Light Microscopic Studies on the Nature of Hypermelanosis in Patients with Melasma. N.P. Sanchez, M.A. Pathak, M.C. Mihm, Jr., J.L. Sanchez, T.B. Fitzpatrick. Harvard Medical School, Boston, MA, and Univ. of Puerto Rico, San Juan, PR

Melasma is an acquired dark-brown to ashen-gray hypermelanosis with mottled patterns and is found in the exposed areas (forehead, malar eminences, upper lip, chin, neck, etc.). Although melasma is believed to be associated with pregnancy, including several other factors such as genetic, racial, endocrine, and nutritional, exposure to sunlight appears to be one of the primary causes of its exacerbation. Examination of patients with Wood's light (320-400 nm) is invariably helpful in recognizing the specific type of melasma, and this depends upon the distribution of pigment granules (melanosomes) as epidermal, dermal, or mixed. Histological studies of skin biopsies and sodium bromide-split, Dopa incubated specimens of epidermis obtained from 13 Hispanic patients with melasma (face and unexposed buttock skin) revealed the following: (1) Increased melanization and distribution of melanin in the skin can be detected with Fontana-Masson stain not only in the basal, suprabasal, and granular cell layers but also in the superficial and deep dermis in the form of melanophages. (2) The basement membrane appeared intact, although in at least three biopsies we could discern the discontinuity of the basement membrane zone and vacuolization of the basal cells. (3) Comparison of the biopsies of the melasma skin with unexposed areas after sodium bromide treatment and Dopa incubation revealed a significantly increased population of melanocytes in patients with melasma. These pigment-producing cells exhibited enlarged perikarya and abundant dendritic arborization. The type-specific pigment-producing cells appeared to be engaged in increased formation, melanization, and transfer of pigment granules to the epidermis as well as to the dermis. It would appear that melasma is a circumscribed hypermelanosis primarily of the epidermis with minimal to moderate melaninosis of the superficial and deep dermis.

Ultrastructural Observation on Extracellular Sheath of Dermal Melanocytes in Nevus of OTA. Yoshiaki Hori, Kuniaki Ohara, Michihito Niimura, Atsushi Kukita. University of Tokyo, Tokyo, Japan

Okawa et al. have found that dermal melanocytes in nevus of ITO possess an extracellular sheath composed of both finefilaments and granules.

Under the electron microscope, we observed dermal melanocytes in lesions of five cases of nevus of OTA, and also those in common type blue nevus and nevus caeruleus tardus associated with progressive systemic scleroderma.

A similar extracellular sheath was recognized as surrounding most of dermal melanocytes in nevus of OTA in older patients (21, 25 and 30 years old). Some dermal melanocytes possessed extracellular sheaths as well as basal laminae. Some possessed only an extracellular sheath. The thickness of the extracellular sheath varied in each dermal melanocyte.

However, not all dermal melanocytes possessed extracellular sheaths. In particular, only a small number of dermal melanocytes in the young patients (9 months and 10 years old) possessed extracellular sheaths which were thinner than those of the older patients. Fibrous long-spacing collagen was recognized in some parts of the extracellular sheath of dermal melanocytes.

In contrast, dermal melanocytes in the blue nevus of the common type were not surrounded by either extracellular sheath or basal lamina. Dermal melanocytes in nevus caeruleus tardus associated with PSS were surrounded by a thin extracellular sheath but not by a basal lamina.

From these findings, we suggest that the extracellular sheath surrounding dermal melanocytes may be produced with advancing age or in the lasting period of dermal melanocytes or with no active movement of dermal melanocytes. In an actively proliferating nevus such as blue nevus of common type, no extracellular sheath is recognized around dermal melanocytes. The extracellular sheath is composed of fine filaments, 20–40 Å in diameter, and appears to be made from collagen.

Electron Microscopy of Dermal Melanocytes in Nevus Ota. Y. Okawa, M. Okawa, A. Yamauchi. Okawa Dermatologic Clinic, Morioka, and Iwate Medical University School of Medicine, Morioka, Japan

