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Patricia L. Crotwell and H. Eugene Hoyme
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Core Concepts: Chromosome Aneuploidies

Patricia L. Crotwell, PhD,*† H. Eugene Hoyme, MD*†‡

Author Disclosure
Drs Crotwell and Hoyme have disclosed no financial relationships relevant to this article. This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

Abstract
Aneuploidy, or deviation from the diploid human chromosome complement of 46, may have physical effects ranging from mild or undetectable, as in a male infant with 47 chromosomes including an additional Y chromosome, to severe, as occurs in infants with an additional chromosome 13 or 18. We discuss the autosomal (13, 18, and 21) and sex chromosome (X, Y) aneuploidies that can be expected in the neonatal health care setting, including clinical signs and symptoms that may be indications for further study. We review appropriate diagnostic testing including chromosome, fluorescent in situ hybridization, and microarray comparative genomic hybridization studies, indicating where parental follow-up studies are necessary to provide accurate recurrence risk counseling. For each aneuploid condition that is likely to be encountered in a living infant, we review appropriate clinical management strategies. Suggested readings and family resources are provided for the aneuploidies that are commonly observed in the newborn, and the reader is directed to additional resources for partial aneuploidies, which are beyond the scope of this review.

Objectives
After completing this article, readers should be able to:

1. Describe the autosomal and sex chromosome aneuploidies that can be expected in live-born infants.
2. Recognize the minor dysmorphisms and major malformations that might indicate a numerical chromosome abnormality.
3. Determine the appropriate diagnostic testing methodology, including identifying the cases that indicate parental follow-up studies.
4. Develop an appropriate referral and/or long-term follow-up care strategy for each of the chromosome aneuploidies described.

Introduction
Approximately 1 in 120 newborns has a chromosome abnormality, ranging from balanced structural rearrangements with normal phenotypes to gains or losses of entire chromosomes or chromosome arms with associated phenotypic and intellectual effects varying from mild to severe. In the absence of prenatal chromosome studies, balanced structural rearrangements, which account for approximately one-half of chromosome abnormalities in newborns, are not likely to be detected in otherwise healthy infants. Most infants with balanced chromosome rearrangements and a benign family history are not diagnosed until they themselves are grown and encounter reproductive difficulty. In contrast, unbalanced chromosome complements, which occur in ~1 in 250 newborn infants, are often, although not always in the case of sex chromosome aneuploidies, associated with adverse physical and/or developmental effects that are readily apparent in the newborn.

The human diploid chromosome number of 46 is achieved by the fusion of a haploid egg and sperm, each bearing 1 to 22 normal autosomes and a single normal X (egg or sperm) or Y (sperm) sex chromosome. Aneuploidy...
arises when an abnormal full or partial chromosome complement occurs. Full aneuploid chromosome complements in the live-born infant may involve either the sex chromosomes X and Y; the autosomes 13, 18, or 21; or, rarely, an additional full haploid set of chromosomes (triploidy). Partial aneuploidy can occur in a whole chromosome mosaic form, or may involve any chromosome or chromosome arm; for example, mosaic trisomy 8, partial monosomy 13 (deletion of a portion of one of the chromosomes 13), or partial tetrasomy 15 (presence of a bisatellited, inverted, duplicated, partial chromosome 15 in addition to two normal chromosomes 15) (Fig 1), to list just a few. Partial and mosaic aneuploidy are beyond the scope of this review; however, the cardinal signs described herein may point to a partial aneuploidy, and laboratory diagnostics can identify and in many cases quantify mosaic and partial aneuploidy.

Here, we describe the key signs that may suggest aneuploidy in the newborn infant, discuss current laboratory diagnostic and testing methods, and review the sex and full autosome aneuploidies that are compatible with live birth and thus can be expected to be encountered in the neonatal health care setting.

