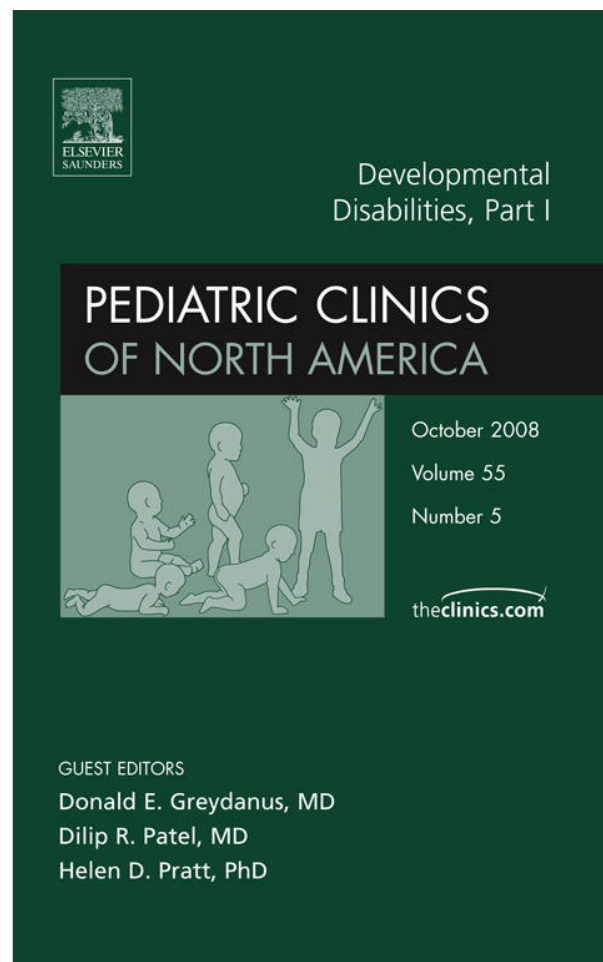


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# Role of the Dysmorphologic Evaluation in the Child with Developmental Delay

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## KEYWORDS

• Syndrome • Diagnosis • Anomaly • Variant

Developmental delay (DD) or cognitive impairment (CI) is a common reason for referral to a genetics unit. The term *developmental delay* is usually used in children younger than 5 years, whereas *cognitive impairment* (mental retardation) is reserved for those 5 years and older. Although DD may predict later CI, occasionally the delays are mild or transient. It is estimated that 1% to 3% of children have CI; the frequency of DD is higher.<sup>1,2</sup> Among the evaluations done on children who have DD in attempt to determine etiology are family and medical history (both pre- and postnatal), neurologic evaluation, dysmorphologic evaluation, and assessment of behavior. Based on these findings, appropriate imaging studies or laboratory tests may be ordered. Using this approach, various studies have found that a cause of DD can be identified in 40% to 60% of the children evaluated.<sup>3</sup> This article focuses on the dysmorphologic evaluation of the child who has DD or CI. Attention is focused on minor anomalies, because those are often considered to be the dysmorphic features that are the component manifestations of a particular syndrome.

Anomalies can occur by way of four modes of pathogenesis: deformation, disruption, dysplasia, or malformation. Deformations are caused by mechanical forces and may be of prenatal or postnatal onset. For example, joint contractures might occur secondary to oligohydramnios; plagiocephaly might occur secondary to sleep position.<sup>4</sup> Disruptions occur in previously normal structures in which some agent has caused cell death to occur. One classic example of this is the amniotic band sequence. Dysplasias are abnormal development of a particular tissue. Ectodermal

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dysplasia refers to that group of conditions that affects structures derived from the ectoderm; notably, skin, teeth, hair, and nails. A malformation is an inherently abnormal developmental process of a particular structure. The malformed structure might be too small (eg, microphthalmia), redundant (eg, polydactyly), or incompletely developed (eg, cleft lip). Anomalies can be classified as major or minor. A major anomaly can be defined as one that will usually require medical or surgical intervention (eg, pyloric stenosis, club foot, cleft palate). A minor anomaly will generally not require intervention but may be of cosmetic concern. In general, each true minor anomaly is found in less than 4% of otherwise normal individuals. It is also estimated that as many as 13% of newborns have at least one minor anomaly; however, among those who have three or more minor anomalies, the chance of having a major anomaly, a dysmorphic syndrome, or both greatly increases.<sup>5,6</sup>