Thin sections of the skin lesion from three cases of nevus Ota in Japanese (25- and 47-year-old
Tokyo, Japan
Toshio
The
Ultrastructural
444
studied
Japanese
case
macules
dermal
features
nevus.
normally
pigmented
ous,
nevus
embedded
keratinocytes
within
spot.
External
occur
pattern
occurred,
interconnecting
dendrites
with
menstruous
creased.
Palade and
females
By
Premelanosomes
case
active
Hamada,
large,
The
Haloe and
Premelanosomes
was
reported
previously
(see
the
above
reference).
Elastic
fiber
and
collagen
fibrils
were
observed
to
be
direct
apposition
to
the
surface
dermal
melanocytes,
or
to
be
embedded
within
the
dermal
melanocyte
sheath.
Under
such
circumstances,
it
was
at
times
difficult
to
distinguish
between
the
sheath
filaments
on
the
one
hand
and
the
microfilaments
interconnecting
collagen
fibrils,
or
the
microfibrillar
component
of
elastic
fibers,
on
the
other.
External
laminae,
which
seemed
to
represent
a
local
condensation
of
the
sheath
substance,
occurring,
though
patchily,
on
the
surface
dermal
melanocytes.
Furthermore,
a
banding
pattern
with
about
130
nm
periodicity
and
reminiscent
of
the
"special
fibrils"
described
by
Palade
and
Farquhar
(J
Cell
Biol
27:215-224,
1965)
existed
within
the
dermal
melanocyte
sheath.
Premelanosomes
were
detected
in
dermal
melanocytes
in
cases
of
nevus
Ota
examined.
Interestingly,
they
were
much
more
frequently
encountered
in
the
sample
obtained
at
the
menstruous
stage
than
in
the
sample
obtained
at
the
interphase
of
the
uterine
cycle.
Together
with
the
finding
of
granular
endoplasmic
reticulum
and
Golgi
apparatus
being
well
developed
within
dermal
melanocytes
it
seems
reasonable
to
assume
that
dermal
melanocytes
in
the
nevus
are
active
in
producing
melanin
even
in
human
beings
more
than
25
years
of
age.

Ultrastructural
Studies
on
Pigmented
Macules
of
Peutz-Jeghers
Syndrome.
Kiyoshi
Yamada,
Ataru
Matsukawa,
Yoshiaki
Hori,
Atsushi
Kukita.
University
of
Tokyo,
Tokyo,
Japan
Pigmented
macules
in
the
lips
and
fingers
of
three
cases
with
Peutz-Jeghers
syndrome
were
studied
by
light
and
electron
microscopes.
The
number
of
DOPA
positive
epidermal
melanocytes
per
square
millimeter
in
pigmented
macules
was
almost
the
same
as
that
in
normally
pigmented
control
area
of
the
same
patient.
Dendritic
processes
in
pigmented
macules
of
the
fingers
were,
however,
longer
than
those
in
normally
pigmented
control
skin.
By
electron
microscopic
observations
of
pigmented
macules
in
the
lips,
various
stages
of
melanosomes
and
well-developed
Golgi
apparatus
were
recognized
in
the
melanocytes.
Numerous,
large,
elloipoidal
melanosomes
were
individually
dispersed
in
basal
and
suprabasal
cells
of
pigmented
macules
in
the
lips.
In
contrast,
many
dendrites
filled
with
mature
melanosomes
were
recognized
among
keratinocytes
in
the
squamous
cell
layer
of
pigmented
macules
of
the
fingers.
Almost
no
melanosomes
were
recognized
in
the
keratinocytes
of
pigmented
macules
of
the
fingers.
These
features
may
be
called
as
"imperfect
pigment
blockade."
Some
of
melanosomes
in
dendrites
of
the
upper
eridermis
exhibited
positive
acid
phosphatase
activity.

The
Phenomenon
of
Halo-Like
Disappearance
of
Mongolian
Spot
on
the
Lesions
of
Mongolian
Spot
Combined
with
Café
au
Rait
Spot
or
Acquired
Pigmented
Nevus.
Toshio
Hamada,
Shinsuke
Suzuki.
Osaka
City
University
Medical
School,
Osaka,
Japan
When
café
au
rait
spots
or
pigmented
nevus
combined
with
the
lesions
of
Mongolian
spot,
whitish
haloes
were
observed
on
the
surrounding
areas
of
these
café
au
rait
spots
and
pigmented
nevus.
The
pathogenesis
of
such
halo-like
phenomenon
was
investigated.
The
materials
were
two
Japanese
girls
whose
Mongolian
spots
were
present
at
birth
over
the
sacrum
and
buttocks.
In
case
1,
eight-month-old,
café
au
rait
spots
and,
in
case
2,
six-month-old,
brownish
black
pigmented
spots
have
appeared
since
about
one
month
after
birth
and
gradually
increased
in
size
and
number
on
the
trunk
and
extremities.
On
the
lesions
of
café
au
rait
spot
and
pigmented
nevus
(histologically
compound
type)
and
these
boundary
areas
of
whitish
halo-like
zone,
dermal
melanocytes
were
marked
small
and
round,
compared
with
the
lesions
of
surrounding
Mongolian
spots,
although
only
slightly
decreased
in
number.
The
characteristic
bipolar
dendrites
had
almost
disappeared.
The
dopa
reaction
of
dermal
melanocytes
was
also
de-
creased.
On
the
boundary
areas
of
halo-like
zone
in
both
cases,
edpidermal
melanin
granules
and
dopa-positive
melanocytes
were
almost
equivalent
to
the
lesions
of
the
surrounding
Mongolian
spot.
Mongolian spots were already present at birth in both cases, and café au lait spots and pigmented nevi firmly suggested to occurred on the lesions of these Mongolian spot after birth later. As the results, Mongolian spots might become to disappear on the lesions of café au lait spots, pigmented nevi, and these boundary areas, and it was regarded as a kind of Sutton's phenomenon.