Clinical Signs Suggesting Aneuploidies

Aneuploidies can result in a spectrum of phenotypic effects, both internal and external. Infants can display intrauterine growth restriction (IUGR), persisting postnatally. Organs and/or organ systems can be malformed, with or without limb abnormalities, and facial dysmorphisms (Fig 2) are commonly present. Central nervous system abnormalities, such as seizures or holoprosencephaly; cardiovascular abnormalities, such as ventricular septal defect or atrial septal defect; diaphragmatic or inguinal hernias; small or large bowel anomalies; and polycystic kidneys are a few of several cardinal signs that may suggest aneuploidy in the newborn. Limb abnormalities (Figs 3 and 4) may range from the profound (absent or additional limbs or digits) to the moderate (clenched fists with unusual finger positions) to the mild (narrow, hyperconvex fingernails), with certain findings, such as transverse palmar creases, occurring in the general population as well as in a subset of patients with aneuploidy. Facial dysmorphisms are common findings in infants with aneuploidies, and as with the systems mentioned previously, may range from mild to severe. Micronathia, epicanthal folds, eye anomalies, cleft lip with or without cleft palate, and low-set or abnormally formed ears with or without pits or tags (Fig 5) are among the facial findings observed in infants with aneuploidy.

Because there is significant diversity in the physical and neurological abnormalities that can be associated with aneuploidy, and because unbalanced chromosome complements occur in \( \sim 1 \) in 250 newborn infants, a low threshold of suspicion is appropriate in the neonatal health care setting. Trisomies 13, 18, and 21 occur at a frequency, and with sufficient consistent clinical findings, that the experienced practitioner can often make the diagnosis at the bedside. Diagnostic testing is nevertheless indicated, as unbalanced chromosome abnormalities may be inherited from a balanced, phenotypically normal parent, leading to an increased recurrence risk with future pregnancies. Other less common syndromes may mimic well-known aneuploidies (for example, infants with Bowen-Conradi syndrome demonstrate many of the features of trisomy 18), or mosaicism or partial aneuploidy may be the cause of the identified abnormalities.

Laboratory Diagnostics

Banded chromosome studies have been the gold standard for diagnosis of chromosome aneuploidies since banding techniques were developed in the 1970s. Following cell culture, cells are fixed, dropped on glass slides, stained with Giemsa (predominantly, although there are other

Figure 1. Partial karyogram for chromosome 15. The arrow indicates an additional bisatellited chromosome, which was identified using array CGH and G-banded chromosome studies as a duplicated portion (partial tetrasomy) of chromosome 15.

Figure 2. Facial dysmorphisms in two unrelated infants. A. Note the smooth philtrum and thin upper lip in this infant. B. Micronathia is severe, and the slope of the forehead is flat in this infant.
staining techniques), and the G-banded chromosomes are counted and analyzed at the light microscope. Images of the chromosomes are captured, and software programs are used to create the karyograms that will illustrate the additional or missing chromosomes and the numerous structural and numerical abnormalities that can occur. The process generally takes 7 to 10 days, although a rapid turnaround can often be arranged in critical cases. For the common aneuploidies (13, 18, 21, X, Y), fluorescence in situ hybridization (FISH) studies may be used. In FISH testing for aneuploidy, labeled DNA probes are used to enumerate the centromeres of chromosomes 13, 18, 21, X, and Y, with results generally obtained in 24 to 48 hours.

Increasingly, G-banded chromosome and FISH studies are being replaced by microarray studies. Microarrays, also referred to as array comparative genomic hybridization (CGH) studies or molecular karyotypes, consist of many thousands to many millions of small DNA probes adhered to a glass slide or chip. Patient DNA is processed, fluorescently labeled, and hybridized to the array, and the resulting data are read by a scanner and interpreted in the laboratory via a software interface. These microarray studies can detect gains (duplications) and losses (deletions) of DNA, typically >200 kilobases in size (Fig 6). Additionally, the technology can detect gains or losses of or within individual genes, if the gene is large enough or if the array used is designed to include a probe for every exon of every gene. A single-nucleotide polymorphism microarray can identify loss of heterozygosity, which allows for detection of uniparental disomy, or which may be useful in studying children who are products of consanguineous relationships. In contrast, G-banded chromosome analysis typically can detect gains and losses >5 megabases (5000 kilobases), but cannot determine loss of heterozygosity, and certainly would not identify disruption of a single gene unless that gene were involved in a translocation or inversion.

