c. Dermis

1. Inflammatory cell infiltration

Inflammatory cell infiltration occurs when inflammatory cells such as neutrophils, eosinophils, lymphocytes, plasmacytes, macrophages and mast cells infiltrate around the blood vessels (perivascular infiltration). There are several infiltration patterns, such as lichenoid infiltration (the cells infiltrate in a band resembling that in lichen planus), vasculitis (the cells cause fibrinoid degeneration, blood clots, or bleeding in the blood vessels), and nodular infiltration.

The principal infiltrating cells and the causative diseases are shown in **Table. 2.2**.

2. Granuloma

A granuloma is a thick aggregation of histiocytes (mostly macrophages) that form focal chronic infiltration. The macrophages in granulomas are called epithelioid cells. Besides macrophages, in granulomas one can observe lymphocytes, fibroblasts, degenerated connective tissue, and blood vessels. Granulomas are classified according to the distribution patterns and subtypes of inflammatory cells, as below.

Sarcoidal granuloma: The main components are epitheliod cells

Table 2.2 Diseases with inflammatory infiltration into the skin.

Infiltrated cells	Disorders
Neutrophils	early-stage inflammation; irritant contact dermatitis, erythema nodosum, etc.
	infections; impetigo, candidiasis, etc.
	disorders associated with reactions of immunocomplex and complements; cutaneous small-vessel vasculitis, Sweet's disease, Behçet's disease
Eosinophils	early inflammation; incontinentia pigmenti
	autoimmune diseases; pemphigus, bullous pemphigoid, etc.
	type I allergy
	malignant diseases; mycosis fungoides, Langerhans cell histiocytosis
Lymphocytes	inflammations; allergic diseases, etc.
Plasma cells	infections; syphilis, lymphogranuloma venereum deep fungal infection
	actinic keratosis, syringocystadenoma papilliferum, etc.
Histiocytes	granulomatous diseases; sarcoidosis, granuloma annulare, etc.
Mast cells	inflammations; atopic dermatitis, chronic eczema, lichen planus, etc.
	other; wounds (especially during healing), neurofibroma, etc.

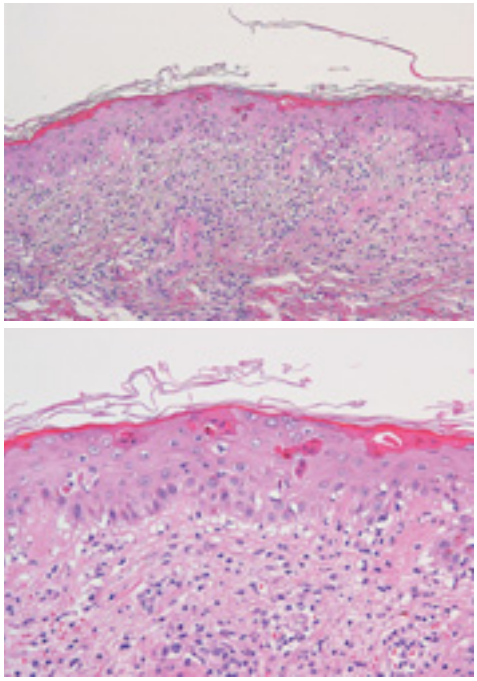

Fig. 2.18 Vacuolar degeneration.
Graft-versus-host disease. Dyskeratosis is also seen, from the apotosis of the epidermal keratinocytes.

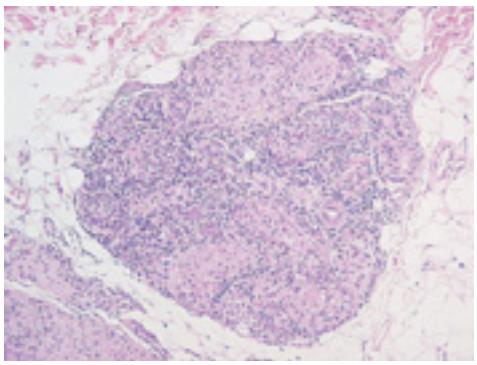

Fig. 2.19 Sarcoidal granuloma.
Cutaneous sarcoidosis. In sarcoidosis, epithelioid cell granuloma is accompanied by few inflammatory cell infiltration, which is also called "naked granuloma."

