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The Importance of Minor Anomalies in the Evaluation of the Newborn

Margaret Adam, MD*,
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Objectives  After completing this article, readers should be able to:

1. List the number of minor anomalies associated with an increased risk of an associated major malformation.
2. Describe the tests that should be conducted in patients who have preauricular ear pits or tags.
3. Delineate which dorsal cutaneous stigmata require further evaluation.
4. Delineate the evaluation that should be undertaken in any infant who has asymmetric crying facies.
5. Describe the potential disease in any Caucasian child who has three or more café au lait spots or any African-American child who has five or more café au lait spots.

Introduction
The identification of congenital anomalies has important diagnostic and prognostic implications for neonates. Because many children who have congenital anomalies are identified in the neonatal period, the neonatologist often is the clinician to whom families turn for initial information about the significance of such anomalies. Another reason for neonatologists to be familiar with minor anomalies is that identification of certain minor anomalies may suggest the need for further diagnostic studies and the search for related conditions. The purpose of this article is to review the significance of minor anomalies, with particular attention to five commonly encountered findings.

The term “congenital” simply means that the finding is present at birth, regardless of cause. This should not be confused with the term “genetic”; congenital does not imply a cause. An anomaly is a structural defect that deviates from the normal standard and can be classified as major or minor. A major anomaly has surgical, medical, or cosmetic importance. A minor anomaly has no major surgical or cosmetic importance.

As might be expected, the prevalence of a given feature in the general population can vary, based on race, ethnic background, and gender of the individual. A minor anomaly typically refers to physical differences that occur in fewer than 4% of the general population; normal phenotypic variant describes features that are present in 4% or more of the general population. Therefore, minor anomalies can overlap with normal phenotypic variants, depending on the demographics of the population being studied. Classifying a physical finding as either a major anomaly, minor anomaly, or normal phenotypic variant is important because it has different implications for the patient.

Major anomalies, such as cleft lip or palate, often can be identified easily. Minor anomalies by definition are more difficult to appreciate and frequently are overlooked. They are found more commonly in areas of the body that are more variable and complex, such as the face or the hands. Approximately 70% of minor anomalies are present in these two areas. It is important to identify minor anomalies for several reasons. First, some minor anomalies are markers for occult major malformations, such as sacral hair tufts or sacral skin abnormalities that are associated with occult spinal dysraphism. Second, many genetic syndromes are defined by a specific pattern of minor anom-
alies occurring together. For example, the typical constellation of minor anomalies involving the face, hands, and feet allows for prompt diagnosis of Down syndrome. Therefore, recognizing a constellation of minor anomalies is important in diagnosing many conditions. Third, the presence of three or more minor anomalies is associated with an increased risk of having a major malformation and should prompt a thorough evaluation for occult major abnormalities.

Approximately 15% to 20% of healthy newborns have one minor anomaly. Thus, it is 10 to 20 times more common to find a minor anomaly than a major malformation. It has been estimated that infants who have one minor anomaly have an approximately 3% risk of associated major abnormalities. Approximately 0.8% of healthy newborns have two minor anomalies, with an approximately 10% risk for an accompanying major malformation. Only 0.5% of newborns have three or more minor anomalies. Several studies have shown that such infants have an approximately 20% risk of also having a major malformation. Thus, special attention should be paid to the infant who has three or more minor anomalies, and a search for an occult major malformation may be indicated, depending on the clinical context.

The prevalence of specific minor anomalies varies by racial and ethnic background. For example, mongolian spots (blue spots) are much more frequent in the Asian and African-American population than in the Caucasian population. In fact, the prevalence of certain minor anomalies in particular ethnic and racial groups is so high that the anomaly is considered a normal phenotypic variant for that population. Natal teeth are rare in the Caucasian population, but they are considered a normal variant within the Native American population. Up-slanting palpebral fissures are considered a normal variant within the Chinese population. It also is important to consider the family history when assessing the significance of a minor anomaly, especially when found in isolation. Certain minor anomalies, such as isolated syndactyly of the second and third toes or isolated in-curving of the fifth digit, can be familial.

**Commonly Encountered Minor Anomalies**

**Preauricular Ear Tags and Pits**

Preauricular ear tags and pits are frequent findings on routine physical examination of the neonate. Preauricular tags are small, skin-colored nodules that can be found anywhere along a line drawn between the tragus to the angle of the mouth (Fig. 1). Preauricular pits are small openings at the anterior margin of the crus of the helix (Fig. 2). Both ear tags and pits can be found in isolation or as part of a genetic syndrome. The prevalence of isolated ear tags is estimated to be 1.7 per 1,000 individuals, with bilateral lesions occurring in approximately 6% of affected individuals. The incidence of isolated ear pits is 1% to 5%, with 20% of affected patients having bilateral lesions. Both isolated ear pits and tags can have an autosomal dominant inheritance pattern within families. Therefore, it is very important to examine other immediate family members and to obtain a thorough family history, with particular attention to abnormal ear formation or hearing loss.