It probably is not necessary to order a microarray study to confirm or rule out a clinically well-characterized diagnosis, such as trisomies 13, 18, or 21, or monosomy X (Turner syndrome). Standard chromosome analysis is sufficient; in addition, it will show, for example, whether the three copies of chromosome 21 or 13 are separate, or whether a Robertsonian translocation is present (Fig 7). This is important for recurrence risk counseling. Similarly, chromosome analysis is still the best method to identify mosaicism, such as is often seen in Turner syndrome, where there may be one, two, three, or even (rarely) more cell lines. Although chromosome studies currently are slightly less costly than array CGH, if chromosomes and FISH are required, the costs are similar, and the diagnostic yield may be significantly improved if array CGH is ordered in place of chromosomes plus FISH in cases where a clinical diagnosis cannot easily be made. A clinical genetics consultation is indicated if there is any question about the type of diagnostic testing to order.

Sex Chromosome Aneuploidies

Turner Syndrome

Turner syndrome affects ~1 in 2500 female live births, although most Turner syndrome conceptuses are spontaneously aborted during pregnancy. Although the 45,X chromosome complement is the most commonly associated, mosaicism occurs frequently, and may occur structurally (eg, 45,X/46,X,i[Xq] or 46,X,r[X]), numerically.

Figure 3. Foot anomalies. A. Asymmetry in this infant was most apparent in the foot size/length discrepancy. B. Bilateral abnormal toe positions in this neonate dictate a thorough head-to-toe physical examination. C. Polydactyly can be associated with trisomy 13, or can be an isolated finding, as in this infant.

Figure 4. Hand anomalies. A. Transverse palmar creases may be an isolated finding or associated with an aneuploidy, as in this infant with trisomy 21. B. A clenched fist with the second finger overriding the third, and the fifth overriding the fourth is seen in this infant with trisomy 18.
(eg, 45,X/46,XX/47,XXX or 45,X/46,XY), or from tissue to tissue within an individual patient. The presence of a Y cell line increases the risk for development of gonadoblastoma; in such cases, referral to a pediatric endocrinologist is indicated. Infants with Turner syndrome often present with lymphedema, particularly of the hands and feet. Careful examination of an infant with Turner syndrome will likely reveal hypoplastic nails and short metacarpals and metatarsals. There may be a low posterior hairline and excess skin at the neck, which are results of a cystic hygroma having been present during fetal development. In addition, the infants often have a broad chest with widely spaced nipples.

If a newborn infant is suspected to have Turner syndrome, chromosome studies are indicated to confirm the diagnosis and to determine if mosaicism is present. An echocardiogram is indicated, because congenital heart defects occur in ~30% of patients with Turner syndrome, particularly coarctation of the aorta and bicuspid aortic valve. Gonadal dysgenesis and genitourinary abnormalities are common findings in patients with Turner syndrome; thus, a renal ultrasound is indicated. Because conductive and sensorineural hearing losses can occur, newborn hearing screening should be performed, and follow-up audiograms ordered if indicated. Short stature is nearly universal, so length/height should be plotted on a Turner-specific growth chart. Referral to a geneticist and genetic counselor is indicated to explain the genetic causation and for recurrence risk counseling. In addition, the geneticist can provide psychosocial counseling, accurate information about prognosis and development, and annual reevaluation to address medical concerns as the girl with Turner syndrome grows to adulthood. Mean IQ may be 10 to 15 points lower than siblings, but typically falls well within the normal range. Referral to a pediatric endocrinologist is indicated for management of short stature and delayed pubertal development. Despite the numerous tests and referrals, health care providers can be reassuring to families with an infant with Turner syndrome. These are girls who generally live successful, relatively normal lives; indeed, approximately one-third of patients with Turner syndrome are not diagnosed until adolescence, when they fail to spontaneously menstruate.

Klinefelter Syndrome
Klinefelter syndrome occurs in ~1 in 500 to 1 in 1000 live male births. Because infants with Klinefelter syndrome usually appear normal at birth, identification of affected boys in the neonatal health care setting is likely to be the result of prenatal screening. Alternatively, undescended testes may be noted in an infant boy, and if chromosome studies are ordered before orchiopexy, the boy would be diagnosed at that time. Often, affected males are not diagnosed until adulthood, when infertility and azoospermia manifest. Thus, health care providers should be reassuring to families of infants with Klinefelter syndrome. Certainly, referrals to a geneticist and genetic counselor for psychosocial counseling are appropriate so that parents and family members can...
receive accurate information about prognosis and development of the affected infant, which may in some cases include educational and behavioral difficulties. 