Changes of Melanocytes in Puva Therapy for Vogt-Koyanagi-Harada Syndrome. Ono Tomomichi, Miyamoto Yutaka, Arao Tatsuyoski. Kumamoto Univ. Medical School, Kumamoto, Japan

A 44-year-old Japanese female suddenly developed visual disturbances ten years ago, and a diagnosis of Vogt-Koyanagi-Harada syndrome was given at the Dept. of ophthalmology. Visual acuity has improved with corticosteroid administration, but leucoderma appeared a half year after the onset of the syndrome on the face, chest, and upper back with poliosis on the scalp. Recent ophthalmologic examinations revealed posterior iris synchia and Dalen-Fuchs nodule in the ocular fundus, but there no active lesions have been noted ophthalmologically. For the last five to six years, the leucoderma has persisted unchanged. PUVA therapy was started on this condition. MED was 3 min. 30 sec. on the uninvolved skin, and 1 min. on leucoderma area (UVA 5mW/cm²). PUVA therapy was carried out five days weekly. Spotty follicular repigmentations appeared in the fourth week after the initiation of the therapy and leucoderma almost disappeared two months after. DOPA positive cells in the leucoderma were noted scarcer and weaker than in the normal skin by epidermal-sheet quantitative method of DOPA reaction. On the repigmentation area, DOPA positive cells were larger and increased in number. Electron microscopic observations were made on the melanocytes prior to and after PUVA therapy.

The Effects of Argon Laser Beam on Melanin Granules of the Skin. Tadashi Tezuka, Hiroyuki Yamazaki, Tomomitsu Nakano. Kinki University, Osaka, Japan

The purpose of this experiment is to detect the changes of melanin granules in the basal cells, melanocytes and nevus cells after the treatment of argon laser therapy.

The skin lesions of nevus pigmentosus were treated with an argon laser beam at various mW intensity and time (200, 400, and 800 mW, and 0.2, 0.5 and 2 sec). Biopsy specimens were taken at 2 hours, 48 hours, and 7 days following the treatment. Results: at two hours after the treatment by 400 mW, 0.5 sec, the vacuolar degeneration was remarkable in the basal cells and the melanin granules in these cells were dispersed. By 800 mW, 2 sec, focal vacuolar changes were characteristic in the melanin-laden nevus cells, though the collagen fibers around these cells and other non-melanin-laden nevus cells appeared to be normal. At two days after the treatment, the melanin granules in the degenerated collagen fibers remained granular, though the melanin granules beneath the degenerated dermis were not granular but fragmented and partially dispersed. Electron microscopically the membraneous structure of the melanosome-complex became obscure. As focal vacuolar degeneration was seen in only melanin-laden nevus cells and the melanin granules were fragmented and dispersed, the function of the laser beam is that its energy was absorbed selectively in melanin granules, which caused the disruption of membrane structure of melanosome-complex and also of lysosome at lower intensity, leading to the dispersion of melanin granules, and it caused the degeneration of a cell by heat at higher intensity.

