Malignant melanoma frequently undergoes extensive, subtotal or even complete regression. Although the regression is a continuous biological and morphological process, we describe the two different histological stages separately, for didactic purposes:
- regressing melanoma with an “active” inflammatory infiltrate;
- regressed melanoma in its terminal fibrotic phase.

Clinical features
Extensive (subtotal) regression in malignant melanoma seems to be a process that occurs in adult and elderly subjects only, and is exceedingly rare in the young. Documented regression in melanoma is practically non-existent in under-20 year-old persons. The average age in most studies is around 40.

Regressing melanoma
With a few exceptions, regression in a melanoma affects a large and horizontally oriented lesion. The stereotypical case is a huge plaque of “superficial spreading” melanoma that has irregularly pigmented zones: black, brownish, pink and reddish areas. Within this lesion, an area becomes flatter, and looses much of its color, acquiring an erythematous cast and ending up as gray, gray-pink, or less often, as nearly white. A depigmented halo occasionally surrounds the entire lesion. Regression in an area of melanoma in situ from an invasive lesion or in melanoma in situ is an equally encountered finding, in
which case the same loss of pigmentation occurs without a loss in substance. Regression is less frequent in entirely nodular presentations of melanoma and in mucosal or juxtamucosal melanoma.

Regressed melanoma
In its “cicatricial” stage, regressed melanoma is characterized by large, irregular whitish areas that may keep expanding. These white lesions contain small blue or black dots, which progressively fade away. The terminal stage consists of a large sclerotic, white or skin-colored area or, if the regression is total, of a lesion with a thinned epidermis. Sometimes the epidermis is hyperkeratotic and scaly.

Both clinically and histologically, regression can be partial. Many authors reserve the term regressing or regressed melanoma to neoplasms in which more than 75% of the lesion is affected by the regression; as noted previously, regression has changes on a continuum and there is little difference between a lesion in which 74% of the surface has regressed and one in which 76% is affected. In cases in which it is as extensive as 75%, regression is said to play an unfavorable prognostic role (Demierre, Clemente, Cook, Guitart, Ferry). According to some studies, metastases follow extensive regression between 4 months and up to 4 years later (Avril). One theory is that regression on this scale correlates with a sensitization of lymphocytes to melanoma cells in a lymph node, and a subsequent attack on cutaneous melanoma cells. Another is that the melanoma cells themselves reach neoplastic crisis, and that the lymphocytes are an epiphenomenon (Bastian).

Histological features
Regressing melanoma (inflammatory stage)
A dense, bandlike inflammatory infiltrate characterizes the first active stage of melanoma regression (Fig. 47.1 - 47.3). The infiltrate extends into junctional nests and blurs the dermo-epidermal interface. Inflammatory cells are mostly small mature lymphocytes, but plasma cells can also be present, scattered throughout the lesion; this plasmacytic component is an important clue for the diagnosis. Lymphocytes are occasionally large and “blastic” with abundant amphophilic cytoplasm. Depending on the stage of the process and on the pigmentation of the melanoma cells, melanophages may also be pre-