The first component of the dysmorphologic examination is observation of the entire child. Does the child resemble the parents or other family members? If not, what are the key manifestations that cause phenotypic differences? The second step should be the documentation and detailed description of these features. Measurements should be done when possible. At this point, the clinician might have an idea regarding a possible syndrome diagnosis. Is this impression based on relatively common anomalies (eg, using the presence of a single transverse palmar crease and small epicanthal folds as the basis for suspecting Down syndrome) or on more unusual, often pathognomic findings (eg, long palpebral fissures with ectropion and prominent fingertip pads as the basis for suspecting Kabuki syndrome)? When the clinician has a suspected diagnosis, he or she should look for other manifestations that support the initial diagnostic impression. In the case of Down syndrome, the clinician should look for thickened nuchal skin, flat occiput, “upslanting” palpebral fissures, small ears, apparently large tongue, and hypoplastic breast tissue. This evaluation is especially important in conditions for which testing is not readily available. When no diagnosis is initially suspected, a good list of manifestations can aid in literature or database searches for potential diagnoses, which in turn can lead to a reasonable approach to laboratory testing. This review, therefore, is not meant to be a comprehensive list of dysmorphic features but instead provides a brief discussion of craniofacial, skin, and limb anomalies (which are more likely to be noted not only by clinicians but also by allied health workers) and notes which features are particularly helpful clues to common syndromes (**Table 1**), metabolic disorders (**Table 2**), or autism syndromes (**Table 3**).

#### COMPONENTS OF A DYSMORPHOLOGIC EXAMINATION

There are several sources of lists of dysmorphic features, with two of the more common being the London Dysmorphology Database<sup>7</sup> and “Diagnostic Dysmorphology.”<sup>8</sup> The features described in the following sections are drawn from these references, with assistance from other sources.<sup>9</sup>

##### ***Build and Stature***

A child’s build can be described as obese, slender, or muscular. Obesity in turn can be truncal or generalized. Stature can be described as short or tall; in those who have short stature, further distinction as to proportionate or disproportionated should be made. The same is true for tall stature: it may be proportionate or further defined as disproportionated, with long limbs being present. Truncal obesity coupled with short stature should prompt consideration of Prader-Willi syndrome; a slender build with short stature is a common finding in Dubowitz and Cockayne syndromes; and disproportionated short stature suggests consideration of a skeletal dysplasia (eg,

hypochondroplasia). A muscular build is a relatively uncommon dysmorphic feature but can be found in several forms of lipodystrophy.

### ***Cranium***

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Attention should be paid to size (microcephaly, macrocephaly), shape, sutures, and fontanelles. Microcephaly and macrocephaly are common component manifestations of numerous syndromes, and the size and growth pattern of the head provide useful clues to diagnosis. For example, a girl who has Rett syndrome exhibits a normal head circumference at birth but develops microcephaly between the ages of 6 and 18 months. Macrocephaly has been shown to be a relatively common finding in individuals who have autism; furthermore, it tends to be postnatal in onset in a substantial proportion of those cases.<sup>10</sup> One notable exception is the association of autism with congenital macrocephaly in those who have PTEN mutations.<sup>11</sup> An abnormal skull shape (brachycephaly, trigonocephaly, plagiocephaly, and so forth) may be secondary to a deformational process or indicative of premature suture fusion. Additional sutural anomalies include ridged or wide sutures; furthermore, fontanelles may be small or large and exhibit early or late closure.

### ***Hair Growth, Structure, and Pigmentation***

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Generalized hair growth anomalies include alopecia (partial or total) and hirsutism. For example, sparse hair is found in Coffin-Siris and Noonan syndromes; hirsutism is a common manifestation of fetal alcohol and Cornelia de Lange syndromes. Hair growth anomalies can also include frontal balding, or low or high frontal hairline. A newborn who has hypotonia and frontal balding should be inspected for additional features of Down syndrome, for example. Widow's peak and abnormal placement of cowlicks may also provide clues to a syndrome diagnosis. Widow's peak is often found in those who have hypertelorism; common syndromes with this manifestation include Aarskog syndrome and Opitz-Frias (G/BBB) syndrome. Hair structure differences that should be noted include fine or coarse, soft or brittle, and kinky. Fine, soft, or coarse hair is more likely to be a familial variant, whereas brittle or kinky hair is more often a minor anomaly and could thus provide helpful clues to diagnosis. Menkes syndrome and Netherton syndrome (ichthyosis and kinky, brittle hair) are both conditions to consider in the child who has DD and these hair findings. Finally, pigmentation differences can point to the correct diagnosis. In particular, general hypopigmentation can be found in a number of metabolic conditions (see **Table 2**); patchy depigmentation suggests the diagnosis of Chédiak-Higashi syndrome.