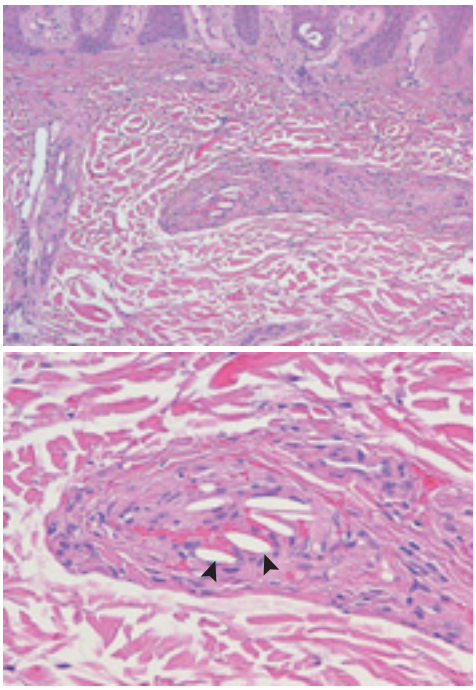

Fig. 2.20 Foreign-body granuloma. Cholesterin deposition (arrows).

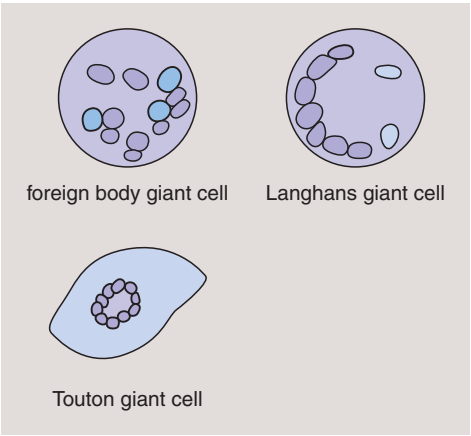

Fig. 2.21 Giant cells originating from histiocytes.

and giant cells. It contains a few necrotic foci and slight lymphocytic infiltration. This is the typical epithelioid cell granuloma observed in sarcoidosis (**Fig. 2.19**).

Tuberculoid granuloma: Epithelioid cell granuloma with caseous necrosis in the center and abundant lymphocytic infiltration at the periphery is observed.

Palisading granuloma: The granuloma contains degenerated collagen fibers and mucin deposition in the center, with peripheral macrophages in a palisade or circular pattern. It is found in granuloma annulare and rheumatoid nodules.

Suppurative granuloma: An abscess (neutrophilic infiltration) surrounded by macrophages and lymphocytes, it is found in deep mycoses.

Foreign-body granuloma: Macrophages, neutrophils and lymphocytes accumulate around an extrinsic body (e.g., glass, suture thread, animal hair, plant fiber) or an intrinsic body (e.g., elastic fiber, calcium deposits, cholesterin crystal). It is a normal reaction to foreign bodies (**Fig. 2.20**). Giant cells that have phagocytosed a foreign body are often observed; however, the foreign substance becomes buried in fibrous tissues over time.

3. Giant cell ★

Giant cell is the general term for cells that contain a characteristically large nucleus. Most giant cells derive from macrophages and are multinuclear from the fusion of macrophages or repeated nuclear division (**Fig. 2.21**). Ballooning observed in viral diseases and Reed-Sternberg cells found in Hodgkin's disease are types of giant cells.

These are other types:

Foreign-body giant cell: Macrophages grow large by phagocytosing foreign substances The nuclei are irregularly arranged (**Fig. 2.20**).

Langhans giant cell: Syncytial macrophages with regularly arranged nuclei in a circular or horseshoe-shaped arrangement. These often found in tuberculosis, sarcoidosis, and lichen nitidus.

Touton giant cell: These macrophages phagocytose fat tissue. The eosinophilic cytoplasm at the center of the cell is surrounded by a nucleus that is further surrounded by foamy light cytoplasm. Touton giant cells are found in juvenile xanthogranuloma and xanthoma.

