

Evaluation of a Dysmorphic Newborn

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Dysmorphology an art in the medical field is primarily a visual specialty. It is the study of disordered development and covers birth defects that are apparent at or before the time of birth and recognizable structural anomalies. There are special terms in conceptualization of dysmorphic features like malformation, deformation, disruption syndrome, sequence and association.

Although reaching an etiologic diagnosis for the newborn with single or multiple malformations is a primary goal of the evaluation process, a specific diagnosis might not be apparent after detailed evaluation and diagnostic testing. This is due to a variety of reasons, such as age-dependent phenotypic or behavioral manifestations or uniqueness of the pattern of malformations. So the diagnosis may not always be reached in the newborn period. Genetic disorders are of three major categories ,chromosomal, single gene and multifactorial. . Most evident birth defects will fall in the multifactorial group.

Definitions

A malformation is a primary defect where there is a basic alteration of structure, usually occurring before 10 weeks of gestation. Example cleft lip, anencephaly or radial agenesis. A malformation could be major which requires surgical intervention e.g. spina bifida / CHD or minor malformation that requires no treatment or can be corrected totally e.g. polydactyly.

A minor variant is a low frequency (1% to 5%) congenital feature that can be found in the normal population or as an integral part of a multiple congenital anomaly (MCA) syndrome. Example: simian crease, clinodactyly of the fifth finger, epicanthic fold, small ears and accessory nipple. Some minor variants are also classified as minor anomalies when part of a syndrome or when no one in the family has similar features. In isolation there variation do not require extensive genetic work up.

Deformations / Secondary defect are anomalies caused by unusual mechanical pressure on the developing fetus, usually during the last trimester of gestation e.g. club feet, torticollis and plagiocephaly.

Disruption occurs when there is a breakdown of normal tissue either due to mechanical, vascular or infectious causes. Example: amniotic band sequence .

Syndrome (Greek word meaning – running together). A dysmorphic syndrome is a recognized pattern of two or more anomalies in an individual due to a common cause. Most of them are made up of one or more major anomalies together with a variable number of minor anomalies. Rarely, any one of these features is diagnostic; instead the entire constellation of defects must be taken into consideration to define the diagnosis.

Recognized dysmorphic syndromes now number in thousands and more seem to be added every month. Example: Marfan syndrome, Apert syndrome, **CHARGE** (Coloboma, Heart defect, Atresia choanae, Growth/MR, genital hypoplasia, Ear abnormalities) syndrome.

Association is a non-random occurrence of the same multiple anomalies for which no consistent cause can be established. The core anomalies usually consist of six to eight features and any individual patient rarely has all the core features. Example: **VATER** (Vertebral Renal dysplasia).

Sequence is used when a single usually undefined event leads to a single anomaly having a cascading effect that causes local and/or distant deformations and/or disruptions, such as Potter sequence (oligohydramnios with beak nose, cartilage-deficient ears, pulmonary hypoplasia) and amniotic band sequence (bands constricting the blood supply to involved limbs with amputation and/or syndactyly), Pierre Robin sequence (micrognathia with glossoptosis and cleft palate).

Dysplasia: Defects resulting from abnormal, cellular organization or function of one tissue type. These may worsen with age e.g. skeletal dysplasia, ectodermal dysplasia.

Complexes refer to anomalies of several different structures all of which lie in the same local body region during embryonic development. Many of them are caused by vascular abnormalities. Risk of recurrence is low e.g. hemifacial microsomia, Poland anomaly, sacral agenesis etc.

Approach for Evaluation

When a newborn with one or more malformations is identified, a detailed history and physical examination must be undertaken to ascertain whether additional malformations are present and to seek a specific etiologic diagnosis. Diagnostic studies should be selected based on the information elicited and a working diagnosis should be developed.