### ***Face, General***

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The child's face shape may be striking, but this feature can often be a familial variant and not be pathologically significant. Facial features that might provide more helpful clues include facial asymmetry, so-called "coarseness" (often attributable to thickened facial tissues), flat facial profile, and midface hypoplasia. Two of the more common syndromes that have facial asymmetry include Goldenhar syndrome and CHARGE syndrome. Coarse facial features are common in many metabolic disorders, particularly those that cause abnormal storage of metabolites. A flat facial profile is common in chromosome 22q13 microdeletion syndrome and in Smith-Magenis and Stickler syndromes. Midface hypoplasia is a pointer toward several chromosome anomalies and a number of prenatal exposures (including alcohol and warfarin). Lastly, facial expression should not be ignored. A child who has an expressionless face could have Möbius syndrome or congenital myotonic dystrophy. Facial grimacing is a component manifestation of a few conditions such as glutaric aciduria type II.

<b>Table 1</b>		
<b>Select syndromes with dysmorphic features</b>		
<b>Condition</b>	<b>Selected Distinctive Features</b>	<b>Comment</b>
Fetal alcohol syndrome	Short palpebral fissures, flat philtrum, relatively thin upper lip	Need facial features plus growth retardation, microcephaly/MR, and maternal alcohol use to make diagnosis
Noonan syndrome	Hypertelorism, deeply grooved philtrum	Caused by mutations in one of several genes—all in the same pathway
Costello syndrome	"Coarse" appearance, sparse curly hair, deep palmar creases	Caused by mutation in HRAS gene
Cardiofaciocutaneous syndrome	Sparse coarse hair, high forehead, relative macrocephaly, hyperkeratotic macules	Caused by mutations in one of at least two genes
Prader-Willi syndrome	Narrow forehead, "upslanting" palpebral fissures, small hands and feet	Methylation studies of chromosome 15q11 region is the suggested first step in the diagnostic evaluation
CHARGE syndrome	Dysplastic ears, which are often asymmetric; unilateral facial palsy	Formerly called CHARGE association, now known to be caused by single gene mutation in CHD7
Kabuki syndrome	Long palpebral fissures, prominent ears, fetal pads	No testing available
Cornelia de Lange syndrome	Synophrys with arched eyebrows, ill-defined alae, thin lips with downturned mouth	Several different genes cause this condition, including one that is X-linked
Sotos syndrome	Macrocephaly, high forehead, "downslanting" palpebral fissures	DD/CI only occasionally found
Angelman syndrome	Large mouth, prominent jaw	Methylation studies of chromosome 15q11 region is the suggested first step in the diagnostic evaluation
Mowat-Wilson syndrome	Deeply set eyes, round nasal tip, uplifted earlobes	Hirschsprung's disease or severe constipation common
Coffin-Lowry syndrome	Full lips, with the upper lip being rounded with minimal vermilion peaks; "puffy," tapered fingers	Female carriers might have milder manifestations
ATRX	Hypertelorism, short philtrum, macrostomia, everted lower lip	Genital anomalies also common

*(continued on next page)*

<b>Table 1 (continued)</b>		
<b>Condition</b>	<b>Selected Distinctive Features</b>	<b>Comment</b>
Williams syndrome	Periorbital puffiness, anteverted nares, full lips	Can be verified by FISH probe
22q deletion syndrome	Short palpebral fissures; broad midnose; long, tapered fingers	Very common cause of DD/learning disabilities
Smith-Magenis syndrome	Short philtrum with upturned upper lip, flat midface	Mutation or deletion of RAI1 gene on chromosome 17
1p36 deletion syndrome	Deep-set eyes, straight eyebrows, flat midface	One of the most common deletion syndromes
9q34 microdeletion syndrome	Long eyebrows with synophrys, upturned nose, short philtrum, low-set ears	—
17q21.31 microdeletion syndrome	Long face, narrow palpebral fissures, bulbous nasal tip, large low-set ears	May account for 1% of those who have CI
9q22.3 microdeletion syndrome	Large size, macrocephaly, small mouth, thin upper lip	—

*Abbreviations:* ATRX, X-linked alpha-thalassemia/mental retardation syndrome; FISH, fluorescent in situ hybridization; MR, mental retardation.