Treatment of Melasma with Hydroquinone. M.A. Pathak, N.P. Sanchez, T.B. Fitzpatrick. Harvard Medical School, Boston, MA

Melasma is an acquired brown hypermelanosis involving the face, forehead, malar eminences, upper lip, and chin. Two controlled double-blind clinical studies involving 175 Hispanic patients and various depigmenting formulations containing hydroquinone (HQ) were carried out to examine the need for the use of retinoic acid (RA) and corticosteroids for safe and effective treatment of melasma. The evaluated formulations contained HQ (2, 4, and 5 percent) with and without RA (0.05–0.1 percent) and corticosteroids (0.05 percent). The need for an effective sunscreen for minimizing exacerbation of melasma during and after the treatment with HQ was also evaluated. Treatment included topical application(s) of cream or lotion either once a day or twice a day for three months. Color photographs and clinical evaluations were obtained before, during (six weeks), and at the end of three months of treatment; and the results
graded as excellent, good, fair, and poor. The following conclusions can be drawn: (1) Exposure to sunlight is one of the primary causes of exacerbation of melasma. (2) Depigmentation of melasma with good results can be achieved by HQ provided the patient avoids sunlight and uses effective sunscreens. (3) Well stabilized 4 or 5 percent HQ without RA can be an effective depigmenting agent, but it is highly irritant. (4) Two percent HQ without RA, corticosteroids, and sunscreens is nonirritant, but a weak formulation for lightening of skin color. Fair to good results can be achieved with twice-a-day application of 2 percent HQ with concomitant use of a sunscreen that filters out 290-400 nm radiation. (5) Anti-inflammatory corticosteroids (fluorinated and non-fluorinated), because of their potential side effects, are not essential in depigmenting formulations. (6) Use of RA (0.05-0.1 percent) in combination with 5 percent HQ with and without steroids can cause more rapid skin depigmentation, but such formulations are irritant and unacceptable to patients. Formulations containing 2 percent HQ and 0.05 or 0.1 percent RA in the form of alcoholic lotion can give consistently good to excellent results provided the patients avoid sun exposure and use sunscreens during and after therapy.

Chemical Vitiligo by Para-Tertiary Butyl Phenol. Hsin-su Yu, Masafumi Iizima, Masako Mizoguchi, Yoshiaki Hori, Yasamasa Ishibashi, Atsushi Kukita. University of Tokyo, Tokyo, Japan

Occupational exposure to para-tertiary butyl phenol (PTBP) produces depigmentation of human skin. Using lyophilized Harding-Passey mouse melanoma tyrosinase and DOPA, we demonstrated that the biochemical basis for this depigmentation might be competitive inhibition of the enzyme tyrosinase. Depigmenting effects of PTBP were investigated by using cultured chick embryonal retinal pigment epithelium and then by electron microscopy. After 24 hours of treatment with PTBP, inhibition of melanogenesis by PTBP was documented by demonstrated of a decrease in the number of melanosomes, especially stage 2 and stage 3 melanosomes. The ultrastructural findings supported that the primary action of PTBP in retinal pigment epithelial cells is directed at the tyrosinase. After 48 hours of treatment, the inhibitory effect of melanogenesis was much enhanced and a decrease in the number of stage I melanosomes was also noticed. In spite of this marked inhibition of melanogenesis, no morphological changes of the nuclei or intracytoplasmic organelles could be found in the retinal pigment epithelial cells by electron microscopic observation. These findings suggest that PTBP may affect not only melanogenesis but also protein synthesis (including tyrosinase and/or matrices of melanosomes) in long time treatment.

Mechanism of Repigmentation of Vitiligo Induced by PUVA Treatment. T. Hirone, S. Fukuda. Kanazawa University School of Medicine, Kanazawa, Japan

In order to investigate the mechanism of PUVA-induced, perifollicular repigmentation in vitiligo, twenty-one patients were studied. Three biopsies were obtained in each patient—from the depigmented skin before treatment, from the repigmented skin in the course of treatment, and from the normal skin in the opposite side. Each biopsy contained a hair follicle at the center. Melanocytes in the perifollicular epidermis were examined by splitting-dopa technique. Follicular melanocytes were examined by paraffin-dopa technique, and counted to be divided into four groups according to Staricco. These melanocytes were observed by electron microscopy.

As the results, average number of melanocytes was greatly higher in the repigmented skin, particularly in the perifollicular epidermis and follicular portions A, B, and D, than in the depigmented skin. Compared with the normal skin, melanocytes in the repigmented skin were much more numerous in follicular portion B, however, there were no significant differences in the follicular portions C and D.

Statistical analysis of the number of melanocytes in the repigmented skin indicated the negative correlation between melanocytes in the perifollicular epidermis and those in follicular portions A and B, and also the minimal positive correlation between melanocytes in portion A and those in portion B.