The family should receive detailed counseling in a setting and with content that is appropriate to their needs. Medical records and reports should reflect available laboratory and clinical data, diagnostic considerations and a plan for ongoing care, evaluation and management. **Fig1 and 2 summarize the overall approach to dysmorphic diagnosis.**

History

A comprehensive history is a critical component of the evaluation of a newborn with dysmorphic features. Certain physical parameters may be assessed further and more carefully based on information derived from historical data. Additionally, results of initial diagnostic testing may suggest the need for further history or physical examination. The following elements should be included:

- Prenatal history
 - Maternal age, parity and health, including maternal illnesses and medications used
 - Fetal movements throughout pregnancy
 - Pregnancy complications
 - History of infections
 - Teratogenic exposures, such as alcohol, tobacco, drugs and medications
 - Periconceptional supplementation with folic acid
 - Prenatal screening/testing (eg antenatal biochemical screening, ultrasonography, invasive testing etc)
- Perinatal history
 - Intrapartum course and duration
 - Intrapartum drug or medication exposure
 - Presentation and mode of delivery
 - Complications of delivery and infant's condition at birth (Apgar score)
 - Description of placenta
 - Birth weight; appropriate for gestational age
 - Neonatal course, including feeding, medications and complications
- Family history
 - A three generation family history with health information about all relatives, including parents, siblings, grandparents, uncles, aunts and cousins and noting any instances of reproductive losses or infertility
 - Specific information in previous babies/relatives
 - Consanguinity in parents
 - Ethnic background

Medical records should be reviewed to corroborate any significant positive findings elicited through the history.

Physical Examination

A complete physical examination must be performed, with particular attention to major and minor malformations and to physical variations. The same areas should be examined in other family members, when appropriate.. Taking a clinical photograph for syndrome search , comparison for evolving phenotype and referral is very useful.

Essential components of the newborn physical examination include:

- Growth parameters
 - Assessment of gestational age by physical parameters
 - Anthropometry
 - Assessment of proportionality and symmetry
 - Specific measurements where indicated by observation, such as inner-canthal distance or upper to lower segment ratio
- General appearance
 - Tone, posture, positioning, alertness, vigor, color, respiratory effort and other observations
- Detailed examination
 - Skin - pigmentation pattern (areas of increased or decreased pigmentation), dimples, vascular or other lesions, or excessive peeling
 - Head - shape, symmetry, fontanelles
 - Scalp - hair patterning and location of hair whorls
 - Facial features
 - Eyes - pupils, orbits (hyper or hypotelorism) including palpebral fissure inclination and length
 - Ears - location, rotation, configuration and size, patency
 - Nose - appearance and patency of nares
 - Appearance of nasal bridge and columella
 - Mouth - appearance of upper lip, philtrum and vermilion border
 - Intra-oral examination of palate, alveolar ridges and tongue
 - Mandible - shape and symmetry
 - Neck - posterior hairline, presence of sinus tracts, torticollis, redundant skin or webbing
 - Chest - shape, symmetry, circumference, location of nipples, accessory nipples
 - Cardiovascular - heart murmurs, pulses, blood pressure

- Lungs - symmetry of breath sounds
- Abdomen - appearance of umbilicus, muscle tone, integrity of wall, enlarged organs or masses
- Genitalia - size, appearance, palpation of testes (in males), presence of ambiguity
- Anus - location and patency
- Back - symmetry, spine, presence of sinuses or hair tufts in inter-gluteal cleft
- Extremities - proportions, appearance, range of motion (including hips), pulses, presence of reduction or duplication of segments
- Hands and feet - nails; creases (palmar, phalangeal and flexion); joints
- Neurological - tone, response, alertness, reflexes

The history and physical findings should lead to an initial impression and differential diagnosis. These will guide selection of preliminary tests, the content of initial counseling of the family and development of an immediate plan for management, which can be modified as new information is developed and synthesized. Few data bases for syndromic diagnosis are also available and may be useful (eg London Dysmorphology data base)

At the end of the history and physical examination impression should fit into one of three categories:

- Single (isolated) malformation
- Multiple malformations, recognizable pattern (syndrome identification)
- Multiple malformations, pattern not recognized

Confirmation of Diagnosis

Diagnostic tests should be selected to clarify or establish a clinical diagnosis when possible. Such tests may be of particular value when a syndrome pattern is not recognized or to facilitate risk assessment for genetic counseling. Select tests in a prioritized order, rather than using a “shotgun” approach; initial results can guide selection of more specific subsequent tests . Single (isolated) malformations or syndromes which are recognized on a clinical basis may not require additional diagnostic tests. It is important to discuss with the family the possible consequences of genetic testing, including the implications for relatives. Consultations with specialists in pertinent fields may be required both for confirmation of diagnosis and multidisciplinary management. .Referral to a Clinical geneticist should be made when a clear working diagnosis is not evident, to confirm a questionable diagnosis, to seek further information about an established diagnosis and to provide detailed genetic counseling.