### **Forehead**

There are a number of minor anomalies involving the forehead, with most being subjective determinations. Specifically, the forehead can be described as prominent, broad, short, or bossed. The frontal hairline may be described as high or low. It is difficult, however, to separate some of these terms from others. For example, an individual who has a prominent forehead may also appear to have a high frontal hairline (eg, as in achondroplasia). Similarly, an individual who has a short forehead could appear to have a low frontal hairline.

In addition, the supraorbital ridges can be hyperplastic or hypoplastic. In an individual who has hyperplastic supraorbital ridges, the eyes may appear deeply set; when the ridges are hypoplastic, the eyes may appear prominent. Examples of conditions that have hyperplastic and hypoplastic supraorbital ridges are frontometaphyseal dysplasia and Zellweger syndrome, respectively. It is unfortunate that there are no tables of normal forehead measurements available.

### **Eyes**

As noted previously, eyes may appear to be deeply set or prominent. The sclerae may have a bluish hue, and variations in pigmentation may affect the iris. Bluish sclerae are a clue to osteogenesis imperfecta, particularly in an older child who has numerous fractures. The iris may show a stellate pattern (a clue to Williams syndrome) or be bicolored (a clue to Waardenburg syndrome when coupled with hearing loss with or without pigmentary anomalies of the hair). Eyelids may exhibit ptosis, ectropion, or entropion. Ptosis is a component manifestation of several hundred syndromes, including Noonan and related syndromes, Dubowitz syndrome, fetal alcohol and hydantoin

<b>Table 2</b>		
<b>Select metabolic conditions with dysmorphic features</b>		
<b>Condition</b>	<b>Dysmorphic Features</b>	<b>Comment</b>
Propionicacidemia	Frontal bossing, depressed nasal bridge, epicanthal folds, open mouth with downturned corners	—
Methylmalonicacidemia	High forehead, broad nasal bridge, epicanthal folds, long smooth philtrum, triangular mouth	—
Multiple carboxylase deficiency	Alopecia, sparse eyebrows and eyelashes	May be caused by holocarboxylase deficiency or biotinidase deficiency
Glutaricaciduria type I	Prenatal- or postnatal-onset macrocephaly, facial grimacing	—
D-2-hydroxyglutaricaciduria	Macrocephaly, epicanthal folds, coarse facial features, single transverse palmar crease	—
Homocystinuria	Tall and thin, depigmented hair	Downward lens dislocation common
Argininosuccinicaciduria	Alopecia, brittle hair	—
Glutaricaciduria type II	High forehead, depressed nasal bridge, short nose, single transverse palmar crease	—
Pyruvate dehydrogenase deficiency	Frontal bossing, short nose, long philtrum, thin upper lip	Face may resemble that of fetal alcohol syndrome
Kearns-Sayre syndrome	Progressive ptosis, short stature	Mitochondrial depletion found in muscle or skin, but not blood
Zellweger syndrome	High forehead, large fontanels, abnormal ears, broad nasal bridge, hypoplastic supraorbital ridges	Other peroxisomal disorders might include some of these features
Menkes syndrome	Depigmented, kinky, or brittle hair; abnormal eyebrow hair	—
Mucopolysaccharidoses	Macrocephaly, coarse facial features, frontal bossing, prominent eyes, depressed nasal bridge, thick lips	Includes Hurler's and Hunter's syndromes, especially. Others have milder, if any, manifestations
I-cell disease	Similar to Hurler syndrome, but earlier onset	—
Mucopolipidosis III	Hirsutism, synophrys, coarse facial features	Two different genes cause this condition

