Skin Findings at Autopsy

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Background

Examining the skin during an autopsy can reveal information about the deceased, ranging from injuries, to underlying medical conditions, to syndromes. It is important to distinguish postmortem artifacts from pathologic findings, document the gross skin examination, and interpret histologic findings in the context of clinical history.

The Fitzpatrick Skin classification is commonly used to identify an individual's skin type and their risk of sunburn or susceptibility to UV-induced skin damage. It is broken into 6 categories as noted below:

Type I	Highly sensitive, always burns, never tans. eg: Red hair with freckles
Type II	Very sun sensitive, burns easily, tans minimally. eg: Fair skinned, fair haired Caucasians
Type III	Sun sensitive skin, sometimes burns, slowly tans to light brown. eg: Darker Caucasians
Type IV	Minimally sun sensitive, burns minimally, always tans to moderate brown. eg: Mediterranean type Caucasians, some Hispanics
Type V	Sun insensitive skin, rarely burns, tans well. eg: Some Hispanics, some Blacks
Type VI	Sun insensitive, never burns, deeply pigmented. eg: Darker Blacks

Table 1: Fitzpatrick skin type scale. (Image credit: University Hospital Dorset).

Although the Fitzpatrick scale is subjective and does not capture the diversities of skin tones, identifying the decedent's' skin type on autopsy may be useful as many conditions appear differently on more pigmented skin and other conditions may be masked.

I. Postmortem Changes

Livor Mortis (postmortem hypostasis, postmortem lividity)

- Passive accumulation of blood within vessels in dependent parts of the body due to gravity that causes discoloration of skin.
- The timing of livor mortis is highly variable and unreliable for determining time of death. It usually begins to be visible 30 minutes to 1 hour after death and is fixed 6-8 hours after death. Blood is initially fluid after death because of the activity of fibrinolysin, but eventually becomes fixed due to hemolysis; once fixed, lividity does not shift its distribution when the position of the body changes.
- Livor mortis spares mechanically compressed areas since pressure prevents blood from filling subcutaneous veins.
    - This may present as odd patterns associated with wrinkled clothes, bedding, or other items.
- Findings may be less apparent if the patient was severely anemic, died of hemorrhage, or has darker skin.
- The color of livor mortis can vary, usually ranging from dark pink to purple. Different colors of livor mortis can be indicators of different disease states.

Color of Livor Mortis	Possible Cause
Pink	Carbon monoxide poisoning

Brown, Dark Blue/Gray	Methemoglobinemia
Bronze hypostasis	Clostridium perfringens septicemia

Table 2: Shades of livor mortis and potential causes

- The presence of extravascular blood differentiates a bruise from livor mortis since livor mortis is caused by intravascularly pooled blood.
    - Bruises result from injured blood vessels, thus, blood will be extravascular. See section on Bruises and Blood, below.

Cutis Anserina (postmortem goosebumps)

- Rigor of the piloerector muscles that are attached to the body's hair follicles. Can serve as an early sign of rigor mortis.

Decomposition

- Decomposition is highly variable and depends on many internal factors, including the decedent's health status, as well as external factors such as the ambient temperature. Each variable can affect the speed of decomposition, with chronically ill-patients / patients in poor health, and higher temperatures accelerating the process.
    - Putrefaction is a type of decomposition from bacterial activity and release of cellular enzymes in anaerobic breakdown of proteins that results in foul odors.
- An early external sign of putrefaction is green discoloration of the anterior wall of the right lower abdominal quadrant, occurring 18-36 hours after death. Here the cecum lies more superficially.
    - Color change occurs due to metabolism of hemoglobin to sulfhemoglobin by intestinal bacteria.
- "Marbling" over the trunk and limbs is another feature of postmortem skin decomposition, where blood vessels are visible on the skin as green-black streaks. This is caused by the spread of bacteria through the venous system and occurs around 24-48 hours after death.
- Livedo reticularis, a mottled or net-like skin discoloration, can be an ante or postmortem finding. It's often a result of the pooling of blood due to gravity and disruption of vascular function.
- Blister formation, with skin and hair breakdown, occurs at 3 to 5 days. From 3 to 4 weeks, hair and nails detach from the body.

Histologic Evaluation of Postmortem Changes

- Normal postmortem tissue changes include:
    - Focal skin slippage: separation at the dermal-epidermal junction
    - Dermal degeneration: can occur within a few days and is characterized by lessening density of tissue, prominence of elastic fibers with splitting, and deterioration into eosinophilic fragments.
    - Eccrine duct necrosis: can occur later (4-7 days) with vacuolization and ballooning of epithelial cells, indistinct cytoplasmic borders, and decrease in nuclear detail.

II. Injuries

Bruises and Blood Collections (contusions, hematomas, ecchymoses)

- Definitions:
  - Contusion: bruising caused by blunt trauma
  - Hematoma: closed space collection of blood
  - Ecchymosis: blood spillage into a space from peripherally associated trauma can appear at the injury site or at a more distant site due to gravity or tissue planes:
    - Periorbital ecchymosis and battle signs from skull fractures vs contusion of the eye (punch to the eye), vs antecubital ecchymosis at a site of venipuncture.
- Bruises (contusions), resulting from broken blood vessels, are often seen with a history of blunt trauma, although they may be associated with impact and/or other types of wounds.
  - It is important to note that dating of contusions, histologically or otherwise, is challenging and without wide consensus.
- Excessive bruising may be a sign of an underlying bleeding disorder:
  - These can be congenital such as hemophilia or Von Willebrand's disease and others.
  - Acquired conditions associated with increased bleeding include:
    - Liver disease, Vitamin K deficiency, disseminated intravascular coagulation, diseases of bone marrow, use of antithrombotic medications, or thrombocytopenias
- Patterned contusions can be associated with different causes / mechanisms of injury, some of which may not be pathologic.
  - Cupping (left) and coin-rolling (right) are practices that result in specific bruise patterns.

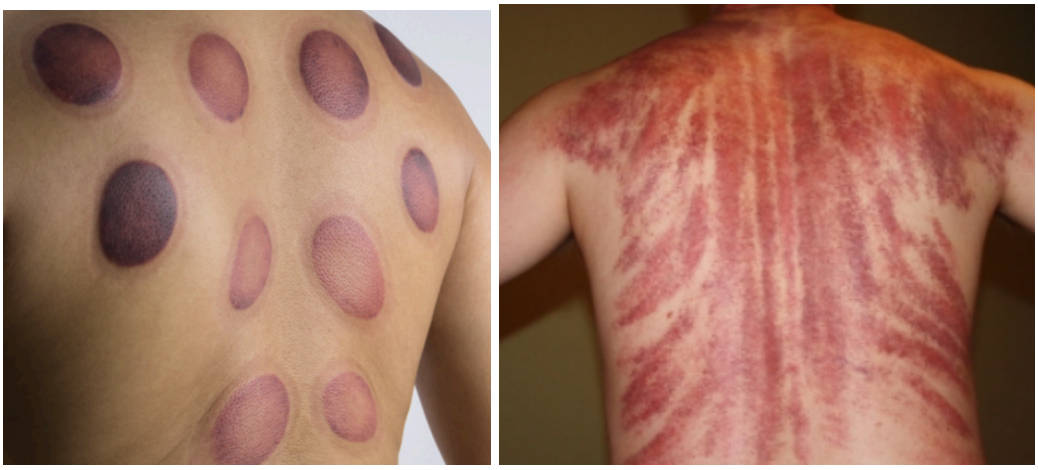

Image: Bruising pattern associated with cupping which is typically used to increase blood flow to muscles to promote improved circulation and healing (Left, Image credit: Hughston Clinic). Example of bruising seen with coin rolling (also known as gua sha)

which is traditionally a South East Asian practice aiming to rid the body of negative energies (Right, Image credit: Stanford Medicine)

- Color - highly variable based on individual physiology and health status:
    - Generally, for rough estimation, red/purple indicate early bruising (0-3 days), green indicates ~7 day old bruising, yellow indicates ~7-14 day old bruising, and bruises are usually resolved in over 2 weeks.
- Accompanying injuries (lesions, abrasions)
    - The amount of bruising at the wound margins is used to determine the sharpness of the injuring object.

Examination of Bruises at Autopsy

- All bruising may not be apparent on the skin's surface and may only be visible deeper in the tissue
    - Factors such as skin tone, age, and location of injury can affect how easily a bruise can be identified externally
    - If trauma is thought to be involved in the cause of death, a more in depth examination may be required to identify hematoma in the musculature.
    - Dedicated neck dissection, examination of the subgaleal tissues of the scalp, or special dissections for impact sights (vehicle) may be required depending on circumstances.