With Klinefelter syndrome, mean IQ may be 10 to 15 points lower than siblings, but typically falls well within the normal range. In addition, patients with Klinefelter syndrome should be evaluated as they approach puberty for hypergonadotrophic hypogonadism, and the infrequent occurrence of gynecomastia. Referral to a pediatric endocrinologist is indicated for testosterone replacement therapy, typically between 11 and 12 years of age. Patients with Klinefelter syndrome generally lead normal, successful lives; indeed, it is likely that many patients are never diagnosed at all.

Triple X Syndrome

Triple X syndrome, like Klinefelter syndrome, is unlikely to be detected or diagnosed in the neonatal health care setting because infants are normal-appearing and the syndrome is not associated with any significant congenital anomalies. It occurs in 1 in 1000 live female births. Referrals to a geneticist and genetic counselor for psychosocial counseling are appropriate so that parents and family members can receive accurate information about prognosis and development of the affected infant, which may in some cases include educational and emotional difficulties. 

Mean IQ may be 10 to 15 points lower than siblings, but typically falls well within the normal range. Although there can be an increased risk of mild speech and language difficulties in childhood and adolescence, most women with triple X syndrome have normal, successful lives. Thus, health care providers should be reassuring to families of infants with triple X syndrome, given that the diagnosis is most likely the result of an incidental finding in prenatal screening.

47,XYY Syndrome

47,XYY syndrome, like triple X and Klinefelter syndrome, is unlikely to be detected or diagnosed in the neonatal health care setting because infants are normal-appearing and the syndrome is not associated with any significant congenital anomalies. It occurs in 1 in 1000 live male births. Although there can be an increased risk of mild motor and language difficulties in childhood and adolescence, most men with XYY syndrome have normal, successful lives. Mean IQ may be 10 to 15 points lower than siblings, but typically falls well within the normal range. Early reports of higher incidence of the XYY chromosome complement in the prison population and in aggressive offenders are now considered to be inaccurate and associated with confirmation bias. Thus, health care providers should be reassuring to families of infants with 47,XYY syndrome, given that the diagnosis is most likely the result of prenatal screening and most patients are undiagnosed.

Sex Chromosome Polysomies

Single sex chromosome aneuploidies, such as 47,XXX; 47,XXY; and 47,XYY, are generally associated with a fairly mild phenotype, if any, as described previously. Sex chromosome polysomies with a diploid chromosome number of 48 or more, however, are often associated with a more severe clinical outcome. Sex chromosome polysomies are not common, occurring at a frequency of 1 in 85,000 for XXXXY and for XXXXX. Patients with XXXX, XXXXX, XXXYY, XXXY, and so forth sex chromosome complements may have growth and developmental retardation, microcephaly, dysmorphic features (which may be mistaken for trisomy 21), and intellectual disabilities that increase in severity with each additional sex chromosome. That is, pentasomy X is more severe than tetrasomy X, for example. Congenital heart defects often occur in...
patients with sex chromosome polysomies; therefore, an echocardiogram and referral to pediatric cardiology are indicated. A renal ultrasound should be ordered to rule out structural kidney anomalies. Radiography and a detailed physical exam will detect various skeletal anomalies such as radio-ulnar defects and vertebral anomalies, among others. Referral to a geneticist and genetic counselor for psychosocial counseling is appropriate so that parents and family members can receive accurate information about prognosis and development of the affected infant, and so that the infant can be evaluated annually as she or he grows to adulthood. Many families will need additional aid, such as that from a social worker and from early childhood intervention specialists, given that the neurodevelopmental prognosis for children with sex chromosome polysomies ranges from moderate to severe.