*(continued on next page)*

Table 2 (continued)		
Condition	Dysmorphic Features	Comment
GM <sub>1</sub> gangliosidosis	Coarse facial features, expressionless face, hirsutism on forehead, long philtrum	—
Multiple sulfatase deficiency	Postnatal microcephaly, coarse facial features, prominent eyes	—
Congenital disorders of glycosylation	Lipodystrophy, high nasal bridge, prominent jaw, inverted nipples	—
Smith-Lemli-Opitz syndrome	High forehead, ptosis, epicanthal folds, short nose, micrognathia, syndactyly toes 2–3	—

syndromes, Kearns-Sayre syndrome, and others. When ectropion is present, the lid appears everted. One common example with this manifestation is Kabuki syndrome. The term *entropion* refers to eyelids that appear to turn inward, with the result that eyelashes rub on the eyeball. This anomaly is relatively rare; most common syndromes in which it is found include chromosome 22q11.2 duplication and Wiedemann-Rautenstrauch syndrome. Palpebral fissures may be described as long or short, wide or narrow. Short palpebral fissures are common to fetal alcohol syndrome; long palpebral fissures are found in Kabuki syndrome. Individuals who have velocardiofacial syndrome (deletion 22q11.2) are described as having narrow palpebral fissures. It is reasonable to measure palpebral fissures using the inner canthus and outer canthus as landmarks to help determine whether they are long or short. In addition, palpebral fissures may slant upward or downward. Down syndrome is one of the most common syndromes that has upward slant; Treacher Collins syndrome and Noonan syndrome show downward slant. A final minor anomaly that may be useful to note is the presence of epicanthal folds.

In addition to paying attention to anomalies of the eye and lids, spacing is well worth documenting. Hypertelorism is the presence of widely spaced orbits; hypotelorism is the presence of closely set orbits. One's impression of hypertelorism may be verified by measuring the inner and outer canthal distances (**Fig. 1**). When both are greater than the 97th centile, hypertelorism is present; when both are less than the third centile, hypotelorism is present. When the inner canthal, but not outer canthal distance, is above the 97th centile, telecanthus is said to be present. Hypertelorism may be an indicator of abnormal facial development, whereas hypotelorism is a strong indicator of abnormal brain development.

### ***Eyebrows and Eyelashes***

Common anomalies of eyebrows include synophrys (confluent growth over the nose), sparseness, disruption, unusual flare, and unusual arch. One particularly notable eyebrow anomaly is the presence of straight eyebrows in chromosome 1p36 deletion (**Fig. 2**). Eyelashes may also be sparse or absent; double eyelashes are an unusual finding found in only a few syndromes. In a child who has lymphedema, however, the presence of double eyelashes leads to a diagnosis of distichiasis-lymphedema syndrome.

### ***Nose***

There are few aspects of the nose that can be measured; most descriptions are based on subjective impressions. For example, the entire nose may be described as large,

<b>Table 3</b>		
<b>Conditions with autism and dysmorphic features</b>		
<b>Condition</b>	<b>Dysmorphic Features</b>	<b>Testing, if Any</b>
Fragile X	Prominent forehead, long face, prominent ears	Molecular testing to determine number of CGG repeats
Classic Rett syndrome	Microcephaly, postnatal onset	Mutation analysis of MECP2 gene
Angelman syndrome	Microcephaly; wide mouth; prominent, pointed chin	Molecular testing (methylation analysis and UBE3 sequencing)
Cornelia de Lange syndrome	Hisutism, synophrys, short nose, thin lips, downturned mouth, small chin, small hands, single palmar crease	Molecular testing for known genes, although not all causative genes identified to date
Smith-Magenis syndrome	Prominent forehead, midface hypoplasia, prominent philtrum, prominent chin, short stature	FISH for deletion 17p11.2; RAI1 gene sequencing if FISH negative
CHARGE syndrome	Short stature, abnormal ears, asymmetric face	Molecular analysis of CHD7 gene, although detection rate 60%–65%
PTEN-related disorders	Macrocephaly, pigmentary skin changes, skin tumors	Molecular analysis PTEN gene
22q deletion (DiGeorge syndrome, Shprintzen syndrome)	Short palpebral fissures; broad nose; hypoplastic alae nasi; micrognathia; slender, tapering fingers	FISH for deletion 22q11.2
Fetal valproate	Metopic ridge, apparent hypertelorism, small nose, long philtrum, "coarse" facial features	None
Kabuki syndrome	Long palpebral fissures, arched eyebrows, depressed nasal tip, small chin, prominent ears, fingertip pads	None
Sotos syndrome	Macrocephaly, large/prominent forehead, "downslanting" palpebral fissures, prominent chin	Molecular testing NSD1 gene
Smith-Lemli-Opitz syndrome	High forehead, ptosis, epicanthal folds, short nose, micrognathia, syndactyly toes 2–3	Determination of 7-dehydrocholesterol level

*Abbreviation:* FISH, fluorescent in situ hybridization.