Histologic Evaluation of Bruises

- Dating of bruises can be **estimated** on histology.
    - Neutrophils seen at around 4 hours after initial bleeding, indicated fresh bleeding
    - Macrophages begin to migrate at around 5 hours after initiation of bruise. Erythrocytes are seen within macrophages around 15-17 hours after the injury
    - Hemosiderin laden macrophages are seen 2-8 days after initial injury.
    - Significant hemosiderin deposits (>20% of the microscopic field) suggest a bruise that is older than 1 week.
    - Hematoidin (bilirubin) is seen in skin and subcutaneous tissue at around 9 days.

Time interval	*Histology*
Less than 4 hours	No distinct signs of inflammation. Histological distinction between antemortem and postmortem skin wounds not possible
4–12 hours	4 hours: some polymorph leucocytes perivascularly 8–12 hours: polymorphs, macrophages, and activated fibroblasts form distinct peripheral wound zone Polymorphs more frequent than macrophages (5:1). Imminent necrosis in central zone
12–48 hours	16–24 hours: relative number of macrophages increases, with polymorph to macrophage ratio falling to 0.4:1 After 16 hours older fibrin stains bright red with Martius scarlet blue, whereas before 16 hours "newer" fibrin stains yellow 24 hours: the number of polymorphs and amount of fibrin increase to maximum (remain at this value for 2–3 days) Cut edge of epidermis shows cytoplasmic processes 24–48 hours: epidermis migrates from the incised edge towards the centre of the wound At 32 hours and after, necrosis is apparent in the central wound zone 48 hours: macrophages reach maximum concentration in peripheral zone
2–4 days	2–4 days: fibroblasts migrate from the nearby connective tissue to the wound periphery 3 days: epithelialisation of small wounds and abrasions complete; thereafter regenerated epidermis becomes highly stratified and thicker than the normal surrounding epidermis 3–4 days: capillary buds appear
4–8 days	4 days: first new collagen fibres seen 4–5 days: profuse ingrowth of new capillaries; capillaries continue to proliferate until 8th day 6 days: lymphocytes reach maximum concentration in wound periphery
8–12 days	Decrease in number of inflammatory cells, fibroblasts, and capillaries; increase in the number and size of collagen fibres
>12 days	12 days: definite stage of regression of cellular activity in both epidermis and dermis. Vascularity of dermis diminishes. Collagen fibres restored. Epithelium shows stainable basement membrane At 14 days fibroplasia reaches its peak. Thereafter there is gradual shrinkage and maturation of connective tissue in the wound

Table 3: Interpreting bruises at autopsy, (Image credit: Vanezis (2001))

Lacerations

- Blunt force applied to the skin, especially over bony structures such as the scalp or joints, causes the skin to stretch, rupture, and tear, resulting in a laceration.
    - Lacerations are characterized by irregular margins and bridging fibers (typically nerves, fibrous bands of fascia, or medium-sized blood vessels that have resisted the injuring force).
- Skin tension must be taken into account when determining a wound's original morphology.
    - Skin tension lines map the direction of maximum tension of the skin. These lines differ from person to person. One well-known map of skin tension lines are Langer lines.

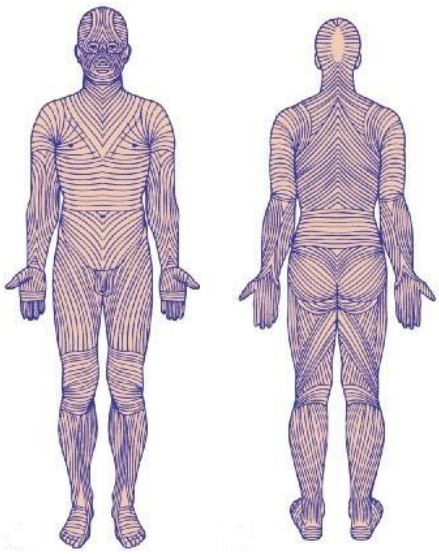

Image: Langer lines, mapping axes of mechanical tension in the skin, produced mostly by dermal connective tissue (Image credit: Primary Care Notebook).

- Elastic fibers perpendicular to the wound cause it to become rounder, while parallel tension lines distort the appearance by lengthening the wound and making it appear more slit-like.

Abrasions (skinned knee / road rash): are the most common blunt force injuries that break skin.

Earliest, Routine, and Latest Appearances of Gross Changes of Abrasions

Gross Changes	Earliest Appearance	Routine Appearance	Latest Appearance
Bright red	10 min	0–4 h	5 h
Reddish scab	6 h	12–24 h	68 h
Brownish scab	18 h	24–72 h	132 h
Dark brown scab	44 h	4–6 d	144 h
Black scab	120 h (5 d)	7–14 d	21 d*
Scab fallen off at margin	144 h (6 d)	7–14 d	15 d†
Scab fallen off completely	11 d	>2 wk	17 d‡

*With comorbid conditions, a black scab was observed up to 35 days.

†With comorbid conditions, a scab has fallen off at margin up to 45 days.

‡With comorbid conditions, a scab has fallen off completely up to 27 days.

Table 4: Color of abrasion relating to timing of injury. (Image credit: Vinay et al (2017))

Earliest and Routine Appearances of Common Histologically Detected Changes of Abrasions

Microscopic Changes	Earliest Appearance	Routine Appearance
Congestion/hemorrhage	10 min	0–4 h
Edema formation	15 min	0–4 h
Margination of polymorph cells	30 min	0–4 h
Early polymorph infiltration	6 h	4–12 h
Predominant polymorph infiltration	12 h	12–24 h
Mononuclear cell infiltration	24 h	24–72 h
Appearance of fibroblast	71 h	71–78 h
Granulation tissue deposition	72 h	4–6 d
Collagen formation	96 h (4 d)	7–14 d
Regression phase	213 h (9 d)	>2 wk

Table 5: Earliest and routine appearances of microscopic changes in abrasions (Image credit: Vinay et al (2017))

III. Non-traumatic skin Findings:

Scars

- Patient may have a history of mechanical injury (blunt force, sharp force, or firearms) or surgery
- Comorbid conditions may also affect wound healing such as diabetes , hypertension, sepsis, malnutrition, etc.

Examination of Scars at Autopsy

- Well-healed traumatic scars can be difficult to distinguish from surgical scars. Surgical scars tend to be more uniform and straight or slightly curved. They are found in areas corresponding to surgical procedures, and scars from common procedures are typically readily identifiable . For example, an open appendectomy will have a scar at the lower right quadrant of the abdomen.

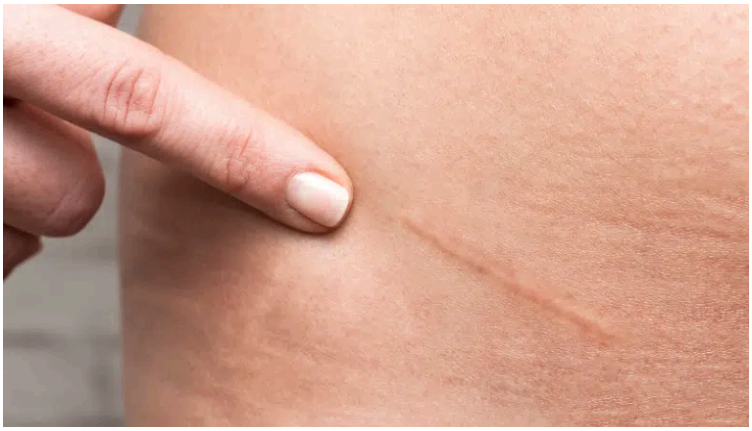

Image: Example of healed appendectomy scar located in the right lower quadrant. (Image credit: Centre for Surgery)

- Surgical scars, especially laparoscopic scars, can easily be overlooked. Laparoscopic scars are frequently 3-4 scars on the abdomen, in the illustrated anatomic positions (figure)

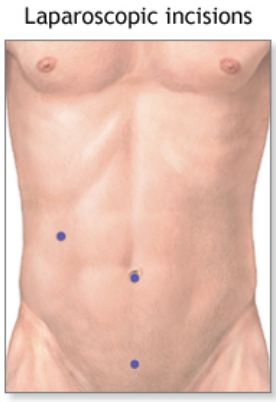

Image: Example of locations of scars from a laparoscopic appendectomy. (Image credit: MedlinePlus)

- The age of a scar can be estimated by counting the number of melanocytes in the epidermal basal layers. The number of melanocytes in the basal layer declines after about 10 years.
- Inflammatory phase (1-3 days after injury)
    - Vascular, hemostatic, and cellular response
- Proliferative phase (up to 10-14 days after injury)
    - Epithelial and connective tissue regeneration
- Reorganization or remodelling phase (several months after injury)

Petechiae:

- Petechiae are small, flat, round, and unraised red, purple, or brown spots that can look like a rash. When pressed, petechiae will remain the same color (non blanching)
    - Most often seen externally in the conjunctiva, oral mucosa, and facial skin; internally on the epicardium and visceral pleura.
- Petechiae are caused by an acute rise in venous pressure → breaking small venules. They are a nonspecific finding and can be caused by a number of things, including:
    - Viral infections like COVID-19, mononucleosis, or the flu, or bacterial infections like strep throat or scarlet fever
    - Some antibiotics, antidepressants, blood thinners, anti-seizure medications, and non-steroidal anti-inflammatory drugs (NSAIDs)
    - Conditions like thrombocytopenia, platelet dysfunction, and coagulation disorders
    - Pressure from severe coughing, or from trauma such as strangulation or choking, which may be associated with facial congestion.
    - Petechiae can also develop post-mortem due to the body's position, developing in dependent areas of the body after death.

