

## Dermatopathologic external agents and artifacts

By Lisa Fronek, DO, Taylor Gray, DO, and Thomas Davis, MD



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H&E Findings Related to Trauma, Treatment, and Metabolic Disorders			
Agent	Histopathologic Findings	May Mimic	Additional Notes
Aluminum chloride	-Light blue to gray histiocytes with a granular cytoplasm +/- calcification -Overlying epidermis may be effaced with horizontal fibrosis, vertical vessels, and collagen alteration indicative of scar -Collagen bundles may appear degenerated	Infectious etiology with parasitized histiocytes (histoplasmosis, leishmaniasis)	-PAS, GMS, Giemsa, and/or CD1a stains may be used to exclude an infectious process if needed -The presence of aluminum chloride can be helpful in identifying the previous biopsy site in the case of subtle or superficial scars
Monsel's solution (ferric subsulfate)	-Brown to black granules of iron-laden pigment within macrophages in the dermis -Overlying epidermis may be effaced with horizontal fibrosis and collagen alteration indicative of scar	Tattoo depending on pigment	Stains <b>positively with iron stains such as Perls/Prussian blue (identifies hemosiderin)</b>
Formalin pigment (acid formaldehyde hematin)	Brown precipitate that occurs due to hemoglobin in formalin with a pH < 6		Commonly seen in areas with numerous red blood cells
Keratin granuloma	-Small fragments of keratin surrounded by granulomatous response +/- cholesterol clefts -May see fragments of an epidermal inclusion cyst or pieces of hair follicle deeper to the granuloma	Poly-L-lactic acid (polarizable spiky translucent islands surrounded by granulomatous inflammation)	<b>Non-polarizable;</b> helps distinguish from foreign body and PLLA
Tattoo	Variably sized particles of pigmented material within the dermis. Pigment may be extracellular or within macrophages, +/- granulomatous response	Blue nevus, Nevus of Ota/Ito (melanin pigment is present within melanocytes and macrophages but not extracellular in location)	Black is most common tattoo color (carbon); less commonly red (mercuric sulfide/cinnabar) or yellow (cadmium)
Splinter	-Square or rectangular brown fragment of plant material with many linear striations throughout -Prominent cell walls	Suture	Consider microbial colonization → look for organisms and perform PAS, GMS stains as needed
Suture	<b>-Birefringent braided suture material</b> -Granulomatous response	Splinter	Polarizable
Amalgam tattoo	-Pigmented lesion in the oral cavity -May see black to brown pigment within the BMZ and deposited on collagen and elastic fibers.	Cosmetic tattoo	No significant inflammatory response
Argyria	Small black pigment granules located in basement membrane of <b>eccrine coils</b>		No significant inflammatory response
Ochronosis	Yellow-light brown " <b>banana-shaped</b> " figures within the dermis	Alkaptonuria (identical histological findings)	
Triamcinolone	Blue amorphous or slightly bubbly and granular material occasionally surrounded by histiocytes or deposited in a scar or keloid	Focal mucinosis (stains positively with mucin stains and may be more superficial in the dermis)	Stains negative for mucin stains (Alcian blue pH 2.5, colloidal iron, etc.)
Gel foam	Amorphous, kite-shaped basophilic material with prominent granulomatous reaction surrounding	HA filler response	Stains negative for mucin stains

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Artifacts Related to Cosmetic Treatments			
Agent	Histological Findings	May Mimic	Additional Notes
Calcium hydroxylapatite (Radiesse)	-Dark <b>brown/green spherical calcific deposits</b> -Generally uniform in size and shape -Variable granulomatous response	Polymethylmethacrylate	<b>Non-birefringent</b>
Hyaluronic acid (Juvederm, Restylane, Revanesse, RHA)	-Pale blue/purple amorphous non-encapsulated material within the dermis -Less granulomatous response	-Focal mucinosis (more superficial in the dermis) -TAC (bubbly and granular)	HA stains (Alcian blue pH 2.5, colloidal iron) positive
Poly-L-lactic acid (Sculptra)	-Multiple well-distributed triangular clear spaces, likened to " <b>spiky translucent islands</b> " within the dermis -Granulomatous response	Keratin granuloma	<b>Polarizable</b>
Polymethylmethacrylate (Artefill, Bellafill)	-Monomorphic clear spheres with surrounding histiocytes	Calcium hydroxylapatite will have more purple, basophilic appearing spheres	Non-birefringent
Silicone	-Empty vacuoles of varying sizes (pseudocystic spaces) surrounded by foreign body giant cells and fibrotic change	-Paraffin -Liposarcoma	
Paraffinoma	-“Swiss cheese”- like holes (pseudocystic spaces) within dermis and fat -Varying amount of fibrosis and granulomatous response	-Silicone	-Secondary to injection of exogenous oils, vitamin E, paraffin injection -Lipid stains (oil red O) will be positive on frozen section material -Also referred to as sclerosing lipogranuloma

Artifacts Related to Mohs Micrographic Surgery	
Agent	Histological Findings
Freeze artifact	Epidermal homogenization with vacuolated keratinocytes; if extensive may produce subepidermal blister
Electrocautery	Keratinocytes appear vertical and parallel to one another; homogenized collagen underneath
Air bubble	Clear spaces due to separation between slide and cover slip
Nicks	Vertical marks made by Mohs surgeon to convey specimen orientation
Venetian blind pattern	Significant tissue folding, wrinkling and bands of light and dark staining within the tissue -Indicative of a particularly dense tissue specimen, loose blade within microtome, or dull surgical blade

### Abbreviations:

H&E: hematoxylin and eosin  
BMZ: basement membrane zone  
PAS: Periodic acid-Schiff  
GMS: Grocott's methenamine silver  
TAC: triamcinolone  
HA: hyaluronic acid  
RHA: resilient hyaluronic acid  
PLLA: Poly-L-lactic acid

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