**Fig. 1.** When measuring inner and outer canthal distances, care must be taken to not loop over the nose, which will artificially increase the measured distance.

small, long, short, broad, narrow, concave, or convex. The bridge may be flat, high, or wide; the tip may be broad, flat, bulbous, or overhanging. The alae can be thick or thin, and there may be a small coloboma present. The nostrils may be broad, small, or anteverted. A flat nasal bridge or a small or short nose is found in several hundred syndromes; conversely, a large nose is markedly less common. Alar notches are another helpful clue and a component manifestation of only a few relatively common syndromes (eg, Johansson-Blizzard and trichorhinophalangeal syndromes).

### ***Lower Jaw***

The two more common descriptions of a dysmorphic jaw are micrognathia and prognathia. In general, a crude means of determining whether a jaw is recessed or



**Fig. 2.** Straight eyebrows in child who has 1p36 deletion.

prominent is to draw a vertical line through the lips—it should intersect the point of the chin. Additional descriptors that can be used to characterize the chin include dimpled, grooved, and pointed.

### ***Philtrum***

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The philtrum can be short or long, smooth or deeply grooved. An apparently long, smooth philtrum is a clue to fetal alcohol syndrome. In addition, a prominent, short philtrum is a common finding in Smith-Magenis syndrome (**Fig. 3**).

### ***Mouth and Lips***

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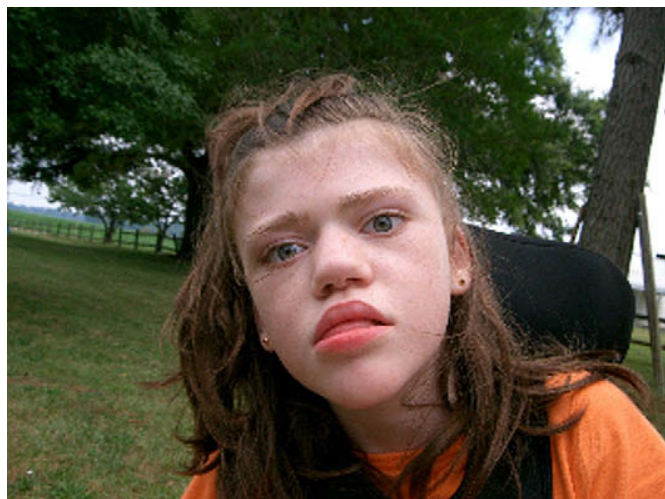
Variations in the appearance of the mouth include large or small size and having corners that appear to turn down. A large mouth is a characteristic finding in Angelman syndrome; a small mouth is common in Freeman-Sheldon syndrome. Downturned corners of the mouth are a typical finding in Cornelia de Lange syndrome. Differences in the appearance of the lips might also provide clues to the diagnosis. Thick or thin lips, although often a familial variant, can occasionally be a useful feature. For example, thick lips that have a rounded upper curve are a cardinal sign of Coffin-Lowry syndrome (**Fig. 4**), whereas a relatively thin upper lip suggests fetal alcohol syndrome.

### ***Ears***

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Anomalies of the ears include size, shape, and position. Large ears are common in fragile X syndrome, particularly if also protruding. Small ears are typical in Down syndrome. Tables of measurements are available, so a subjective impression may be verified. Abnormally shaped ears (which includes the terms lop, cup-shaped, crumpled, and dysplastic) are found in CHARGE syndrome, Treacher Collins syndrome, and many conditions. Differences in ear position can also provide helpful clues to the diagnosis, although low-set ears are perhaps one of the most overcalled findings in the author's personal experience. To determine whether the ears are truly low set, the clinician should draw an imaginary horizontal line from the corner of the eye to the occiput. That line should intersect the upper part of where the ear attaches to the head. A second manifestation that is often erroneously stated to be present is posteriorly rotated ears. A rotation of as much as 30° is within normal variation.