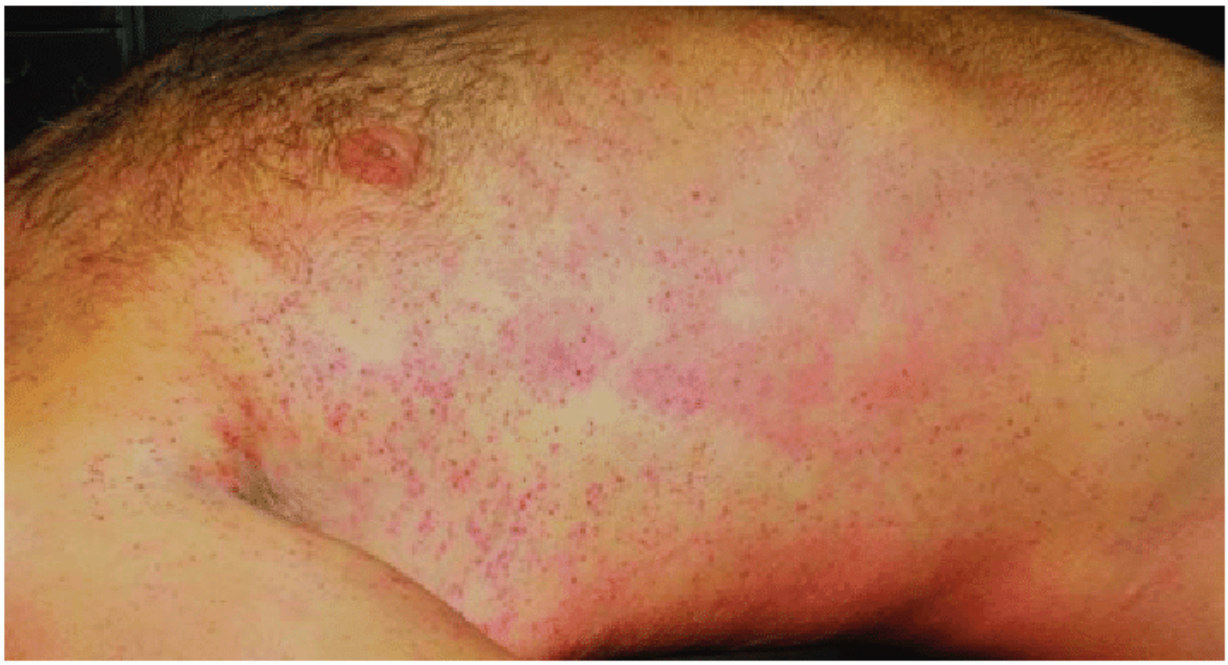

Image: Example of petechiae on torso of descendent who died secondary to DIC. (Image credit: MDPI)

Histologic Evaluation of Petechiae

- Minimal inflammation present when compared to other causes of rash
- Extravasated red blood cells can be seen but vessel walls themselves are usually intact.

Jaundice

- History of cirrhosis is the most common cause of jaundice, however, other etiologies are possible and should be considered.
  - Jaundice appearing over a few days to a week implies hepatitis, whether drug or toxin induced, viral or bacterial (i.e., leptospirosis).
  - Jaundice appearing over the course of weeks is considered subacute and can be caused by - hepatitis or extrahepatic obstruction due to malignancy, gallstone, chronic pancreatitis, or stricture in the common bile duct.
  - Jaundice of fluctuating intensity implicates gallstones, ampullary carcinoma, or possible drug hepatitis.
  - A past history of jaundice may implicate chronic hepatitis, cirrhosis, benign recurrent intrahepatic cholestasis, or a genetic nonhemolytic hyperbilirubinemia (i.e., Gilbert's or Dubin–Johnson syndrome).
- Surgical history; within the first three postoperative weeks, jaundice may be due to a variety of problems that include:
  - (1) increased bilirubin load related to hemolysis of transfused erythrocytes (especially stored blood), resorption of hematomas or hemoperitoneum and rarely to hemolysis of the patient's erythrocytes due to G-6PD deficiency, drug reactions or malarial parasites in transfused blood

    - (2) impaired hepatocellular function, which may be related to administration of halogenated anesthesia agents, exposure to other hepatotoxic drugs, sepsis, or hepatic ischemia associated with preoperative or intraoperative hypotension or hypoxia
    - (3) extrahepatic biliary obstruction, which may be secondary to inadvertent surgical injury to the common bile duct or occasionally to an unsuspected biliary calculus or to cholecystitis. Biliary tract surgery in the remote past may have produced a biliary stricture, although these are usually clinically evident within 2 years of operation.
- Other systemic conditions may have complications related to the liver. For example, patients with inflammatory bowel disease are predisposed to primary sclerosing cholangitis, cholangiocarcinoma, chronic hepatitis, cirrhosis, and hepatic amyloid. If a significant section of terminal ileum has been involved by or resected for Crohn's disease, the patient may also have gallstones. Cystic fibrosis, hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency and other hereditary metabolic diseases with prominent hepatic effects.

Examination of Jaundice at Autopsy

- Jaundice is often seen visually when bilirubin is >2-3 mg/dL.
    - It is classically appreciated in the sclera but can also be present in mucous membranes and skin (especially palms and soles).

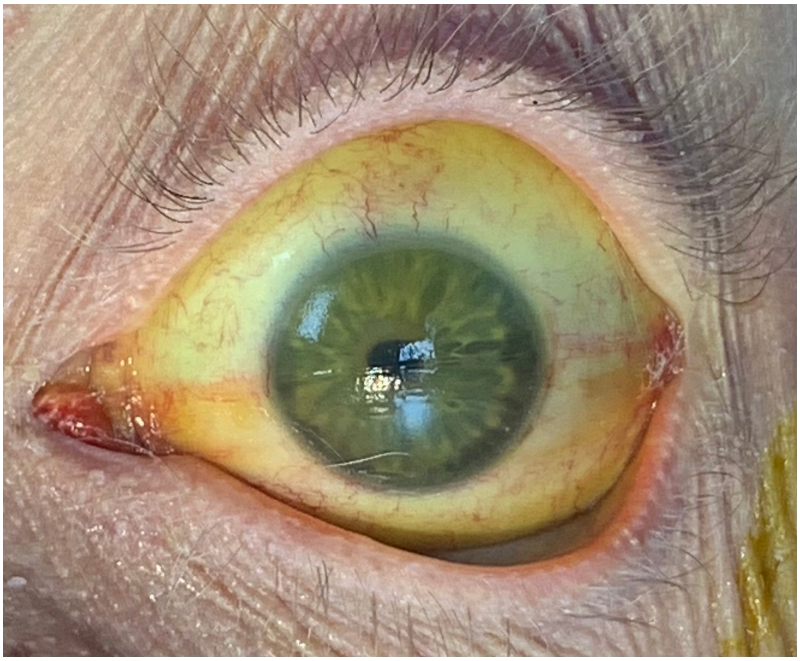

Image: Example of yellowing of the sclera due to jaundice. (Image credit: Darin Wolfe, MD)

- Yellowing of the skin in carotenemia (excessive carrot consumption) can be distinguished from jaundice by the absence of yellow discoloration in the sclera in the former.

Histologic Evaluation of Jaundice

- Skin biopsy usually is generally not required ante or postmortem to diagnose jaundice.
- If unknown, liver biopsy can be performed to identify the cause of jaundice.

