and the sex ratio was 8 : 3 for the cases with cerebellar hypoplasia. The perinatal findings of 20 cases with CNS anomalies and fetal trisomy 18 are shown in Table 1.

The present study represents the largest known series of consecutive fetuses with trisomy 18 and documents the type and frequency of sonographically detectable CNS anomalies associated with fetal trisomy 18. In this presentation, hydrocephalus, HPE, and NTD were detected sonographically either in the second trimester or in the third trimester. However, most cases with cerebellar hypoplasia presenting as an enlarged cisterna magna or Dandy–Walker malformation were detected in the third trimester. A male preponderance was noted in cerebellar hypoplasia associated with fetal trisomy 18. The sex ratio is defined as the number of males divided by the number of females. For trisomy 18 conceptuses, there is a significant excess of females in both fetuses and livebirths due to a prenatal selection against trisomy 18 males (Huether *et al*., 1996). In prenatal normal controls, the sex ratio is 1.07, while the sex ratio for fetal trisomy 18 is 0.90, and, for livebirths with trisomy 18, it is 0.63 (Bianchi *et al*., 2000). The sex ratio of 0.93 for the 89 cases with fetal trisomy in this study is in accordance with the previous observation. Many congenital anomalies have sex biases (Lubinsky, 1997). A sex ratio of 8 : 3 in the present cases with cerebellar hypoplasia provides evidence for a male preponderance and sex bias in cerebellar hypoplasia associated with fetal trisomy 18.

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Omphalocele and congenital diaphragmatic hernia associated with fetal trisomy 18

During the study period (1988–2004), 89 consecutive cases of fetal trisomy 18 were detected at the Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan, following perinatal karyotyping because of advanced maternal age, fetal anomalies, abnormal obstetric sonographic findings, abnormal maternal serum screen results, or elective reasons. Of the 89 cases, 41 cases had a karyotype of 47,XY,+18, one had 47,XY,inv(2)(p22q21),+18, one had 47,XY,+18/46,XY, 44 had 47,XX,+18, one had 48,XXX,+18, and one had 46,XX,i(18)(q10), giving a male to female sex ratio of 43 : 46, or 0.935. The average gestational age at diagnosis was 23.5 ± 7.4 (mean $\pm$ SD) weeks. Twelve cases (13.48%) had omphalocele and four cases (4.49%) had congenital diaphragmatic hernia (CDH). The male to female sex ratio was 8 : 4 for the cases with omphalocele, and the ratio was 3 : 1 for the cases with CDH. The perinatal findings of the 12 cases with omphalocele and the four cases with CDH associated with fetal trisomy 18 are shown in Table 1. Among 12 cases with omphalocele, 8 cases (66.7%) had extracorporeal intestines, three cases (25%) had extracorporeal intestines and liver, and one case (8.3%) had extracorporeal liver. All four cases with CDH were associated with a diaphragmatic defect on the left side.

In this presentation, a male preponderance was noted in both omphalocele and CDH associated with fetal trisomy 18. This finding has not been described previously. The sex ratio is defined as the number of males divided by the number of females. For trisomy 18 conceptuses, there is a significant excess of females in both fetuses and livebirths due to a prenatal selection against trisomy 18 males (Huether *et al*., 1996). In prenatal normal controls, the sex ratio is 1.07, while the sex ratio for fetal trisomy 18 is 0.90, and for livebirths with trisomy 18, it is 0.63 (Bianchi *et al*., 2000). Many congenital anomalies have sex biases (Lubinsky, 1997). Early developmental anomalies reviewed by Arena and Smith (1978) have been shown to have a sex ratio of 1.2 for omphalocele (Hay, 1971) and a ratio of 1.9 for diaphragmatic hernia (Johnson *et al*., 1967). A sex ratio of 8 : 4 in the present cases with omphalocele and a ratio of 3 : 1 in the present

Table 1—Perinatal findings of the cases with omphalocele or congenital diaphragmatic hernia (CDH) associated with fetal trisomy 18

