Alcian blue

Alcian blue is a family member of basic polyvalent dyes, of which the Alcian blue 8G has been historically the most reliable member and the most common [36]. It is used to stain acidic polysaccharides such as glycosaminoglycans in cartilages and other body structures, some types of mucopolysaccharides, sialylated glycocalyx of cells, etc

4. Trypan blue

It is derived from toluidine, and it is so-called because it can kill the parasites that cause sleeping sickness trypanosomes. An analog of trypan blue, suramin, is used pharmacologically against trypanosomiasis. It is commonly used in microscopy (for cell counting) and laboratory mice to assess tissue viability [37]. The method cannot distinguish between necrotic and apoptotic cells. It also may be used to observe fungal hyphae [38] and stramenopiles.

5. Evans blue

A passive cutaneous anaphylaxis test (an animal model test for inflammatory reaction) can detect IgG antibodies, which cannot form precipitates with the antigen [39].

Here, the patient's serum containing the antibodies is injected intradermally into the skin of a guinea pig. After an interval of 4–6 hours during which the IgG antibodies get fixed to the guinea pig's cutaneous mast cells in that area, the guinea pig is given an intravenous injection containing the antigen mixed with an aqueous solution of Evans blue. Evans blue has an affinity for serum albumin and remains in the circulation. When the antigen combines with the antibody on the guinea pig's cutaneous mast cells, the mast cells release their histamine, which increases the permeability of cutaneous capillaries and causes leakage

of Evans blue. This produces a blue spot on the skin at the site where the patient's serum had been injected.

6. Luxol fast blue

It is a copper-phthalocyanine dye soluble in alcohol and is attracted to bases found in the myelin sheath's lipoproteins [40,41]. Under the stain, myelin fibers appear blue, neutrophil appears pink, and nerve cells appear purple. It is as used as staining for the detection of nerve involvement (myelin) in leprosy.

7. Lactophenol cotton blue

It is the most used staining method and for the observation of fungi. Lactic acid preserves the fungal structure and clears the tissue while phenol acts as a disinfectant, and cotton blue imparts blue coloration to the fungal spores and hyphae [42].

8. Chicago blue stain

It is a direct disazo dye compound. It stains the fungal hyphae and spores a contrast blue against a light purplish background of cellular debris [43]. In immunofluorescence histochemistry, it is also used as a counterstain for background autofluorescence.

g) Miscellaneous

a. Blue kit

In Genital Ulcer Disease Non-Herpetic (GUD-NH) - for patients allergic to penicillin blue kit containing 30 tablets/capsules of Doxycycline (100mg) BD for 15 days & 1 tablet of Azithromycin (1 gram) is given (Fig. 4).

b. Blue color blister pack - MDT PB

In Hansen disease, MDT PB type in children (10–14years) blue color blister pack has been given, and it contains once a month: Day 1 – 2 capsules of rifampicin (300 mg+150 mg) – 1 tablet of dapsone (50 mg) Once a day: Days 2–28 – 1 tablet of dapsone (50 mg); (Fig. 5).

c. Blue cheese - EAC

Erythema annulare centrifugum is a chronic reactive form of annular erythema characterized by erythematous, circular, arciform, and polycyclic lesions, with a characteristic delicate scale behind the advancing edge ('trailing scale') and was noted to occur as a hypersensitivity reaction to mold in blue cheese [44].



Figure 4: Blue kit.

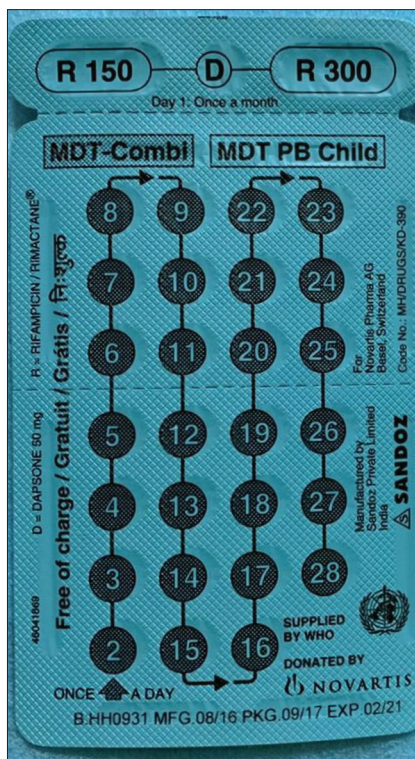


Figure 5: Blue color blister pack – MDT PB.

CONCLUSION

We see here that there are several blues in dermatology, and as a dermatologist, it would be imperative to know

how various blues present to arrive at a conclusive diagnosis and use it in multiple indications, follow-up, and better therapeutic outcomes.

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Source of Support: Nil, **Conflict of Interest:** None declared.