Ceruloderma

- Blue skin can be caused by drug-induced pigmentation/deposition and is most commonly associated with amiodarone.
- Other causes include:
    - silver, minocycline, phenothiazines,, antimalarials, or clofazimine

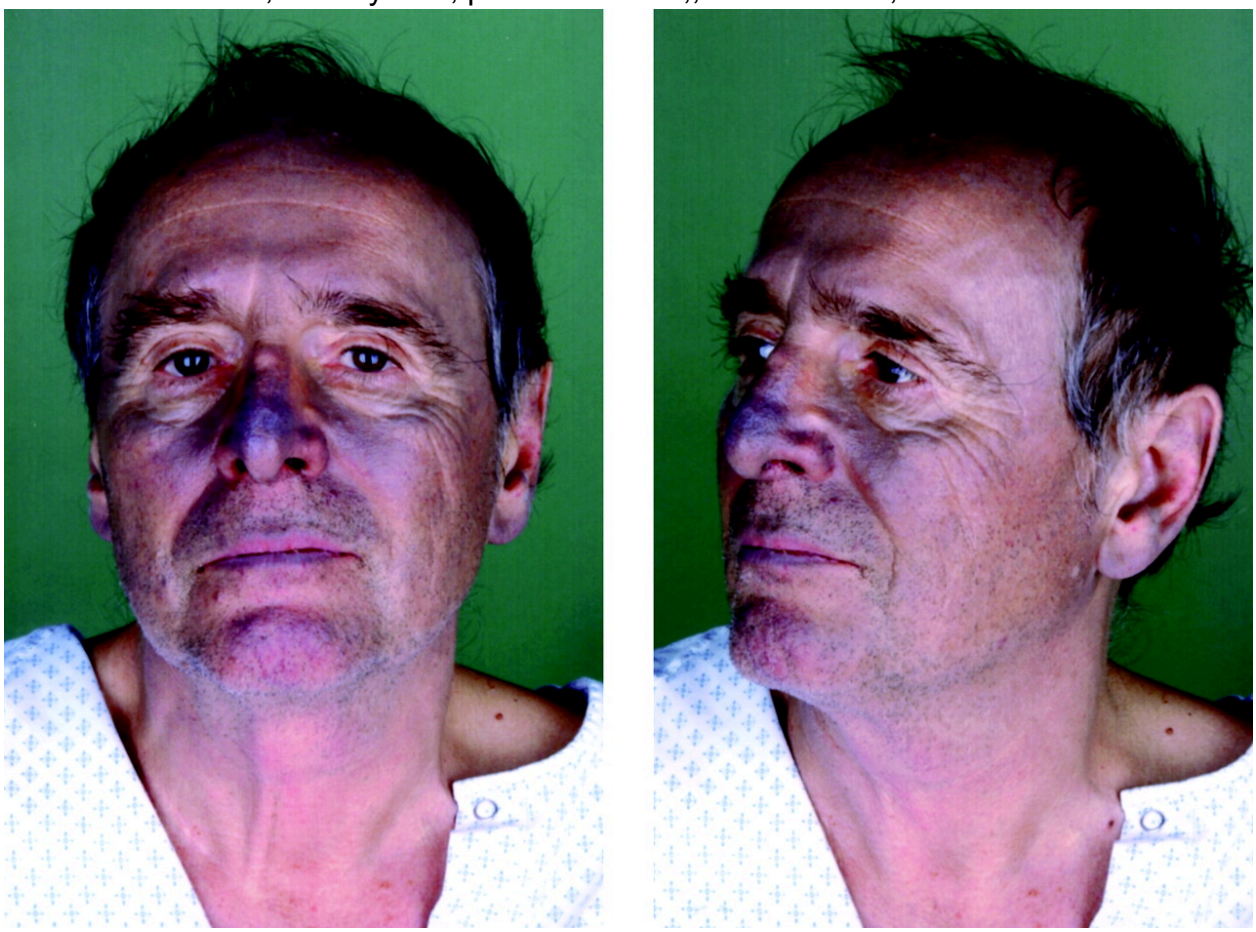

Image: Example of patient with ceruloderma secondary to amiodarone use. (Image credit: Journal of American Heart Association)

Ulcers

There are several types of ulcers that may be present at autopsy:

- Pressure Ulcers (Decubitus Ulcers):

    - These are caused by prolonged pressure on the skin, often in bedridden or immobile individuals, leading to tissue damage and ulceration.
    - Additionally, cachexia can increase the risk of pressure ulcers over bony prominences.
    - Decreased mobility, skin moisture, poor nutritional status, and loss of sensory perception are the most common risk factors.
    - Duration of immobility, diabetes, peripheral vascular disease, or malignancy can also make pressure ulcers more likely
- Lower extremity ulcers
    - Arterial Ulcers:
        - These ulcers result from poor blood circulation due to blocked arteries in the lower extremities. A decedent will likely have a history of peripheral artery disease.
        - Arterial ulceration often occurs after seemingly trivial trauma or as the result of localised pressure
    - Venous Ulcers:
        - These ulcers are caused by weakened veins, leading to poor blood flow.
        - Direct risk factors include: Varicose veins, deep vein thrombosis, chronic venous insufficiency, poor calf muscle function, arterio-venous fistulae, obesity, history of leg fracture
        - Chronic venous disease is the most frequent cause of leg ulcers.
    - Diabetic Foot Ulcer:
        - These ulcers are a specific type of neuropathic ulcer found in diabetic individuals.Multiple risk factors for these ulcers as diabetes itself is a risk factor for PAD, diabetic microangiopathy, and peripheral neuropathy.

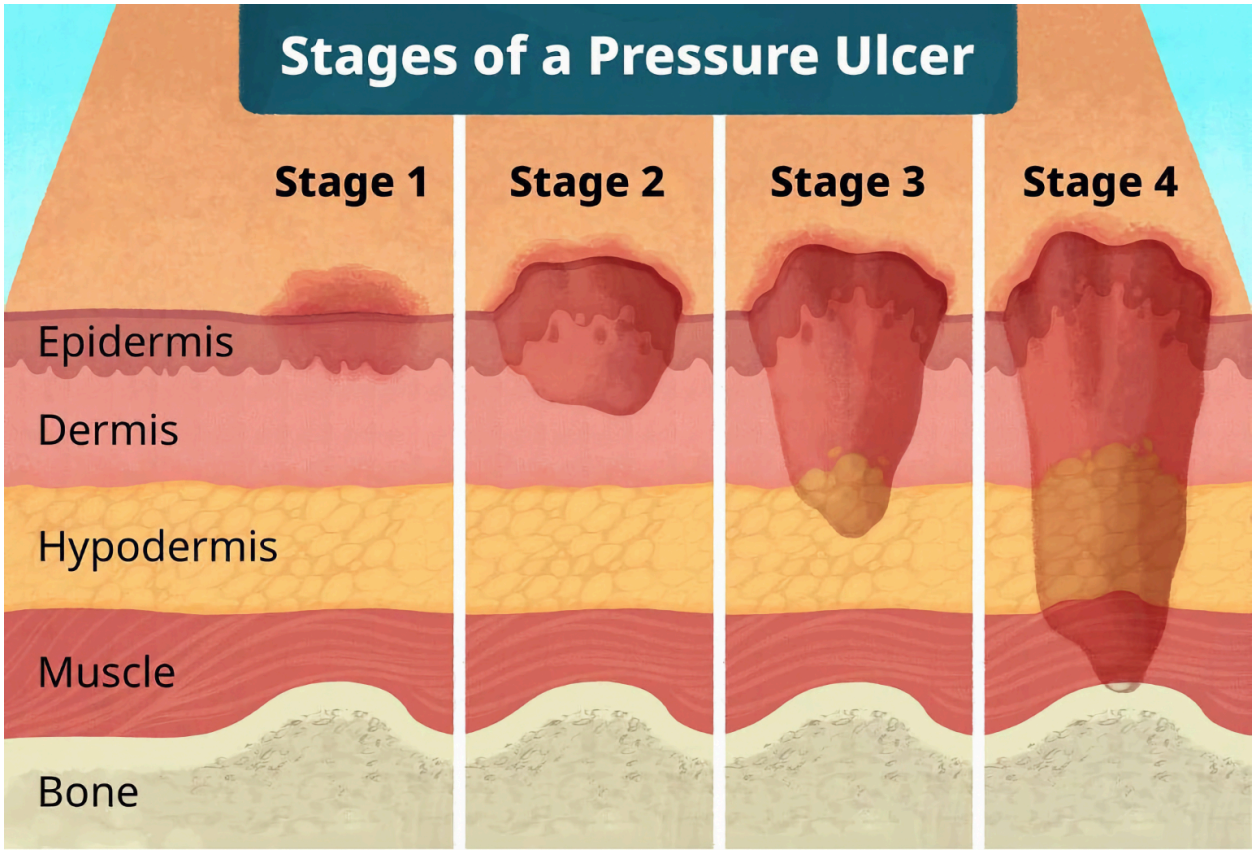

Image: Stages of a pressure ulcer depend on the depth of tissue affected. Note that Stage 1 ulcers do not have any erosion and are limited to superficial erythema. (Image credit: Mira Norian for Verywell Health).