When evaluating a patient who has ear pits or tags, it is of utmost importance to assess hearing in both ears. Abnormalities of the external ears can be an indication of occult abnormalities involving the middle or inner ear, which can lead to decreased auditory acuity. A thorough examination of the external ears and face should exclude microtia and facial asymmetry, which can be suggestive of oculoauriculovertebral spectrum, also known as hemifacial microsomia and Goldenhar syndrome. Patients who have this condition also can have epibulbar dermoids and vertebral anomalies, so an ophthalmologic examination and spinal radiographs should be considered. It is important to examine the neck of any patient who has ear pits for evidence of branchial cleft fistulae. The association of ear pits and branchial pits is seen in branchio-oto-renal (BOR) syndrome, an autosomal dominant genetically heterogeneous disorder. Renal ultrasonography should be performed to assess for renal anomalies in patients in whom a diagnosis of BOR is being entertained. In the past it was recommended that all patients who have ear pits or tags undergo routine renal ultrasonography because of the association of ear and renal anomalies in certain genetic syndromes. However, evidence is mounting that it is unnecessary to obtain routine renal ultrasonography in patients who have isolated preauricular ear pits or tags.

A recent study by Kugelman and associates evaluated the utility of renal ultrasonography in newborns who had isolated preauricular ear pits or tags. The investigators compared renal ultrasonography results from 92 infants who had isolated ear pits or tags with those from 95 healthy infants. The incidence of renal abnormalities detected on ultrasonography was 2.2% among infants who had isolated ear pits or tags compared with 3.1% among healthy newborns. Furthermore, the renal abnormalities consisted of mild unilateral pelviectasis in the group that had isolated ear pits or tags and mild pelviectasis and renal calculi in the group of healthy newborns. Therefore, it appears that routine renal ultrasonography is not indicated for patients who have isolated ear pits or
tags. In contrast, renal ultrasonography is a reasonable consideration for patients who have three or more minor anomalies that include ear pits or tags or for patients in whom a genetic syndrome is suspected.

**Sacral Dimples**

Cutaneous abnormalities in the sacral area of the newborn may indicate occult spinal dysraphism. Identification of occult spinal lesions is important because early diagnosis and treatment can prevent progressive and irreversible neurologic dysfunction. The best method of assessing spinal cord involvement in high-risk infants younger than 3 months of age is spinal ultrasonography; after 3 months of age, magnetic resonance imaging of the spine is the suggested diagnostic modality. It is important to distinguish sacral stigmata that are more likely to be associated with an underlying spinal abnormality from those that are not.

A recent study by Kriss and Desai examining 1,449 consecutive term infants noted an approximately 4.8% incidence of dorsal cutaneous stigmata in this otherwise normal population. The most common finding was a simple dimple, which was defined as a midline dimple measuring less than 5 mm that was located within 2.5 cm of the anus and not associated with other cutaneous findings (Fig. 3). This was identified in 74% of patients. None of the affected patients was found to have occult spinal dysraphism on ultrasonography. Accordingly, the authors concluded that routine spinal ultrasonography is not warranted in patients who meet the definition of simple sacral dimple. High-risk dorsal cutaneous stigmata for occult spinal dysraphism in the study population included hemangiomas, cutis aplasia, raised lesions (masses, tail-like appendages, and hairy patches), the presence of multiple cutaneous lesions in a given patient, and atypical dimples, defined as dimples that are large (>5 mm) or high on the back (>2.5 cm from the anus).

**Asymmetric Crying Facies**

Congenital absence or hypoplasia of the depressor anguli oris muscle (DAOM) is a common cause of asymmetric crying facies in neonates. Patients who have asymmetric crying facies have drooping of the corner of the mouth on the unaffected side when crying or grimacing. These patients can be distinguished from patients who have the less common finding of facial nerve palsy by the ability of the former patients to wrinkle the forehead and close the eye equally well on both sides of the face. In addition, the nasolabial fold depth remains intact and equal on both sides in patients in whom the DAOM is absent (Fig. 4).

The incidence of congenital absence or hypoplasia of the DAOM is estimated to be between 0.63% and 0.82% of the general population. There appears to be an increased male-to-female ratio and a predilection for the left side of the face to be affected. The pathogenesis of the anomaly is unknown, although intrauterine molding and subclinical viral infections have been suggested. Family studies have shown an increased incidence among first- and second-degree relatives, suggesting at least a genetic contribution in some cases. A multifactorial etiology seems most likely.