4. Changes in connective tissue

Fibrosis (irregular proliferation of fibroblasts and collagen fibers such as in scarring and dermatofibroma) and sclerosis (decrease of fibroblasts, swelling or homogenization of collagen fibers, radiation dermatitis, scleredema) are observed in changes of collagen fibers. Elastic fibers decrease in size and number, fracture, and degenerate in senile skin and pseudoxanthoma elasticum. Edema with detachment of connective tissue and accumu-

lation of serous fluid (scleredema) and dermis elevation caused by projected dermal papillae (papillomatosis) are also changes of connective tissues.

5. Deposition of foreign substances

Substances that deposit in the dermis include amyloids (e.g., in macular amyloidosis, lichen amyloydosis), mucins (e.g., myxedema, lupus erythematosus), calcium (e.g., in carcinosis cutis, pseudoxanthoma elasticum, CREST syndrome), hemosiderins (e.g., in bruising, angiitis, hemochromatosis), uric acid, porphyrin and hyaline.

d. Subcutaneous fat tissue

1. Panniculitis ★

Panniculitis is an inflammation of the subcutaneous fat tissue (**Figs. 2.22** and **2.23**). It is categorized by the site of inflammation. In septal panniculitis, inflammation occurs mostly in the septa of the subcutaneous fat tissue, such as seen in erythema nodosum. In lobular panniculitis, inflammation occurs in the lobules of the fat tissue, such as seen in erythema induratum. Panniculits can also occur in acute pancreatitis from the fat necrosis that occurs as a complication.

2. Other changes in fat tissue

Lipogranuloma, lipoatrophy, liponecrosis, lipolysis, lipoma and liposarcoma are other changes of fat tissue.

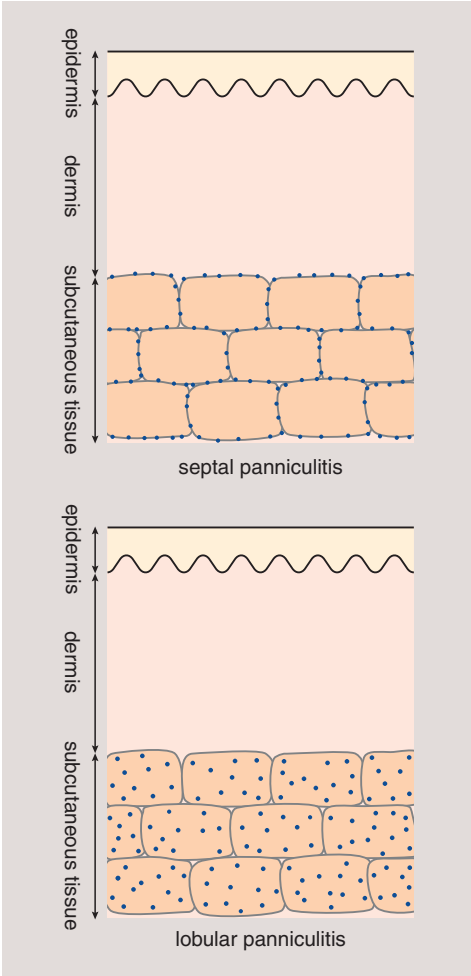

Fig. 2.22 Differences between septal panniculitis and lobular panniculitis.
Black dots are the infiltrated inflammatory cells.

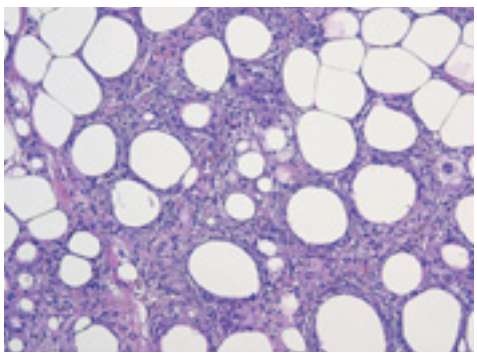

Fig. 2.23 Septal panniculitis.
Erythema nodosum.