See Ash Leaf Macules, Think Tuberous Sclerosis

BY DOUG BRUNK

PORTLAND, Ore. — If an infant pres-
ents with at least three hypopigmented
macules, think tuberous sclerosis.

Tuberous sclerosis is described as a tri-
ad of neurologic impairment, multisys-
tem hamartomas, and skin findings (such as
ash leaf macules and facial angiofi-
bromas). The disease is of autosomal
dominant inheritance, with an incidence
of 1:6,000 to 1:10,000. Spontaneous mu-
tation occurs in 70%–75% of cases.

Ash leaf spots or hypopigmented macu-
els occur in 90% of patients with the
disease, Dr. Dawn Siegel said at the an-
nual meeting of the Pacific Dermato-
logic Association. They can range in size
from 1 to 12 cm in diameter and “are
rounded at one end and tapered at the
other, resembling the leaf of an ash tree.

They can vary quite a bit in their pre-
sentation. In some cases, they present as
confetti macules, which are only 1-2 mm
in diameter,” she said.

If an infant presents with more than
three hypopigmented macules, she rec-
ommends screening evaluations, which
could include a renal ultrasound, an eye
exam, and a cardiac echocardiogram. “I
usually reserve head MRI or CT for ba-
bies who are developing seizures, or who
have a positive finding on one of the
other screening tests, or if I have a
high clinical suspicion,” said Dr. Siegel,
assistant professor of dermatology and
pediatrics at Oregon Health and Science
University, Portland.

Infantile spasms, the most common
presenting neurologic sign, tend to de-
velop by 4-5 months of age in about 70%
patients.

Establishing a definitive diagnosis of
tuberous sclerosis requires the presence
of two major clinical diagnostic criteria
or one major and two minor criteria.

Major criteria include facial angiofi-
bromas or forehead plaque, nontrau-
matic ungual fibroma, three or more
hypomelanotic macules, shagreen patch
(most commonly on the back and chest),
multiple retinal nodular hamar-
tomas, cortical tuber, subependymal
nodule, subependymal giant cell astro-
cyteoma, single or multiple cardiac rhab-
domyoma, renal angiomyolipoma, and
pulmonary lymphangiomatosis, said Dr.
Siegel.

Minor clinical criteria include multiple
randomly distributed pits in dental
enamel, hamartomatous rectal polyps,
bone cysts, cerebral white matter radial
migration lines, gingival fibromas, non-
renal hamartoma, retinal achromatic
patch, “confetti” skin lesions, and mul-
tiple renal cysts.

Current treatments for the facial
angiofibromas include pulsed dye laser and
pulsed KTP (532 nm) laser. “Some peo-
lie use a CO2 laser or the erbium:YAG
laser to try and flatten down the lesions,”
Dr. Siegel said.

Studies of oral and topical rapamycin
are underway after a published case re-
port demonstrated that the agent signif-
ically improved angiofibroma lesions in
a patient with tuberous sclerosis complex
who took rapamycin after undergoing re-
nal transplantation (Br. J. Dermatol.
2008;159:473-5).

“This would be exciting, because an-
giofibromas are so disfiguring and treat-
ment has been frustrating,” she said.

Incontinentia Pigmenti

Dr. Siegel went on to discuss inconti-
enta pigmenti, which is caused by a ge-
netic rearrangement of the gene for nu-
clear factor kappa B essential modulator
and has an incidence of 1:40,000. The
skin disorder is marked by four stages
that occur in most patients.

In stage I, vesicles in linear streaks fol-
low the lines of Blaschko. These lesions
are present at birth in 50% of cases and
wax and wane for up to 1 year. In stage
II, verrucous hyperkeratotic streaks usu-
ally appear at 2-6 months of age. Stage
III is marked by hyperpigmentation in
streaks along the lines of Blaschko in a so-
called “marble-cake pattern,” she said.

Cutaneous findings in stage IV typi-
cally involve atrophy and hypopigmen-
tation that may be subtle. Affected in-
fants may have a lack of hair along the
lines of Blaschko.

Recurrence of the vesicular phase
may occur, but this typically lasts only
1-2 weeks and is often preceded by a vi-
ral illness. “Sometimes these lesions are
mistraken for herpes zoster,” Dr. Siegel
noted.

Additional findings of incontinentia
pigmenti may include scarring alopecia,
most commonly on the vertex; conical or
peg-shaped teeth; absence of teeth; nail
dystrophy; and abnormal sweating.

“The management of incontinentia
pigmenti in the newborn period should
focus on skin care with emollients and
monitoring for skin infection,” she said.