Diagnostic tests which should be considered include:

1. Imaging

Radiographs, computed tomography, magnetic resonance imaging or ultrasonography should not be considered routine, but should be employed as indicated by the differential diagnosis. Infantogram is useful in suspected skeletal dysplasias.

2. Chromosomal analysis - Table 1 gives risk of chromosomal abnormalities with structural malformations. Usually a routine G banded karyotype is done, high resolution chromosome banding is required in situations where the phenotype is "Chromosomal" but not fitting in a particular chromosomal phenotype and G banded karyotype is normal. Chromosomal analysis should definitely be obtained in the following situations:

- Infants with two or more major malformations
- Infants with a single major malformation or multiple minor malformations who are also small-for-dates
- Infants with a single major malformation who also have multiple minor anomalies
- In selected cases, fluorescence *in situ* hybridization (FISH) may be indicated to detect sub-microscopic structural chromosome changes or microdeletions (as in DiGeorge or Williams Syndrome) if the phenotype is suggestive.
- Metabolic testing – Some features might suggest the possibility of a metabolic disorder in presence of dysmorphism. (Table 2).

3. Molecular studies – Are required for diagnosis of single gene disorders for which the gene has been identified (eg Achondroplasia),

Counseling the Family

The American Society of Human Genetics (ASHG) defined genetic counseling as a communication process that deals with the human problems associated with the occurrence or the risk of recurrence of a genetic disorder in a family. The main principle of genetic counseling is nondirectiveness which is the art of presenting facts without influencing decision.

The process involves an attempt by one or more appropriately trained persons to help the individual or family to

- 1) Comprehend the medical facts including the diagnosis, probable course of the disorder, and the available management

- 2) Appreciate the way heredity contributes to the disorder and the risk of recurrence in the specified relatives
- 3) Understand the alternatives for dealing with the risk of recurrence
- 4) Choose a course of action which seems to them appropriate in view of their risk , their family goals , and their ethical and religious standards and act in accordance with the decision
- 5) Make the best possible adjustments to the disorder in an affected family member and/ or to the risk of recurrence of that disorder

Counseling is an ongoing process; its staging and depth should be tailored to each family. The most difficult step is breaking the news which should always be done with great caution and passion depending on the preparedness of the family(eg prior suspicion on fetal ultrasound). Always discuss the positive aspects like what can be done for the baby. The family should be informed all about you know and more importantly you do not know. The approach taken in counseling the family of a newborn with congenital anomalies should be such that it sets the stage for future interactions and multiple follow up sessions.

Table-1 Aneuploidy risk with major structural fetal malformation

Malformation	Aneuploidy risk
Cystic hygroma	60-75%
Hydrops	30-80%
Hydrocephalus	3-8%
Holoprosencephaly	40-60%
Cardiac defects	5-30%
Diaphragmatic hernia	20-25%
Omphalocele	30-40%
Gastroschisis	None- minimal
Duodenal atresia	20-30%
Facial cleft	1%
bladder outlet obstruction	20-25%
Limb reduction	8%
Club foot	20-30%
Single umbilical artery	minimal

Table 2. Situations Suggesting the Need for Metabolic Testing in the Newborn with Malformations:

Selected clinical findings	Selected laboratory findings	Selected radiologic findings
Ambiguous genitalia	Metabolic acidosis	Punctate calcifications
Enlarged fontanelle	Abnormal liver function tests	Severe osteopenia
Seizures	Persistent hyperbilirubinemia	
Severe hypotonia	Hyperammonemia	
Cataracts	Hypocholesterolemia	
Coarse facies	Hypoglycemia	
Hepatosplenomegaly		
Lethargy or coma		
Persistent vomiting		
Unusual odor		

Table 3 Empiric Risk of Recurrence of Isolated Malformation

Malformation	Frequency per 1000 births	Recurrence for normal parents of one affected child