Trisomies Compatible With Life

Trisomy 13: Patau Syndrome

Trisomy 13 occurs in ~1 in 9500 live births. Most trisomy 13 conceptuses are miscarried or associated with stillbirth. Approximately 75% of affected infants die within the first year of life, though survival to childhood and mid-to-late teens has been reported in certain cases. Surviving patients have significant intellectual disabilities with limited or no self-care; families may require extensive support in those cases. In the neonatal health care setting, suspicion of trisomy 13 will be raised for infants with any combination of holoprosencephaly, orofacial clefting, polydactyly, congenital heart defects, renal anomalies, omphalocele, and cutis aplasia (Figs 8 and 9). Numerous additional dysmorphisms have been observed in trisomy 13, including clenched and overlapping fingers and rocker-bottom feet. G-banded chromosome studies, with or without FISH for rapid confirmation of the diagnosis, should be ordered. Although microarray testing would certainly identify trisomy 13, an array would not identify the genetic mechanism associated with the ~1 in 5 cases of trisomy 13 that are characterized by a Robertsonian translocation. Such translocations may be either inherited or de novo. Parental follow-up studies are indicated in all cases of trisomy 13 where Robertsonian translocations are identified, because if a parent carries the balanced translocation, he or she has an increased recurrence risk with subsequent pregnancies.

An echocardiogram is indicated, because congenital heart defects occur in ~80% of infants with trisomy 13. Because renal abnormalities are common findings in patients with trisomy 13, a renal ultrasound also is indicated. Growth deficiencies are the rule, rather than the exception; therefore, length/height should be plotted on a trisomy 13–specific growth chart. Referral to a geneticist and genetic counselor for psychosocial counseling is appropriate so that parents and family members can receive accurate information about prognosis and development of the affected infant, and so that the infants who survive their neonatal period can be evaluated annually. Throughout the neonatal course, all treatment decisions, which may range from surgical interventions to comfort care, should be discussed with the parents regularly. Treatment plans are often subject to change, even daily, based on the prognosis and development of the affected infant. Families may benefit from support organizations, such as SOFT (the Support Organization for Trisomy 18, 13, and Related Disorders), regardless of the life expectancy of their child. Genetic counselors can provide additional resources as well.

Trisomy 18: Edward Syndrome

Trisomy 18 occurs in ~1 in 7900 live births, making it the second most common autosomal trisomy after trisomy 21. The clinical picture is severe, with fewer than 1 in 10 affected infants surviving their first year of life; indeed, average survival is ~2 weeks. Infants with trisomy 18 are small for gestational age, and survivors have significant feeding difficulties, growth and developmental delays, and marked intellectual impairment. Suspicion for
Trisomy 18 (Fig 10) should be raised in infants with IUGR, microcephaly, a short sternum, and camptodactyly with a clenched hand posture, where the index finger overrides the middle finger and the fifth finger overrides the fourth finger.

G-banded chromosome studies or microarray studies, with or without FISH for rapid confirmation of the diagnosis, should be ordered. An echocardiogram is indicated, because congenital heart defects occur in ~90% of infants with trisomy 18. Renal and genital abnormalities are common findings in patients with trisomy 18; thus, an abdominal ultrasound is indicated. Because feeding difficulties occur in most affected infants, a barium swallow study may be indicated. Length/height should be plotted on a trisomy 18–specific growth chart. Referral to a geneticist and genetic counselor for psychosocial counseling is appropriate so that parents and family members can receive accurate information about prognosis and development of the affected infant, and so that the infants who survive their neonatal period can be evaluated annually. As is the case for infants with trisomy 13, health care providers for infants with trisomy 18 should discuss all treatment decisions, ranging from surgical interventions to comfort care, with the parents regularly. Treatment plans are often subject to change, even daily, based on the prognosis and development of the affected infant. Information for support organizations, such as SOFT, should be provided regardless of the life expectancy of the infant. Genetic counselors can provide additional resources as well.

