“Brown spots on Babies”

Jonathan A. Dyer, MD
Associate Professor
Departments of Dermatology and Child Health
University of Missouri

Objectives
- Recognize common hyperpigmented skin lesions in infants
- Discuss new findings and practical pearls pertaining to pigmented lesions
- Manage hyperpigmented lesions in infants

“Brown spots on Babies”

Dirt
Marker
Food
Chocolate
Excrement

Hyperpigmented lesions
- Café au lait macule (CALM)
- Becker’s nevi
- Patterned dyschromia/pigmentary mosaicism
- Nevi
  - Congenital melanocytic nevi (CMN)
  - Speckled lentiginous nevi/ nevus spilus
- Mastocytoma

DISCLOSURES
Investigator: Scioderm, Allergan
Café au lait macules (CALM)

• “Coffee with milk”
• Congenital/ acquired
• Isolated lesions very common
  – ~20-25%
• Sporadic may fade in adults
• Histo: increased melanin of MC and KC, macromelanosomes*

Neurofibromatosis (NF)

• “Coast of California”
• May develop new lesions after age 6
• Don’t fade with time

Table 2

<table>
<thead>
<tr>
<th>Symptoma</th>
<th>Clinical features</th>
<th>Genes or Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurofibromatosis type 1</td>
<td>Multiple café-au-lait, skin-fold freckling, lisch nodules, optic pathway glioma, skeletal dysplasia, stigmata and plexiform neurofibroma, microscopic cafe-au-lait spots, meningioma, Schwartz-Jampel syndrome, congenital pseudarthrosis of tibia, von Recklinghausen disease, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
<td>NF1</td>
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<tr>
<td>Neurofibromatosis type 2</td>
<td>Multiple café-au-lait, absence of café au lait spots, juvenile xanthogranuloma, neurofibromatosis, neurofibromatosis, von Recklinghausen disease, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
<td>NF2</td>
</tr>
<tr>
<td>Multiple café-au-lait without other stigmata of NF1</td>
<td>Multiple café-au-lait without other stigmata of NF1</td>
<td>1</td>
</tr>
<tr>
<td>Multiple café-au-lait with at least one other developmental defect</td>
<td>Multiple café-au-lait with at least one other developmental defect</td>
<td>SF3601</td>
</tr>
<tr>
<td>Segmental café-au-lait</td>
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<td>SF3611</td>
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<tr>
<td>Multiple café-au-lait, adenoma sebaceum, polyposis, multiple epidermal naevi, multiple plexiform neurofibromas, adolescence and neurofibromatosis type 1 (NF1).</td>
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<td>SF3621</td>
</tr>
<tr>
<td>Multiple café-au-lait, non-streamline superstitious naevi, neurofibromatosis, leptomeningeal angiofibroma, neurofibromatosis type 2 (NF2).</td>
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<td>SF3631</td>
</tr>
<tr>
<td>Multiple café-au-lait, neurofibromatosis, mental retardation, shunt states, joint anomalies</td>
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<td>SF3641</td>
</tr>
<tr>
<td>Café-au-lait, café-con, lichenoid, cafe-au-lait naevi, psoriasis, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
<td>Café-au-lait, café-con, lichenoid, cafe-au-lait naevi, psoriasis, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
<td>SF3651</td>
</tr>
<tr>
<td>Lisch nodules; café-au-lait spots; neurofibromatosis type 1 (NF1).</td>
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<td>SF3661</td>
</tr>
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<td>Café-au-lait, café-con, lichenoid, cafe-au-lait naevi, psoriasis, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
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<td>Café-au-lait, café-con, lichenoid, cafe-au-lait naevi, psoriasis, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
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<td>Café-au-lait, café-con, lichenoid, cafe-au-lait naevi, psoriasis, neurofibromatosis, phemiscranial anomalies, osteoporosis, cranial dysostosis, acanthosis nigricans, and neurofibromatosis type 1 (NF1).</td>
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<td>SF3691</td>
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* Macromelanosomes are melanosome-sized brown melanosomes.
**Legius syndrome**