These data strongly suggest that melanocytes responsible for perifollicular repigmentation in vitiliginous skin are derived from the portion B of hair follicles, in which inactive melanocytes are activated and increased by the treatment.
Ultrastructural Studies of Vitiligo with Inflammatory Raised Borders. Masamitsu Ishii, Toshio Hamada. Osaka City University Medical School, Osaka, Japan

Vitiligo with inflammatory raised borders has rarely been described under the level of light microscopy. However, slight redness or itching are sometimes observed at the borders of early or progressive vitiligo lesions. The purpose of this study is to describe the ultrastructural findings of vitiligo with inflammatory raised borders and to further the understanding of the etiology of vitiligo. The case was a 41-year-old Japanese female whose vitiligo had occurred on the back and nuchal region about six months ago and had gradually been developed. Slight elevated red borders were observed on the periphery of some lesions of vitiligo. Electron microscopic findings showed a few melanocytes with decreased and irregular melanosomes in basal layer and the dissociation of keratinocytes in spinous layers. Melanosomes in keratinocytes also markedly decreased. Lymphocytes were intraepidermally frequently observed, and the process which lymphocytes passed on the basal lamina from dermis were also observed. Some melanocytes contacted with lymphocytes in basal layer. These melanocytes as the results, might fall into degeneration with many vacuoles formation in the cytoplasm were observed. In epidermis, the cells which had many dense granules in the cytoplasm were frequently observed. These cells had many cup-like bodies and lysosome structures in their cytoplasm; therefore, they were concluded to be macrophages. Many typical Langerhans cells with many racket bodies were observed on the upper spinous layers. On the other hand, on the basal layer, Langerhans cells with only a few racket bodies were pretty observed. These Langerhans cells contacted with lymphocytes were also frequently observed.

Recently autoimmune concept has been proposed for the etiology of vitiligo, although none have been established as yet. These ultrastructural findings were firmly suggested to relate to some immunological mechanism on the occurrence of vitiligo.

Prevalence of Vitiligo in Patients with Uveitis. A.B. Lerner, N. Todes-Taylor, J.J. Nordlund, D. Albert. Yale Univ. School of Medicine and Ophthalmology, Mass. Eye and Ear Infirmary (MEEI), Boston, MA

In vitiligo, the loss of epidermal pigment cells (PC) leaves white spots on the skin. We reported that 44 of 112 patients with vitiligo had discrete lesions of the PC visible in the eyes by fundus examination. The patients had no symptoms of eye disease. We suggested that vitiligo is a systemic disease in which PC in any part of the body may be lost. We tested this hypothesis by examining for vitiligo the skin of all patients with uveitis seen at MEEI during a period of four months. 107 patients were examined. 22 patients had uveitis caused by an infectious agent and 12 had an associated systemic disease like sarcoidosis, rheumatoid spondylitis, or ulcerative colitis. None of these 34 patients had vitiligo. 73 other patients had idiopathic uveitis. 44 of these had anterior uveitis; 10 posterior disease; 7 peripheral uveitis, i.e., pars planitis; 8 panuveitis; and 4 sympathetic ophthalmia. Six of the 73 (8 percent) had vitiligo, a prevalence higher than expected in the general population (0.5 percent) and statistically significant ($p<0.025$). Six of another group of patients with idiopathic uveitis were also found to have vitiligo. Four of the 12 patients with uveitis and vitiligo had the onset of both diseases within a few years of each other. For the other patients, the vitiligo antedated the uveitis by 5 or more years. Ten patients had white spots on the skin. Two of the 12 had depigmentation only of the hair of the scalp, eyebrow, and eyelashes. Patients with vitiligo have discrete pigmented lesions of the fundus and patients with uveitis have a high incidence of vitiligo. These observations support our hypothesis that these two skin and eye diseases are part of one systemic disease process, probably immunologic in origin.