Examination of Ulcers at Autopsy

- Pressure Ulcers (Decubitus Ulcers):
    - These ulcers are present 70% of the time at the sacrum, ischial tuberosity, and greater trochanter.
        - However, they can also occur in the occiput, scapula, elbow, heel, lateral malleolus, shoulder, and ear or any area where the decedent may have had prolonged pressure on the body.
    - Can vary in size, depth, and chronicity.
- Arterial Ulcers:
    - The ulcer appears “punched out,” with well demarcated edges and a pale, non-granulating, often necrotic base.
    - Typically found on the toes, heels, and bony prominences of the foot. The surrounding skin may be hairless, thin, and brittle, with a shiny texture (evidence of peripheral artery disease).
    - The toenails may thicken and become opaque and may be lost. Gangrene of the extremities may also occur.

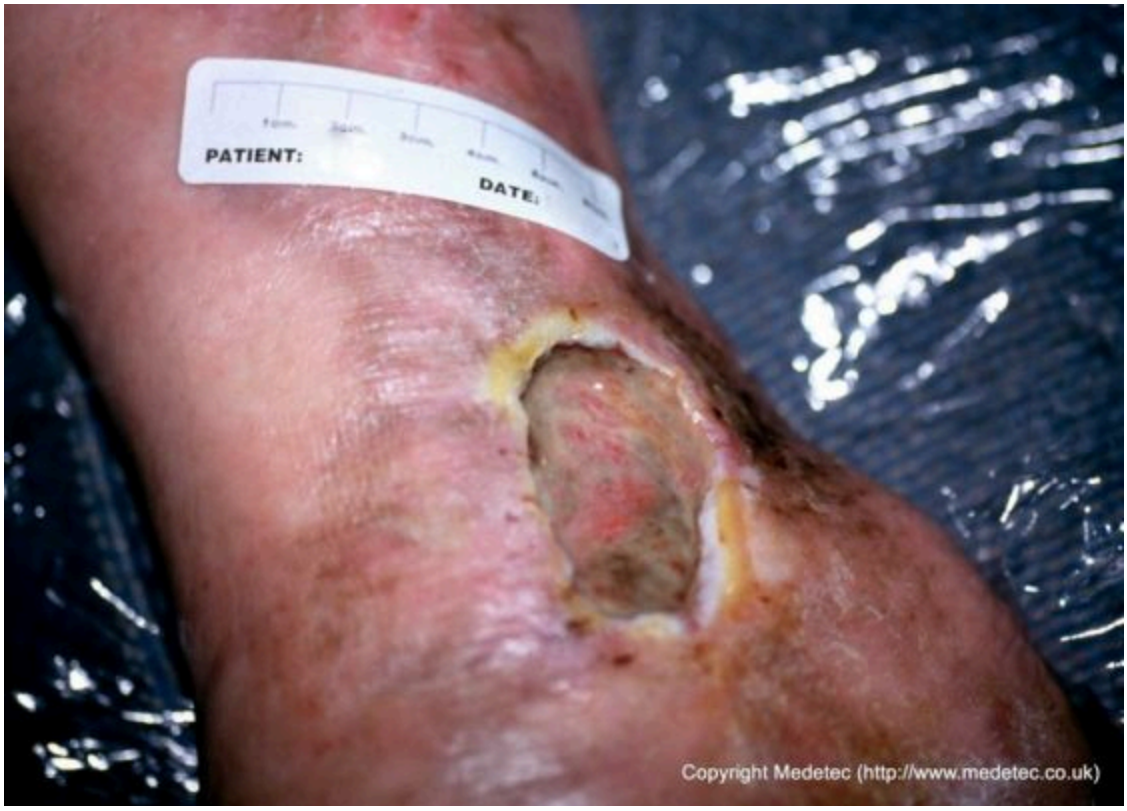

Image: Example of punched out arterial ulcer. (Image credit: Wound Source)

- Evidence of Peripheral Vascular Disease
    - Absence of hair on the distal lower extremities with shiny/smooth skin texture, toenail changes, edema or lipodermatosclerosis, and varicose veins.
- Venous Ulcers:
    - Often found on the lower legs and ankles, most commonly over the medial malleolus
    - Usually have more sloping edges (not as punched out)
    - Associated with limb edema, venous eczema, lipodermatosclerosis, and hemosiderosis.

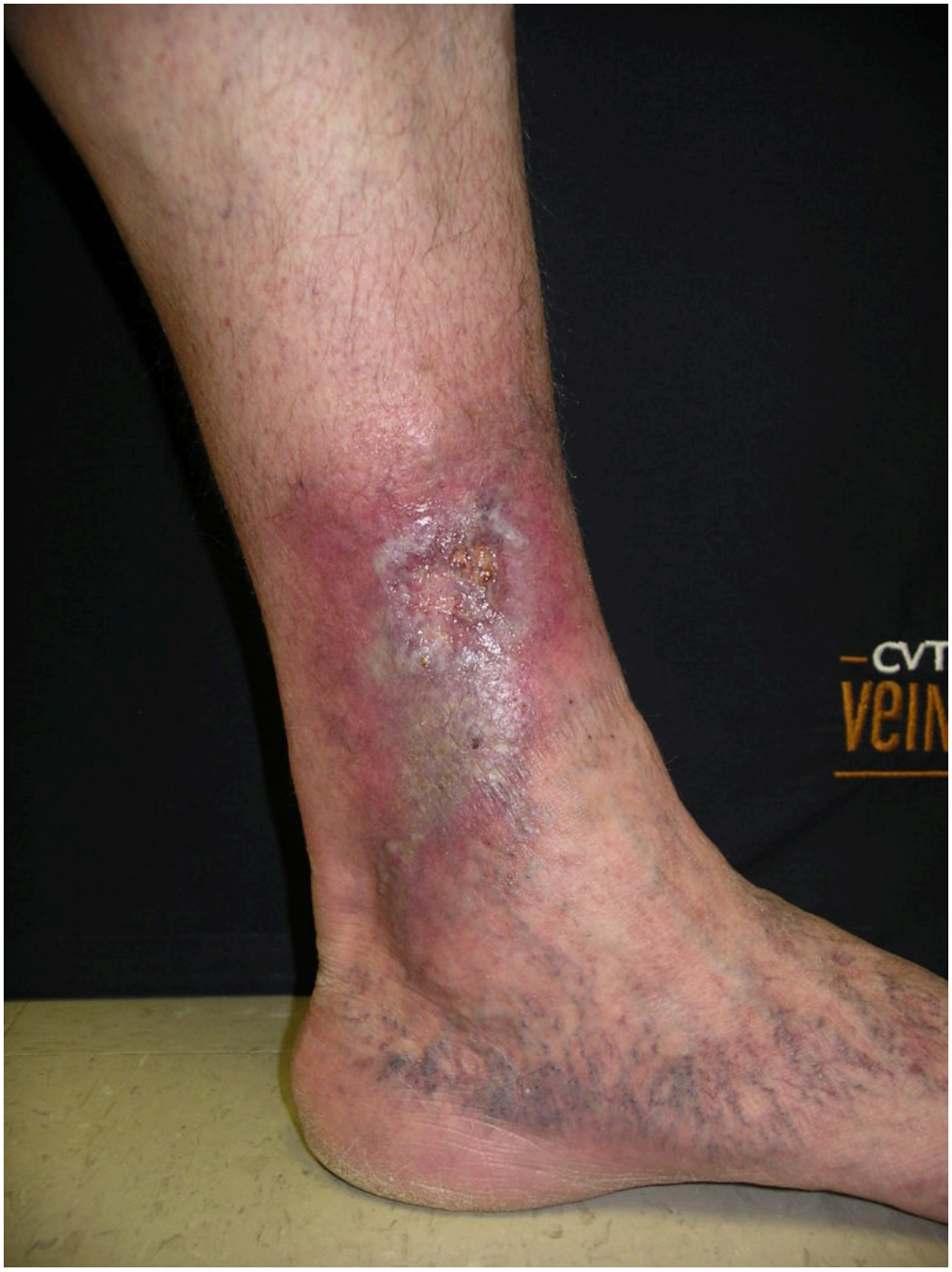

Image: Example of venous ulcer on the medial malleolus. (Image credit: CVT Surgical Center)

- Diabetic Foot Ulcers:
    - Often located on the feet, heels, or toes.