Trisomy 21: Down Syndrome
Trisomy 21 is the most common chromosome aneuploidy, occurring in ~1 in 800 live births. There is a significant maternal age effect, with older mothers (>35 years) more likely to have an affected infant than younger mothers; however, because younger women have children more often than do older women, most infants with trisomy 21 are born to women who are younger than 35 years of age. Most infants (85%) with trisomy 21 survive their first year of life, and ~50% of patients live to 50 years of age. In the neonatal setting, common findings include upslanting palpebral fissures, Brushfield spots, a protruding tongue, decreased muscle tone, soft or doughy skin texture, brachydactyly, single transverse palmar creases, and/or a gap between the first and second toes. Congenital heart defects occur in ~50% of infants with trisomy 21, with variable types (eg, endocardial cushion/atrioventricular canal defects or ventricular septal defect) and severity. Multiple heart defects occur in ~30% of infants. Reduced life expectancy is associated not only with congenital heart defects, but also with esophageal atresia (with or without tracheoesophageal fistula), the presence of Hirschsprung disease or duodenal atresia, leukemia, and/or infection.

G-banded chromosome studies, with or without FISH for rapid confirmation of the diagnosis, should be ordered. Although a microarray test would certainly identify trisomy 21 (Fig 6), an array would not identify the mechanism of the ~2% to 5% of cases of trisomy 21 that are characterized by a Robertsonian translocation (Fig 7), which may be either inherited or de novo.

Figure 9. Two unrelated infants with trisomy 13. A. Cutis aplasia may be mild and readily apparent, or B, pronounced though somewhat obscured by hair. Careful examination of the scalp is indicated.

Figure 10. Suspected trisomy 18. Clockwise from left, the arrows indicate foot abnormalities, a dysmorphic ear, a depressed nasal bridge with a short nose, and unusual finger positions. Together with IUGR and microcephaly, a concern was raised for trisomy 18. Chromosome studies were normal. Because this infant was born to parents from a Hutterite colony, a clinical diagnosis of Bowen-Conradi syndrome was made.
Parental follow-up studies are indicated in all cases of trisomy 21 where Robertsonian translocations are identified. All infants with trisomy 21 should receive an echocardiogram and be followed by a pediatric cardiologist until it has been determined whether cardiac anomalies are present. Short stature is nearly universal, so length/height should be plotted on a Down syndrome–specific growth chart. Referral to a geneticist and genetic counselor for psychosocial counseling is appropriate so that parents and family members can receive accurate information about prognosis and development of the affected infant, and so that the infant can be evaluated annually as she or he grows to adulthood. IQ can range from 20 to 85; thus, affected children generally have moderate to severe mental retardation. Many surviving infants can be expected to grow into children and adults who attend and graduate from mainstream schools, obtain jobs, and live semi-independent lives. This is increasingly the case in communities where acceptance of individuals with developmental and intellectual disabilities is the norm, and because affected children receive health care and treatment equal to that of their unaffected peers. Numerous resources are available for families, and these can be provided by genetic counselors.

**Triploidy**

Rarely (1 in 100,000 live-born infants), an infant will be born with three full haploid sets of chromosomes. Infants with evidence of significant IUGR, hypotonia, hydrops, poly- or oligohydramnios, and multiple congenital anomalies including dysmorphic features, should undergo genetic studies, including G-banded chromosome studies with or without FISH. Karyotypes in affected infants will show 69 chromosomes, with XXX, XXXY, or XYY sex chromosome complements. (Note: microarrays may “miss” triploidy because of comparative DNA levels). There is no treatment available for true triploidy; it is a lethal condition. Supportive therapy is indicated for diploid/triploid mosaicism, where life expectancy may be longer.

**Concluding Remarks**

The clinical phenotypes associated with chromosome aneuploidy range from the mild, often missed end of the spectrum (such as that seen in triple X syndrome or XYY syndrome) to the severe (such as that seen in trisomies 13 and 18, and triploidy). In the neonatal health care setting, clinicians will identify infants with growth restriction, neurological abnormalities, and major and minor anomalies, and coordinate genetic testing as appropriate. When an affected infant is diagnosed, a team approach is necessary to provide comprehensive medical and psychosocial care to the infant and family. Numerous resources are available to health care providers and families of affected infants. A list of suggested reading is provided at the end of this article, ranging from excellent reviews to extensive and detailed population studies that are the source of information regarding the frequencies of the individual aneuploidies described herein. Although online resources are numerous as well, those are not specifically referenced in the list of suggested reading.