Additional variations of the ear are those of the helices and the lobes. Helices can appear to be overfolded or unfolded (although these, too, may be familial variants);



**Fig. 3.** Short, upturned philtrum in Smith-Magenis syndrome.



**Fig. 4.** Full lips with poorly defined vermilion peaks, giving upper lip a rounded appearance, in Coffin-Lowry syndrome.

the lobe may be uplifted or have creases. Uplifted lobes, particularly with what appears to be a small mound in the lobe, are characteristic of Mowat-Wilson syndrome (**Fig. 5**); creased earlobes are common to Beckwith-Wiedemann syndrome. Finally, ear pits and tags are often helpful clues to diagnosis.

### ***Nipples***

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Nipples are mentioned here because they are often stated to be widely spaced; measurements are available to verify that subjective impression. If they are found to be widely spaced, the clinician should consider Turner syndrome when found in a female patient. Another helpful dysmorphic feature of the nipples is inversion, which is a pointer toward the group of metabolic disorders termed the congenital disorders of glycosylation.

### ***Limbs***

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Disproportion of limbs should be noted, if present, as should asymmetry (eg, apparent overgrowth of one). Restriction of elbow movement is also a good manifestation to note, particularly because it is a common finding in such conditions as Emery-Dreifuss muscular dystrophy and Marfan syndrome. Contractures in general are another significant anomaly to note.



**Fig. 5.** Characteristic ear in Mowat-Wilson syndrome.

### **Hands and Feet**

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Variations in size of the hands and feet and anomalies of the digits and creases should be assessed. Hands and feet that appear disproportionately small (and measurements should be done to verify) are common in Prader-Willi syndrome. Large hands and feet are an uncommon component manifestation but, when present, can be a very helpful clue to the diagnosis. Digits may also show variations in size (short or long), shape (tapered, broad, or with wide fingertips or fetal pads), and position (clinodactyly, camptodactyly) (**Fig. 6**). In addition, toes can sometimes be described as malimplanted (**Fig. 7**), although this seems to be a relatively common, nonspecific finding. A relatively slender middle toe is also a common finding, the significance of which is unknown. One very useful finding, however, is significant syndactyly between toes 2 and 3, which in a child who has DD and a dysmorphic facial appearance should lead to a strong suspicion for Smith-Lemli-Opitz syndrome. Finally, creases should be assessed, although a single transverse palmar crease (previously called a “simian” crease) (**Fig. 8**) is a relatively common finding in the general population. Deep or shallow palmar creases are also helpful clues (eg, deep palmar creases suggest mosaic trisomy 8).

### **Skin**

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Attention should be paid to pigmentary and vascular differences. The pigmentary differences might be general (eg, albinism) or localized (café au lait macules, areas of hypopigmentation). Vascular anomalies include capillary malformations and hemangiomas.

As alluded to earlier, some dysmorphic features are better diagnostic clues than others. **Table 1** lists several common syndromes and the features that are particularly helpful in suggesting the diagnosis. Although metabolic screening is usually not a recommended part of the evaluation of the child who has DD,<sup>12</sup> in some cases, the presence of dysmorphic features may help point toward a particular metabolic diagnosis and lead to appropriate laboratory evaluation. **Table 2** lists the metabolic conditions that have associated phenotypic anomalies. It has been suggested that the evaluation of children who have autism could yield diagnostic information in up to 40%. Approximately 15% of the yield would be attributable to chromosome studies, array comparative genomic hybridization studies, or both; the remaining would be attributable to a number of syndromes, which are listed in **Table 3**.



**Fig. 6.** Camptodactyly of fifth finger.



**Fig. 7.** Malimplanted toes.

Finally, it has recently been shown that without experience in dysmorphology, the determination of whether a structure is truly abnormal is difficult. A better approach, as suggested by Miles and colleagues,<sup>13</sup> is to recognize that a body part is abnormal (eg, noting that the lip and philtrum area appears abnormal, rather than specifying that the philtrum is short and the upper lip appears pulled up) and noting how many body parts are dysmorphic (thus, a reason for referral or laboratory evaluation might state, “cognitive impairment with anomalies of the eye, ear, and hands”). Further research is being done to determine whether this approach has validity.<sup>13</sup> Until then, the bottom line is that any individual who has DD or CI should be evaluated for the presence of



**Fig. 8.** Single transverse palmar crease.

dysmorphic features that might point toward the correct diagnosis and provide the family with information regarding recurrence risk, prognosis, and medical management issues for that particular individual.

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