Histologic Evaluation of Ulcers

- Biopsy is usually not required, but may be considered if the lesion is at an uncommon site or the decedent does not have the appropriate risk factors
- Pressure Ulcer
    - Histopathological analysis of the edges and marginal areas of clinically advanced decubitus ulcers (clinical grade IV) shows heterogeneous features. The ulcer center can have varying appearances depending on the stage of disease. Early wounds exhibit a hemorrhagic crust, a perivascular lymphocytic infiltrate and a diffuse polymorphonuclear cell infiltrate. Healing decubitus ulcers show granulation tissue and edema as well as fibroblast and capillary proliferation. Long-standing, persistent decubitus ulcers are characterized by diffuse fibrosis, coagulation necrosis on the surface and the loss of epidermal appendages
- Arterial Ulcer
    - Biopsy of an ulcer related to PAD often shows necrosis and epidermal thinning in the epidermis and sclerosis and necrosis in the dermis. There may also be vessel thrombosis.
- Venous Ulcer:
    - On histology, venous ulcers may demonstrate spongiosis, hyperkeratosis and acanthosis in the epidermis and inflammatory infiltrate, edema, hemosiderosis and collagen bundle degeneration in the dermis. The vessels may appear dilated with reduced capillary density and extravasated red cells.
- Diabetic Foot Ulcer
    - Histopathological patterns for diabetic foot ulcers are not pathognomonic. Capillary thickening in non-ulcerated skin could hint to microangiopathic involvement in wound development, but are seen in other conditions . Fibrin cuffs, as seen in VLUs, have been both found in ischemic and non-ischemic diabetic ulcers

Black eschars

- Due to insufficient blood supply
- Most frequently seen in pressure ulcer wounds
    - Also seen in burns, infections (cutaneous anthrax, fungal infections), necrotizing spider bite sounds, and tick bites associated with spotted fevers.
- Calciphylaxis, a condition caused by calcium deposition in small arteries, can also cause black eschars:
        - Painful skin lesions that develop over several days to weeks will likely be in the patient's clinical history
    - Most commonly seen in end stage renal disease and hyperparathyroidism, although the exact etiology is unknown

Examination of Eschars Autopsy

- Crusted tissue that appears dark brown, black, or tan in color on the skin.
- May be boggy if associated with an ulcer

- Not to be confused with a scab, eschars are adherent

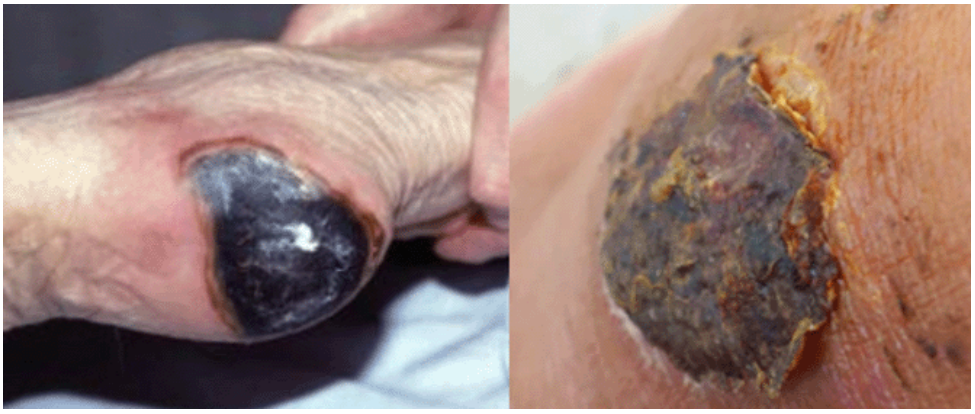

Image: The image on the left shows an eschar which is adherent to the skin compared to the image on the right which is a scab. (Image Credit: https://www.sharedhealthservices.com/post/scab-versus-eschar)

- Calciphylaxis will appear as large, purple/black web-like areas on the skin.

<u>Histologic Evaluation of Eschars</u>

- Histologic evaluation is often not revealing of the etiology of the eschar.
- Eschars appear as a layer of necrotic cells and debris on the surface with a loss of normal tissue architecture. Depending on the stage, inflammatory cells may be present.
- In calciphylaxis, calcium deposits are seen in the intima of blood vessels and are associated with thrombi. Interstitial calcification is rare.

Cellulitis

- Cellulitis is a bacterial infection of the skin that can be caused by anything leading to breaks in the skin
  - Most commonly due to Streptococcus Pyogenes and Staphylococcus Aureus
  - Can be due to a wound, insect bite, or cracking of the skin due to eczema
- Symptoms include swelling, pain and tenderness and warmth at the site.
  - Patients may have evidence of systemic infection with symptoms such as fever, chills, low blood pressure, etc.
- Risk factors include diabetes, HIV/AIDS, obesity, leukemia, corticosteroid use, tobacco or injection drug use, etc.

<u>Examination of Cellulitis at Autopsy</u>

- Cellulitis typically presents as a poorly demarcated, erythematous area with associated edema and is frequently not bilateral
- Culture may be considered, but is often not necessary post mortem given the risk of bacterial migration and contamination

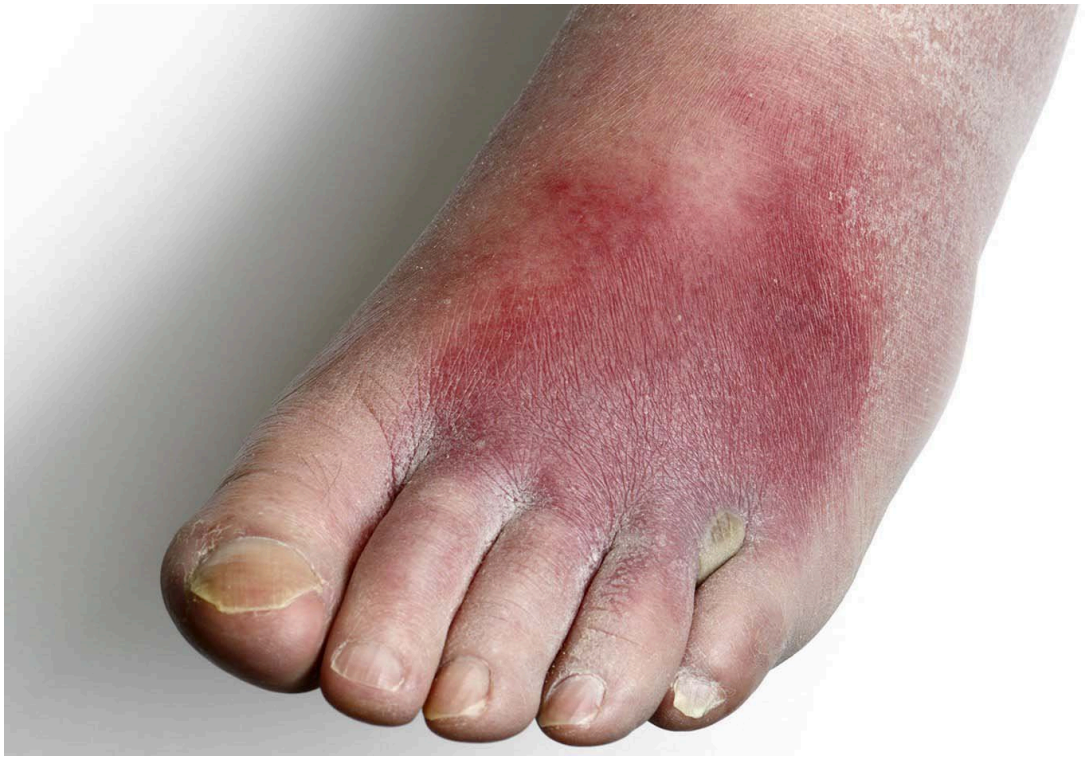

Image: Cellulitis on foot demonstrating redness and swelling. (Image credit: NHS UK)

Histologic Evaluation of Cellulitis

- Histology demonstrates deep dermal inflammatory infiltrate, neutrophils, edema between collagen fibers, and dilated blood vessels

IV. Evidence of Syndromes

Acquired Syndromes

Many systemic diseases and medication effects manifest on the skin and may provide diagnostic clues during autopsy. Recognition of these features can guide towards underlying endocrine, autoimmune, infectious, or toxicologic conditions, particularly when clinical history is limited. Table 6 (below) summarizes notable cutaneous findings associated with common acquired syndromes.