This review was focused specifically on the full aneuploidies that can be expected in neonates. We must point out, however, that there are infinite varieties of partial and mosaic aneuploidies that are beyond the scope of this review. When a partial or mosaic aneuploidy is observed in the neonate, we suggest Schinzel (2001) (full reference in the list of suggested reading) for a brief summary of the published literature, and referral to a geneticist and genetic counselor for a thorough review of the literature (if any) and information pertaining to prognosis and clinical management.

**American Board of Pediatrics Neonatal-Perinatal Content Specifications**

- Recognize the physical findings and chromosomal pattern in trisomy 13.
- Identify the physical characteristics and chromosomal pattern in trisomy 18.
- Be aware of the maternal factors, incidence, and clinical manifestations of Down syndrome.
- Know the implications of a prenatal diagnosis of sex chromosome aneuploidy for the long-term developmental outcome of an infant.
- Recognize the physical characteristics and chromosomal pattern of sex chromosome aneuploidy.
- Know fetal and placental manifestations of triploidy.
- Know the indications and limitations of molecular cytogenetic studies (eg, FISH), specifically in the diagnosis of aneuploidy and microdeletion.

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Suggested Reading


NeoReviews Quiz

New minimum performance level requirements

Per the 2010 revision of the American Medical Association (AMA) Physician’s Recognition Award (PRA) and credit system, a minimum performance level must be established on enduring material and journal-based CME activities that are certified for AMA PRA Category 1 Credit™. In order to successfully complete 2012 NeoReviews articles for AMA PRA Category 1 Credit™, learners must demonstrate a minimum performance level of 60% or higher on this assessment, which measures achievement of the educational purpose and/or objectives of this activity.

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6. A newborn infant has phenotypic features that include generalized hypotonia, almond-shaped eyes, small hands and feet, and hypogonadism. Parents of this infant are first cousins. Uniparental disomy (UDP), in which both copies of a chromosome are inherited from the same parent, is suspected. Of the following, the genetic test most likely to confirm UDP in this infant is
   A. Array comparative genomic hybridization.
   B. Fluorescence in situ hybridization.
   C. G-banded karyotype analysis.
   D. Gene linkage analysis.
   E. Single nucleotide polymorphism microarray.

7. Turner syndrome affects approximately 1 in 2,500 female live births. Although 45,X is the most common chromosomal complement in this syndrome, mosaicism may occur structurally, numerically, or from tissue to tissue within an individual patient. Of the following, the mosaicism pattern in Turner syndrome most associated with an increased risk for the development of gonadoblastoma is
   A. 45,X/46,X,i(Xq).
   B. 45,X/46,X,r(X).
   C. 45,X/46,XX.
   D. 45,X/46,XY.
   E. 45,X/47,XXX.

8. Klinefelter syndrome affects approximately 1 in 500 to 1,000 male live births. Most patients with this syndrome are diagnosed in adulthood, although a few are identified in infancy based on prenatal karyotype screening for 47,XXY chromosomal complement. Of the following, the most common presenting clinical manifestation in Klinefelter syndrome is
   A. Dysmorphic facies.
   B. Gynecomastia.
   C. Infertility from azospermia.
   D. Mental retardation.
   E. Short stature.

9. A newborn infant has phenotypic features that include intrauterine growth restriction, microcephaly, short sternum, and camptodactyly with a clenched hand posture, in which the index finger overrides the middle finger and the fifth finger overrides the fourth finger. Abdominal ultrasonography reveals multicystic/dysplastic kidneys. Of the following, the most likely chromosomal diagnosis in this infant is
   A. Trisomy 8.
   B. Trisomy 13.
   C. Trisomy 16.
   D. Trisomy 18.
   E. Trisomy 21.

10. A 21-year-old primigravid woman seeks consultation in her 24th week of pregnancy. Her pregnancy is complicated by oligohydramnios, and by fetal growth restriction, hydrops, and multiple congenital anomalies including renal defects. A fetal blood sample is obtained by cordocentesis for chromosomal analysis. Of the following, the most likely chromosomal complement in this fetus is
    A. 47,XXX.
    B. 47,XXY.
    C. 48,XXX.
    D. 48,XXXY.
    E. 69,XXX.
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