Antibodies to Melanocytes in Patients with Vitiligo. J.-C. Bystryn, N. Howanitz, J. Nordlund. New York Univ. School of Medicine, New York, NY, and Yale Univ. School of Medicine, New Haven, CT

Some patients with vitiligo associated with chronic mucocutaneous candidiasis and multiple endocrinopathies have complement-fixing antibodies to normal melanocytes in their serum. Because it has been suggested that these antibodies are involved in the pathogenesis of vitiligo, we have studied their prevalence in a large number of individuals with different types of vitiligo and other pigmentary disorders.
Antibodies to melanocytes were measured by immunofluorescence complement fixation in 294 individuals. The sera were tested at 1/2 and 1/50 dilutions. The substrate was normal human skin, frozen in liquid nitrogen, stored at ~35°C, and used within three days. No antibodies to melanocytes were found in 69 persons with vitiligo. Of these, 31 had common vitiligo. In the others, vitiligo was associated with melanoma (17 persons), thyroiditis (7 persons), uveitis (7 persons), halo nevi (4 persons), alopecia areata (2 persons), or Vogt-Koyanagi syndrome (1 person). Nor were antibodies to melanocytes found in control groups of 82 patients with various nonpigmentary dermatosis, in 71 patients with malignant melanoma, or in 55 patients with inflammatory diseases of the ocular pigment system, i.e., anterior or posterior uveitis. However, antibodies to melanocytes were present in 5 (29 percent) of 17 persons with chronic mucocutaneous candidiasis. These included 2 of 3 patients who also had vitiligo and multiple endocrinopathies, 1 of 4 patients who also had endocrinopathies but no vitiligo, and 2 of 7 patients without vitiligo or other autoimmune or endocrine problems.

In summary, all 5 patients with complement-fixing antibodies to melanocytes had chronic mucocutaneous candidiasis. Only 2 of the patients also had vitiligo. These findings suggest that antibodies to normal melanocytes are not involved in the pathogenesis of common vitiligo, inflammatory pigmentary diseases of the eye, or melanoma.

**Demonstration of IgG Deposit in the Sutton's Leukoderma and Vitiligo Vulgaris with the Use of Peroxidase-Antiperoxidase Technique.** H. Uda. Osaka Univ. Faculty of Med., Osaka  M. Takei, Y. Mishima. Kobe Univ. School of Med., Kobe, Japan

The primary defect of Sutton's leukoderma and vitiligo vulgaris has been found to be a loss of premelanosome formation in the melanocytes. Autoimmune mechanisms have been thought to be involved at least in some of these processes. We reported the deposit of small quantities of IgG detected by direct immunofluorescent technique in the basement membrane zone of some depigmented lesions from patients unassociated with autoimmune diseases. Purposes of present study are to report further the IgG deposit in vitiligo, Sutton's leukoderma, and melanoma associated vitiligo at cellular and subcellular level using highly sensitive and specific PAP immunoperoxidase method which can utilize prefixed paraffin embedded tissue. This process includes the protease digestion of deparaffinized sections as well as inhibition of endogenous peroxidase activity by methanol-H₂O₂ pretreatment prior to the incubation with anti-IgG. After examination of more than 20 cases of Sutton's leukoderma, 30 cases of vitiligo vulgaris, and 3 cases of melanoma associated vitiligo, we have found distinct deposit of IgG and its permeation into the lower epidermis. Furthermore, the frequency and intensity of positive reaction for IgG are found to be higher in the Sutton's leukoderma than vitiligo. Deposit of these IgG are suggested to participate in immunological dysmelanogenesis.

**Possible Lymphocyte Mediated Melanocyte and Keratinocyte Damage in Vitiligo.** Jag Bhawan, L.K. Bhutani. Univ. of Massachusetts Medical School, Worcester, MA, and All India Institute of Medical Sciences, New Delhi, India

Light and electron microscopic studies were performed on the amelanotic and adjacent normal-appearing skin from nine patients with vitiligo. The light microscopy of amelanotic skin revealed complete loss of pigment. Electron microscopy confirmed the absence of melanocytes. Langerhans cells were observed with ease but did not appear to be greatly increased in number. Mast cells were present in normal numbers in the dermis and no intra-epidermal mast cells were found.

Light microscopy of the normal-appearing skin revealed increased cellularity and vascularity of the upper dermis. Focal areas of vacuolation were seen in the basal layer of the epidermis, associated with vacuolation of the underlying dermal cellular infiltrate. Electron microscopy showed the cellular infiltrate to consist of lymphocytes and other mononuclear cells. Some lymphocytes had the configuration of Ségary cells. These cells were frequently seen within the lower layers of the epidermis in close contact with melanocytes and/or keratinocytes. Varying degree of destructive changes were observed in melanocytes as well as in keratinocytes. At times, lymphocytes were found in close contact with normal-appearing melanocytes and keratinocytes. The upper dermis contained many nerves and nerve endings, without any significant pathologic change.

These findings support the hypothesis that an immune mechanism plays a role in the pathogenesis of vitiligo, and suggest that lymphocytes are involved in the destruction of melanocytes and keratinocytes.