Acquired Syndrome	Skin Findings at Autopsy	Associated Internal Findings/Relevance
Diabetes Mellitus	Diabetic dermopathy (atrophic pigmented pretibial patches), necrobiosis lipoidica, acanthosis nigricans, candidiasis, poor wound healing, and diabetic foot ulcers (see section above)	Renal disease, atherosclerosis, possible pancreatic pathology
Systemic Lupus	Malar rash (may persist	Nephritis, CNS involvement,

Erythematosus	postmortem), discoid lesions, alopecia	thrombotic phenomena
Dermatomyositis	Heliotrope rash, Gottron papules, periungual erythema	Skeletal muscle inflammation interstitial lung disease, malignancy risk
Scleroderma	Skin thickening, shiny taut skin, sclerodactyly, digital ulcers, calcinosis	Pulmonary fibrosis, renal crisis, cardiac fibrosis
Hypothyroidism	Coarse, pale skin; non-pitting edema; thinning hair; loss of lateral eyebrows	Cardiomegaly, pericardial effusion
Hyperthyroidism	Pretibial myxedema, onycholysis	Goiter, exophthalmos, possible atrial fibrillation
Chronic Kidney Disease	Xerosis, uremic frost, pruritis-related excoriations, calciphylaxis (see section above)	Pericardial effusion, uremia, hypercalcemia
Liver Failure/Cirrhosis	Jaundice (see section above), spider angiomas, palmar erythema, caput medusae	Portal hypertension, ascites, coagulopathy
Infective Endocarditis	Janeway lesions, Osler nodes, splinter hemorrhages, petechiae	Valvular vegetations, septic emboli, infarcts
Medication Reactions	Fixed drug eruptions and epidermal detachment disorders (see SJS, TEN, and EMM section below)	History of recent drug exposure, internal mucosal involvement, and multi-organ failure in TEN

Table 6: Cutaneous manifestations of acquired syndromes and systemic disease processes.

Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and erythema multiforme major (EMM)

- If a case was suspected by unconfirmed, postmortem sampling should be done. Postmortem sampling can often be more revealing than antemortem; A negative antemortem biopsy is not proof of ruling out SJS/TEN.
- Usually drug induced, thus medication history is important
    - A list of implicated drugs can be found here: https://pmc.ncbi.nlm.nih.gov/articles/PMC10718167/
- Other differential diagnoses include:
    - Other drug rashes

- Toxic shock syndrome - usually present with early multi organ failures and unique cutaneous manifestations in the form of macular rashes affecting palm and soles that later on evolve to desquamation over the period of 14 days
- Paraneoplastic pemphigus as a mucocutaneous manifestation of malignancy
- Exfoliative erythroderma - usually affects skin only and spares mucous membrane and is painless in most of the cases

Examination of SJS/TEN at Autopsy

- SJS and TEN are characterized by ill-defined erythematous macular rash and bullae, which coalesce to form sheet-like blisters. These blisters can easily slough off / detach, leaving a characteristic moist denuded dermis. They usually start in the face and presternal area before affecting the whole torso. However, the scalp area remains spared in almost all cases.
- Two or more mucous membranes are involved in 90% of SJS and TEN cases.
- EMM is characterized by the symmetric acral distribution of target lesions with or without blister formation.

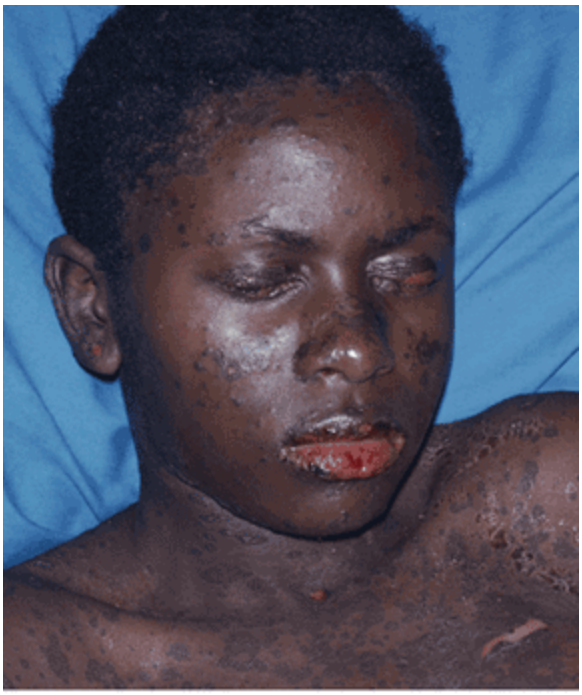

Image: Skin findings in a patient with SJS/TEN with mucocutaneous involvement. (Image credit: US Pharmacist)

Histologic Evaluation of SJS/TEN

- Sampling for histologic evaluation should target the edge of lesions and be guided by clinical context.
- Postmortem sloughing is a common decompositional change and not all blistering or sloughing skin needs biopsy.
- Early lesions: **apoptotic keratinocytes** scattered in basal epidermis

- Later lesions: numerous necrotic keratinocytes, full thickness epidermal necrosis and subepidermal bullae
- Epidermal changes are often accompanied by a moderate or dense **lymphocyte predominant dermal infiltrate** (as opposed to skin sloughing as a normal postmortem change)
- Notably, decompositional sloughing will not have apoptotic keratinocytes and inflammatory infiltrate.
- Gross correlation is essential to distinguish erythema multiforme, SJS and TEN using body surface area, as they may look nearly identical histologically
    - Cannot reliably distinguish based on full thickness epidermal necrosis / necrolysis, because EM may have it and SJS / TEN may not, depending on the site of the biopsy

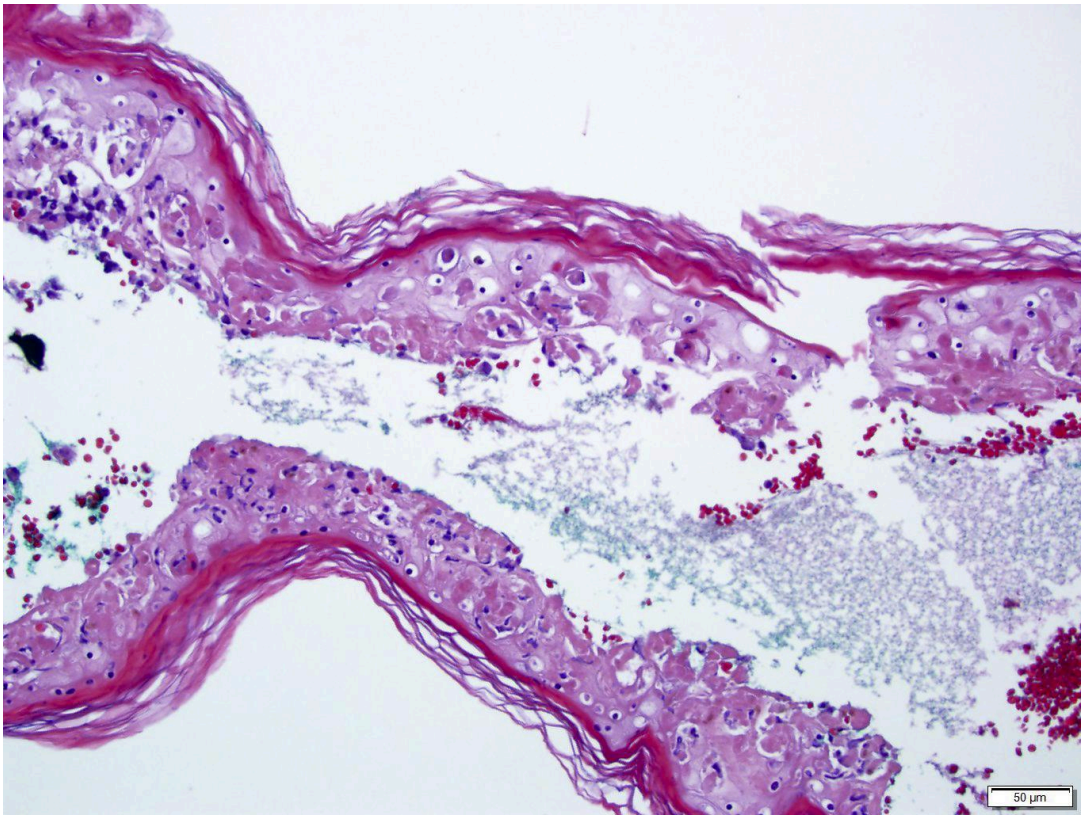

Image: H&E image of patient with SJS demonstrating detached epidermis with full thickness necrosis and dyskeratotic cells. (Image credit: Pathology Outlines).