Anencephaly/Spina bifida	4 – 5	5 %
Cardiac malformation	6 – 8	3 – 4 %
Cleft lip and cleft palate	2	4 – 5 %
Cleft palate alone	0.5	2 – 6 %
Pyloric stenosis	2 – 3	3 %
Talipes equinovarus	3 – 4	2 – 8 %
Dislocation of hip	3 – 4	3 – 4 %
Hirschsprung disease	0.1	6 %

Approach to a Dysmorphic Newborn I

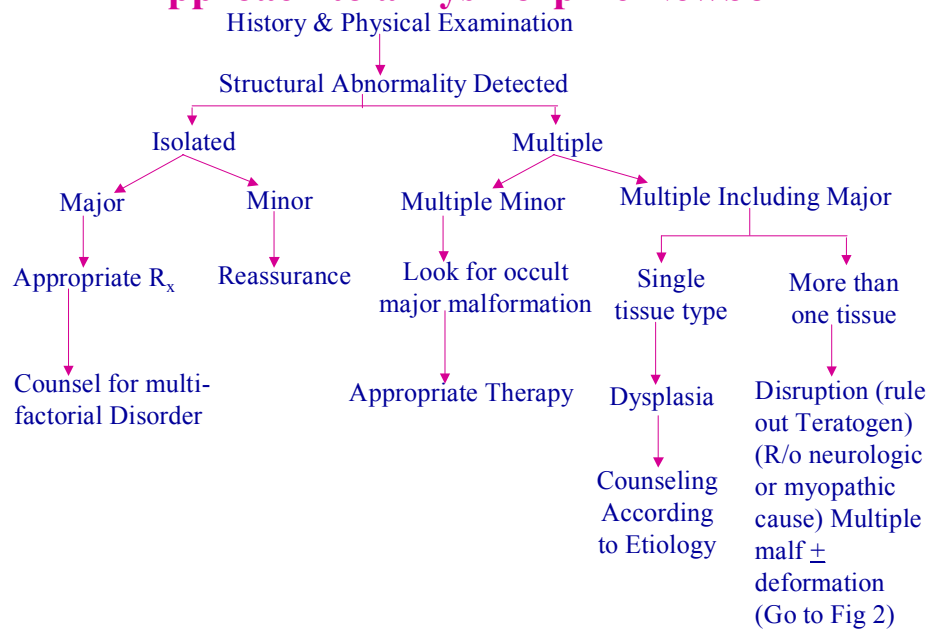


Figure 1

Approach to a Dysmorphic Newborn II

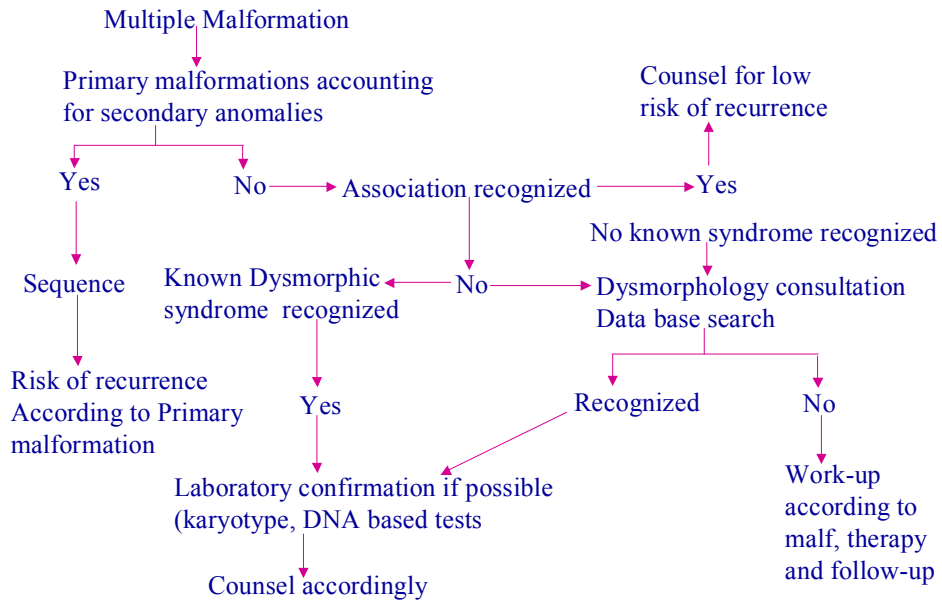


Figure 2