- SPRED1

**McCune-Albright syndrome**

- Fibrous dysplasia; CALM; precocious puberty
- GNAS
  - Mosaicism for somatic activating mutations
    - Alpha subunit of stimulatory G-protein
- Incidence: 1/100,000-1x10^6
  - Diagnosis by 5yo

**McCune-Albright syndrome**

- Polyostotic fibrous dysplasia
  - Scoliosis
- Precocious puberty
  - Vaginal spotting/bleeding
  - Testicular/ penis enlargement
  - Precocious sexual behaviour
- Variable hyperfunctional endocrinopathies
  - Cushing syndrome

**Pigmentary Mosaicism/ Patterned Dyschromia**

- Heterogeneous
  - Hypo and/or hyperpigmented
  - May follow Blaschko’s lines
- Associated clinical abnormalities in 30% (literature)
  - Esp. CNS, eye, bone
    - Nehal et al. Arch Derm 1996; 132:1167
    - Likely an overestimate

**Congenital melanocytic nevi**

- 2-3% of neonates
- Large CMN rarer
  - 1: 20-50,000 live births
- Tardive or late onset CMN
  - Onset <3 yo
- Smaller lesions – BRAF V600E
  - Only MAPK activation
- Large/giant CMN – NRAS
  - MAPK and PI3K/AKT activation
    - PI3K/AKT – promotes MC survival/ directional migration
    - Rapamycin???
Congenital Melanocytic Nevi (CMN)

- Largest expected adult diameter
  - Small <1.5cm
  - Medium 1.5-10cm
  - Large
    - L1 >20-30
    - L2 >30-40

- Giant
  - G1 40-60
  - G2 >60

How to predict adult size?
- CMN increase factors:
  - Head – 1.7x
  - Legs – 3.3x
  - Other – 2.8x

Satellite nevi
- S1 <20
- S2 20-60
- S3 >60

Congenital melanocytic nevi

Evolution
- Scalp CMN may lighten/ regress over time
- Small-medium CMN
  - Melanoma risk – after puberty
  - <1% over lifetime
    - Background risk in population is 2%
- Large/Giant CMN
  - <5%; 50% in first 5 yrs; >40cm 75%

Which CMN patients are at risk for neurocutaneous melanosis?
- Numerous CMN
  - 66% large/giant primary lesion with many satellites
  - >20 satellites = 5x higher NCM risk
  - CMN >40cm final size in posterior axial locations
  - 33% numerous small/medium CMN (>10)

Speckled lentiginous nevi

- AKA; Nevus spilus; CMN subtype
  - Incidence: 2-3%
- CALM-like background in childhood
  - Neviod papules appearing with time
    - Lentigenes; nevi; Spitz; blue nevi

Genetics
- Conventional SpLN
  - HRAS
- Large CMN like SpLN
  - NRAS
- Melanoma risk
  - Likely proportionate to size
Pediatric melanoma

- 0.5% of melanoma occurs <20 yo
  - <0.05% in <10 yo
  - Amelanotic
  - Nodular
  - PG; keloid; wart
- Prepubertal melanoma incidence stable
- Adolescent/adult incidence rising

Mastocytosis

- Clonal mast cell expansion
  - Activating KIT mutations
- Cutaneous
  - Onset typically <6 mo
    - Occ. Congenital
  - Typically gradually regress
    - Puberty
- Systemic
  - Adult

Mastocytoma

- Yellow-tan-brown
  - Plaques
- Darier’s sign
  - Scalp

Mastocytosis

- Childhood-onset MPCM
  - “Urticaria pigmentosa”
  - Heterogeneous lesions

Mastocytosis

- Large maculopapular lesions:
  - lower tryptase levels
  - Low anaphylaxis risk
  - shorter disease duration
  - earlier disease onset
  - spontaneous resolution
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Thank you for attending!

Please contact me should you have any questions.

Jonathan A. Dyer, MD
Associate Professor of Dermatology and Child Health
University of Missouri - Columbia
1 Hospital Drive, Room MA111
Columbia, MO. 65212
phone: 573-882-8578 fax: 573-884-5947
E-mail: DyerJA@health.missouri.edu