Genetic Syndromes

Certain genetic syndromes present with characteristic dermatologic manifestations that may prompt further investigation at autopsy, including targeted internal examination, review of medical or family history, or additional postmortem testing. Table 6 summarizes select syndromes with notable cutaneous features and associated internal neoplasms. Awareness of these patterns can help identify occult diagnoses with implications for family counseling, heritable risk, and public health.

Genetic Syndrome	Skin Findings at Autopsy	Associated Internal Neoplasms
Cowden	Perinasal and central-facial trichilemmomas, keratotic papules on the face, neck, ears, and hands; multiple papules on the oral mucosa; lipomas; hemangiomas	Breast cancer, thyroid adenocarcinoma, and uterine cancers, among others
Muire-Torre	Sebaceous tumors (adenomas, adenocarcinomas, epitheliomas)	Gastrointestinal, endometrial, ovarian, urothelial, and biliary cancers
Gardner's	Epidermoid cysts; fibromas; lipomas; desmoid tumors	malignant transformation of adenomatous intestinal polyps and CNS neoplasia
Birt-Hogg-Dube	Acrochordons and benign follicular tumors of the head and neck	kidney cancer risk
Multiple Endocrine Neoplasia Type I	Multiple facial angiofibromas, collagenomas, cafe-au-lait spots, gingival papules, lipomas	parathyroid adenoma, pituitary tumors, pancreatic neoplasms
Multiple Endocrine Neoplasia Type II	Lichen amyloidosis	Parathyroid adenoma, pheochromocytoma, medullary thyroid carcinoma.
Peutz-Jeghers Syndrome	Pigmented mucocutaneous macules and gynecomastia	Intestinal, breast, pancreatic, ovarian, testicular, and cervical malignancies
von Recklinghausen's disease	Cafe-au-lait spots, axillary and inguinal freckles, cutaneous neurofibromas, and plexiform neuromas	Malignant degeneration of neurofibroma, astrocytoma, glioblastoma, meningioma, and bilateral pheochromocytoma.

Table 8 Cutaneous manifestations of genetic syndromes associated with internal neoplasms (adapted from Leal et al. 2021).

Other genetic syndromes with skin findings include:

- Basal cell nevus syndrome (Gorlin Syndrome)
    - Numerous basal cell carcinomas and jaw cysts
- Tuberous Sclerosis:
    - Collagenomas, ash-leaf macules, and angiofibromas
- Neurofibromatosis:

    - Café au lait spots, freckling in the armpits and groin (Crowe's sign), and neurofibromas
- Fabry Disease:
    - Angiokeratomas, often clustered
- Lamellar Ichthyosis:
    - Large dry patches of scaly skin, especially on palms and soles, may have hair loss
- Focal Dermal Hypoplasia (Goltz syndrome):
    - Linear hypoplastic streaks and other skin findings including verrucoid papillomas, pyogenic granuloma-like lesions, palmar and plantar hyperkeratosis, and localized total loss of skin.
- Epidermolysis Bullosa:
    - Thickened skin on palms and soles from repeated blistering, nail abnormalities, and intraoral blisters.

V. Tattoo documentation

- Tattoos must be appropriately documented in the autopsy report to include location, size, design and color
    - Photographs can be considered, for example, documenting may be phrased as "tattoos, located X, Y, Z, are photographically documented".
    - Tattoos can be critical in aiding to identify an unknown descendent, however, are not a form of scientific identification.
    - When examining tattoos, it should be remembered that pigments, especially red, green, or blue pigments, fade over time.
- Other types of "tattoos" include traumatic tattooing of lead on the hands of coal miners or radiation therapy tattoos

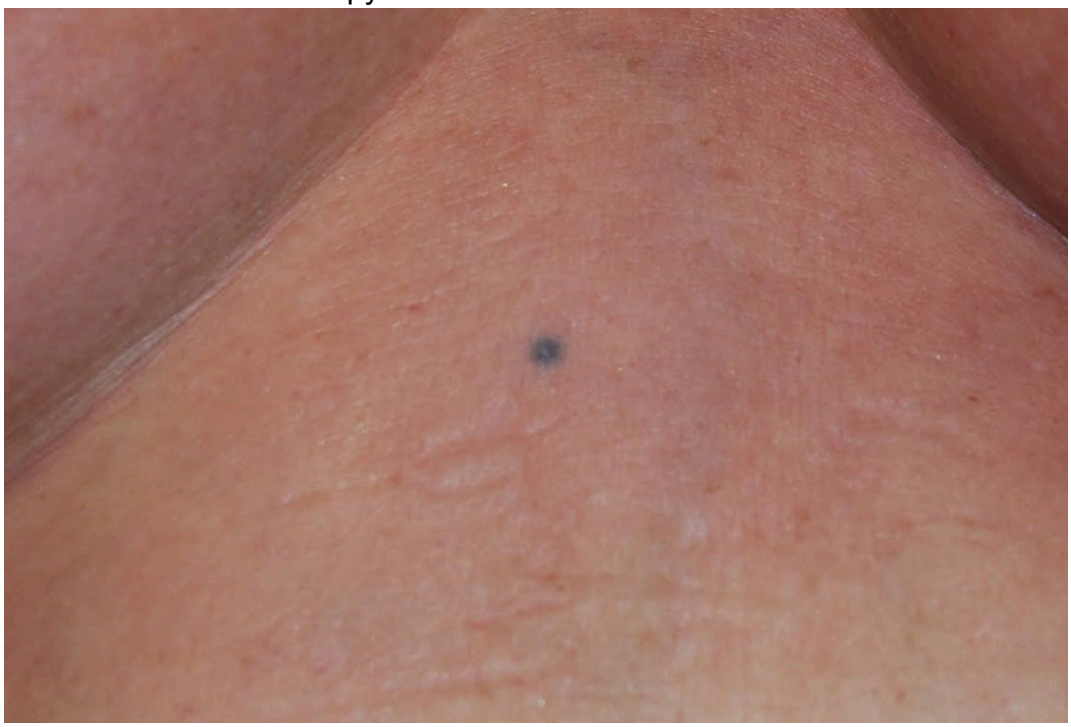

Image: Example of temporary tattoo from a patient undergoing radiation therapy. (Image credit: Salmon Creek Plastic Surgery)

Recommended References

- DermNet NZ. Forensic dermatology. Available at: https://dermnetnz.org/topics/forensic-dermatology. Accessed March 17, 2025.
- StatPearls - NCBI Bookshelf. Livor mortis. Available at: https://www-ncbi-nlm-nih-gov.offcampus.lib.washington.edu/books/NBK554464/#:~:text=Livor%20mortis%2C%20also%20known%20as,from%20pink%20to%20dark%20purplish. Accessed March 17, 2025.
- Bernstein ML, Burkhart CN, Keeling JH, Morgan MB. Cutaneous manifestations of child abuse. *J Am Acad Dermatol.* 2010;62(1):1-18. doi:10.1016/j.jaad.2009.06.026.
- Burkhart CN, Keeling JH, Morgan MB, Bernstein ML. Cutaneous manifestations of elder abuse and neglect. *J Am Acad Dermatol.* 2010;62(3):363-371. doi:10.1016/j.jaad.2009.06.027.
- Jalali A, Rahmani M, Rahmani M. Skin changes in the postmortem period: A comprehensive review. *J Forensic Sci Med.* 2024;10(2):143-150. doi:10.4103/jfsm.jfsm_23_104.
- Vinay J, Harish S, Mangala GSR, Hugar BS. A Study on Postmortem Wound Dating by Gross and Histopathological Examination of Abrasions. Am J Forensic Med Pathol. 2017;38(2):167-173. doi:10.1097/PAF.0000000000000314
- Vanezis P. Interpreting bruises at necropsy. Journal of Clinical Pathology. 2001;54(5):348-355. doi:10.1136/jcp.54.5.348
- Leal JM, de Souza GH, de Marsillac PF, Gripp AC. Skin manifestations associated with systemic diseases - Part II, An Bras Dermatol. 2021;96(6):672-687. doi:10.1016/j.abd.2021.06.003.

Additional References

- Davis JH, Miller KK, Williams SE. Cutaneous findings in victims of interpersonal violence: A forensic perspective. *J Am Acad Dermatol.* 2018;78(2):345-358. doi:10.1016/j.jaad.2017.09.024.
- Rao D. Forensic dermatology: Skin signs in medicolegal context. *Acad Forensic Pathol.* 2015;5(1):120-132. doi:10.23907/2015.029.
- Gilbert JD, Byard RW. Histological assessment of postmortem skin changes. *J Clin Pathol.* 2001;54(5):348-350. doi:10.1136/jcp.54.5.348.

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