“Topical steroids can sometimes be
beneficial for symptomatic relief in the
verrucous phase. Referral to an oph-
thalmologist for a retinal exam is im-
portant. If neurologic symptoms are
present, then evaluation includes an
EEG and an MRI,” she added.

Neurofibromatosis Type 1

Dr. Siegel concluded her presentation by
discussing neurofibromatosis type 1
(NFI), a multisystem disorder caused by
a mutation of a gene on the long arm of
chromosome 17 that occurs in about 1 in
4,000 births.

According to the 1988 National Insti-
tutes of Health Consensus Develop-
ment Conference, a diagnosis of NFI
requires two or more of the following
clinical features: six or more café-au-lait
macules, two or more neurofibromas
or one or more plexiform neurofibro-
mas, freckling in the axilla and inguinal
region (Crowe’s sign), tumor of the
optic nerve pathway, two or more
Lisch nodules (iris hamartomas), and
distinctive osseous lesions.

Café-au-lait macules, the hallmark
clinical feature, are present in nearly all
cases. The size is age dependent, with
macules typically exceeding 5 mm in
prepubertal children and 15 mm in post-
pubertal children.

“They often appear in the first few
months of life and increase in number over
the first couple of years of life,” Dr.
Siegel said.

Axillary or inguinal freckling tends to
present later in childhood, while neu-orfibromas begin to appear in child-
hood or later. “They are not usually
present in infancy,” she said. “They in-
crease in number in puberty and during
pregnancy.”

Plexiform neurofibromas present in
about 25% of cases in infancy. They can
be disfiguring and can cause hypergly-
caemia and hypopigmentation, and can run along the
lines of nerves. “It’s difficult to excise
them for that reason,” she said.

Plexiform neurofibromas also can be
painful and, although rare, there is a risk
that they will develop a malignant pe-
ripheral nerve sheath tumor.

“Because they’re difficult to com-
pletely excise, it’s always hard to know
when they develop to cancer in the
plexiform neurofibroma, or if the lesion
is just growing,” she noted.

“There are a lot of clinical trials go-
ing on right now looking at various med-
cal, nonsurgical treatments for plexifor-
num neurofibromas,” Dr. Siegel added.

Dermatologic exams for children with
NFI should include evaluation for the
presence of café-au-lait spots, neu-
orfibromas, plexiform neurofibromas,
and skinfold freckling. “Enlarging or
disfiguring plexiform neurofibromas
may require referral to a surgical spe-
cialist to discuss debulking or to a spe-
cial center for enrollment in a clinical
trial,” she said.

Dr. Siegel disclosed having no relevant
conflicts of interest.

New Wound Dressing Reduces Pain During Changes

BY KERRI WACHTER

PHILADELPHIA — A new dressing using a lipido-
coated, non-adherent tape reduced pain during
changes and improved quality of life for patients
with epidermolysis bullosa.

The 20 patients involved in the trial reported most of
the dressing changes to be pain-free (91%). The re-
main 9% of dressing changes were reported as mild
to moderately painful, according to the results pres-
ted at the annual meeting of the Society for Pediatric
Dermatology.

The contact layer consists of petrolatum and car-
boxymethylcellulose on a mesh. When exudate comes
in contact with the dressing, the carboxymethylcellu-
lose swells and retains moisture, which keeps the environ-
ment moist, said coauthor Dr. Mary Regan, who is the
director of clinical affairs for Hollister Wound Care (a
joint venture between Hollister Incorporated and Lab-
oratories URGO), which markets and sells the dressing
as the Restore family in the United States. The study was
funded by Laboratories URGO, which markets and
sells the dressing (UrgoCell, Urgotul) in Europe.

This open-label, single-center study involved 11 adults
and 9 children with simplex or dystrophic epidermol-
ysis bullosa. Skin lesions were managed with the lipi-
do-coil contact layer dressing for a maximum of 4
weeks. At dressing changes, the researchers assessed
pain and quality of life.

All 20 patients completed the trial, with a total of 152
dressing changes. Dressing application was considered
by the patients to be “easy” or “very easy” for most of
the dressing changes (95%). Likewise, dressing removal
was considered “easy” or “very easy” for almost all of
the dressing changes (98%). Dry dressing removal was
recorded for 87% of dressing changes; in 13% of
dressing changes saline soaking was used for removal.

Roughly half of patients (55%) reported that using the
experimental dressing had improved their quality of
life, due to easier dressing removal.

“Most adults and children felt less apprehensive
about the procedure than they had with their usual
dressing,” the researchers wrote. All but one patient said
that they would use the experimental dressing to
manage their lesions in the future.