It long has been recognized that patients who have asymmetric crying facies have an increased risk for concomitant congenital heart defects, most commonly ventriculo-septal defects, atrial sepal defects, patent ductus arteriosus, and tetralogy of Fallot. In fact, asymmetric crying facies has been described in patients who have velocardiofacial syndrome (VCFS), also known as 22q11 deletion syndrome. In a patient who has asymmetric crying facies, other signs of VCFS should be sought, such as a cardiac malformation, hypocalcemia, typical facial features, and immune dysfunction, and fluorescence in situ hybridization for 22q11 deletion should be considered.

Recent evidence has surfaced that a subset of patients who have asymmetric crying facies may be at increased risk for other congenital anomalies. The incidence of associated anomalies has been reported to be 20% to 70%. Associated anomalies other than cardiovascular defects have included abnormalities of the skeletal, genitourinary, gastrointestinal, and central nervous systems. In addition, a subset of patients exhibit failure to thrive and developmental disabilities. One recent study found that 50% of affected infants had at least two associated systemic anomalies. Therefore, a thorough physical examination and evaluation, with particular attention to the cardiovascular system, should be undertaken in any infant found to have asymmetric crying facies. Long-term follow-up should focus on evaluation of growth and development.

**Single Transverse Palmar Crease**

The pattern of palmar creases varies substantially within the general population. The formation of palmar creases, which occurs between the second and fifth months of gestation, depends on fetal movement. Once the palmar creases are formed, they remain unchanged throughout life.

More subtle normal variations of palmar creases can occur for a variety of reasons, including family background, age, and race. Many physicians are aware of the association between single transverse or bridged palmar

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creases, previously known as simian creases and Sydney creases, respectively, and the occurrence of Down syndrome (Fig. 5). Although approximately 45% of patients who have Down syndrome have single transverse palmar creases, this finding occurs unilaterally in 4% and bilaterally in 1% of the general Caucasian population. In the Chinese population, single transverse palmar creases may be considered a normal phenotypic variant; a recent study found that 16.8% of 3,345 healthy Chinese newborns had unilateral single transverse creases and 6.6% had bilateral single transverse creases.

Despite the high frequency of single transverse palmar creases in certain populations, aberrations in the flexion creases of the hands have the potential to signify abnormal fetal development. The association of abnormal flexion creases and various congenital disorders has been reported frequently in the literature. Studies have shown an increased incidence of single transverse palmar crease in children who have chromosome abnormalities and in low-birthweight infants. Therefore, it is reasonable to search for other congenital anomalies when evaluating an infant who has a single transverse palmar crease after taking into account the patient’s race and familial background. When the crease occurs in isolation, however, no further evaluation is indicated.

### Café Au Lait Spots

Café au lait spots (CALS) are common in childhood and usually represent a benign birthmark. They are sharply defined, round to oval, homogeneous macules, usually varying in size from 2 mm to 20 cm (Fig. 6). Although their name implies a milky brown color, CALS can vary from tan to dark brown. They are more prevalent on unexposed skin and are found more frequently on the buttocks, trunk, and lower limbs. Histologically, they are characterized by increased melanin in the form of giant melanosomes in both the melanocytes and basal keratinocytes.

The frequency of CALS in the general population varies tremendously, based on the age and ethnic background of the patient. It has been estimated that 2.7% of all newborns have one or more CALS, with the prevalence in the Caucasian and Chinese populations being about 0.3% and that in the African-American population being about 18.3%. The prevalence in the general popu-

### Table. Summary of Selected Minor Anomalies and Associated Findings

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Syndrome(s) to Consider</th>
<th>Associated Findings</th>
<th>Suggested Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear tags</td>
<td>Oculoauriculovertebral spectrum</td>
<td>Microtia, facial asymmetry, epibulbar dermoids, vertebral anomalies</td>
<td>Hearing evaluation, Ophthalmologic evaluation, Spinal radiographs</td>
</tr>
<tr>
<td>Ear pits</td>
<td>Branchio-otorenal syndrome</td>
<td>External ear anomalies, brachial cleft fistulae, renal anomalies</td>
<td>Hearing evaluation, Renal ultrasonography</td>
</tr>
<tr>
<td>High-risk dorsal cutaneous stigmata</td>
<td>—</td>
<td>Occult spinal dysraphism</td>
<td>Spinal ultrasonography (&lt;3 mo of age), Spinal magnetic resonance imaging (&gt;3 mo of age)</td>
</tr>
<tr>
<td>Asymmetric crying facies</td>
<td>Velo-cardio-facial syndrome</td>
<td>Conotruncal cardiac malformation, hypocalcemia, typical minor anomalies</td>
<td>Echocardiography, Serum calcium measurement, Fluorescence in situ hybridization for 22q11 deletion</td>
</tr>
<tr>
<td>Cardiofacial syndrome</td>
<td></td>
<td>Cardiac, skeletal, genitourinary, gastrointestinal, or central nervous system abnormalities; failure to thrive and developmental abnormalities</td>
<td>Echocardiography, Monitor growth and development, Consider: Skeletal survey, Central nervous system imaging</td>
</tr>
<tr>
<td>Single transverse palmar crease</td>
<td>Down syndrome</td>
<td>Cardiac abnormalities, typical facial features, mental retardation</td>
<td>Karyotyping, Echocardiography</td>
</tr>
<tr>
<td>Café au lait spots</td>
<td>Neurofibromatosis type 1</td>
<td>Axillary or inguinal freckling, Lisch nodules, neurofibromas</td>
<td>Monitor for the development of the associated findings</td>
</tr>
</tbody>
</table>
lation increases to approximately 25% to 36% of school-age children and 8% to 13% of adults.

Although it is common to see one spot, the finding of three or more CALS is uncommon. Increased numbers of CALS have been associated with a number of neurocutaneous and genetic disorders, the most common of which is neurofibromatosis type 1 (NF-1). NF-1 is a relatively common autosomal dominant condition that is associated with more than six CALS that are greater than 5 mm in diameter in a prepubertal individual, axillary and inguinal freckling, ophthalmologic abnormalities such as optic gliomas and Lisch nodules, cutaneous neurofibromas, and mild learning difficulties. The diagnosis of NF-1 is based on clinical findings; genetic testing for this disorder is not performed routinely. Among prepubertal children, the prevalence of three or more CALS is estimated at 0.3%. Because of racial differences in the prevalence of CALS, it has been recommended that any Caucasian patient who has more than three CALS or any African-American patient who has more than five CALS be followed for the development of multisystem disease.

Conclusion

Neonatologists often have the unique opportunity to be the first to identify abnormalities in the neonate. The recognition of minor anomalies can be the key to diagnosis and management of a patient. The Table summarizes the minor anomalies discussed in this review, possible associated syndromes and findings, and suggested investigations. However, it is important to consider the age, gender, race, and family background of the patient prior to assigning significance to any given anomaly. When three or more minor anomalies are observed, a thorough investigation for an occult major abnormality should be undertaken. However, obtaining invasive studies, imaging, or laboratory investigations should depend on the clinical context of the patient and the presence or absence of additional symptoms and signs. Certain minor anomalies, including asymmetric crying facies and high-risk dorsal cutaneous stigmata, are associated with an increased risk of an underlying major malformation and should prompt their own investigation. Therefore, a thorough examination of every neonate, with particular attention to the identification of minor anomalies, is essential.

Suggested Reading

**NeoReviews Quiz**

5. A minor anomaly is a structural defect that deviates from the normal standard and has no major surgical, medical, or cosmetic importance. Of the following, a single minor anomaly is **most** likely to be:

   A. Associated with a 20% percent risk of a major malformation.
   B. Found on the face or the hands.
   C. Indicative of a genetic syndrome.
   D. Present in 4% or more of the general population.
   E. Present in 1% of normal newborns.

6. Preauricular ear tags and pits are frequent findings on routine examination of the neonate. Of the following, preauricular ear tags and pits are **most** likely to be:

   A. An indication for echocardiography.
   B. An indication for renal ultrasonography.
   C. Associated with hearing loss.
   D. Bilateral.
   E. Inherited as an autosomal recessive trait.

7. Cutaneous abnormalities in the sacral area can be used as a possible indicator of occult spinal dysraphism. Of the following, the **most** common cutaneous abnormality in the sacral area is:

   A. Cutis aplasia.
   B. Hairy tuft.
   C. Hemangioma.
   D. Simple dimple.
   E. Tail-like appendage.

8. Congenital absence or hypoplasia of the depressor anguli oris muscle (DAOM) is a common cause of asymmetric crying facies in neonates. Of the following, the **most accurate** statement regarding hypoplasia of the DAOM is that the:

   A. Incidence is increased in first- and second-degree relatives.
   B. Patient cannot close the eye on the affected side.
   C. Patient cannot wrinkle the forehead on the affected side.
   D. Predilection is for the right side of the face.
   E. Prevalence is higher among females.
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