Case	Maternal age (years)	Karyotype	Gastrointestinal anomalies	Associated perinatal findings	Main indication of perinatal karyotyping and gestational age at diagnosis
1	33	47,XY,+18	Omphalocele	Arthrogryposis of bilateral wrists, left radial hypoplasia, increased nuchal translucency, extracorporeal intestines	Fetal anomaly; 12 weeks
2	33	47,XY,+18	Omphalocele	Cystic hygroma, imperforate anus, extracorporeal intestines	Fetal anomaly; 16 weeks
3	36	47,XY,+18	Omphalocele	Arthrogryposis of bilateral wrists, PDA, VSD, extracorporeal intestines	Advanced maternal age; 16 weeks
4	44	47,XY,+18	Omphalocele	Choroid plexus cysts, VSD, extracorporeal intestines	Fetal anomaly; 16 weeks
5	33	47,XY,+18	Omphalocele	IUFD, extracorporeal intestines and liver	Fetal anomaly; 17 weeks
6	41	47,XX,+18	Omphalocele	Choroid plexus cysts, extracorporeal intestines	Advanced maternal age; 18 weeks
7	39	47,XY,+18	Omphalocele	IUGR, choroid plexus cysts, nuchal thickening, umbilical cord cyst, extracorporeal intestines and liver	Fetal anomaly; 19 weeks
8	36	47,XX,+18	Omphalocele	IUGR, SUA, extracorporeal intestines and liver	Fetal anomaly; 26 weeks
9	32	47,XX,+18	Omphalocele	Arthrogryposis of bilateral ankles, cleft lip and palate, umbilical cord cyst, IUGR, extracorporeal liver	Fetal anomaly; 28 weeks
10	27	47,XX,+18	Omphalocele	IUFD, SGA, extracorporeal intestines	Fetal anomaly; 29 weeks
11	31	47,XY,+18	Omphalocele	Dandy–Walker malformation, IUGR, right hydrothorax, VSD, PDA, extracorporeal intestines	Fetal anomaly; 29 weeks
12	27	47,XY,+18	Omphalocele	Enlarged cisterna magna, IUGR, cardiomegaly, extracorporeal intestines	Fetal anomaly; 34 weeks
13	37	47,XY,+18	CDH (left)	Choroid plexus cysts, ASD, VSD, SUA, polydactyly	Advanced maternal age; 16 weeks
14	24	47,XY,+18	CDH (left)	Arthrogryposis of bilateral ankles, DORV	Fetal anomaly; 24 weeks
15	31	47,XX,+18	CDH (left)	IUGR, VSD, SUA, hypoplastic left ventricle, polyhydramnios	Fetal anomaly; 26 weeks
16	33	47,XY,+18	CDH (left)	Arthrogryposis of bilateral wrists, lumbosacral myelomeningocele, Arnold–Chiari malformation, polyhydramnios, IUGR	Fetal anomaly; 38 weeks

PDA, patent ductus arteriosus; VSD, ventricular septal defect; ASD, atrial septal defect; IUFD, intrauterine fetal death; SUA, single umbilical artery; SGA, small for gestational age; CDH, congenital diaphragmatic hernia; DORV, double-outlet right ventricle; IUGR, intrauterine growth restriction

cases with CDH indicate a male preponderance and sex bias in the gastrointestinal system anomalies associated with trisomy 18. Prenatal selection against trisomy 18 males may be in part due to the fact that, in fetal trisomy 18, male fetuses are prone to having some major structural anomalies than the females.

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Arthrogryposis of the wrist and ankle associated with fetal trisomy 18

During the study period (1988–2004), 89 cases of fetal trisomy 18 were detected at the Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan, following perinatal karyotyping because of advanced maternal age, fetal anomalies, abnormal obstetric sonographic findings, abnormal maternal serum screen results, or elective reasons. Of the 89 cases, 41 cases had a karyotype of 47,XY,+18, one had

Table 1—Perinatal findings of 23 cases with arthrogryposis of the wrist and/or ankle and fetal trisomy 18

Case	Maternal age (years)	Karyotype	Arthrogryposis of the limb	Associated perinatal findings	Main indication of perinatal karyotyping and outcome
1	42	47,XX,+18	Bilateral wrists, bilateral ankles	Right radial and ulnar hypoplasia, IUGR, cystic hygroma	Fetal anomaly; TOP at 22 weeks, 292 g
2	24	47,XY,+18	Bilateral ankles	Left congenital diaphragmatic hernia, DORV	Fetal anomaly; TOP at 26 weeks, 600 g
3	29	47,XY,+18	Left wrist	Brachycephaly, choroid plexus cysts, unilateral cleft lip	Abnormal maternal serum screen result; TOP at 21 weeks, 366 g
4	28	47,XY,+18	Bilateral wrists	Bilateral cleft lip and palate, bilateral radial aplasia and ulnar hypoplasia	Fetal anomaly; TOP at 24 weeks, 404 g
5	33	47,XY,+18	Bilateral wrists	Left radial hypoplasia, omphalocele, increased NT	Fetal anomaly; TOP at 13 weeks, 20 g
6	33	47,XY,+18	Bilateral wrists	Bilateral radial hypoplasia, VSD, DORV, choroid plexus cysts, IUGR	Abnormal maternal serum screen result; TOP at 25 weeks, 386 g
7	36	47,XY,+18	Bilateral wrists	Omphalocele, PDA, VSD	Advanced maternal age; TOP at 18 weeks, 146 g
8	20	47,XY,+18	Bilateral wrists	HPE-PMA, median facial cleft, TF, right radial aplasia, echogenic bowel	Fetal anomaly; TOP at 20 weeks, 368 g
9	28	47,XY,+18	Bilateral wrists	Enlarged cisterna magna, VSD, ASD, PDA, right ear canal atresia, IUGR	Fetal anomaly; delivery at 35 weeks, 1320 g
10	38	47,XY,+18	Bilateral wrists, bilateral ankles	Bilateral cleft lip and palate, tracheoesophageal fistula, left radial hypoplasia, choroid plexus cysts	Advanced maternal age; TOP at 23 weeks, 368 g
11	41	47,XY,+18	Bilateral wrists	Bilateral cleft lip and palate, left radial aplasia, right radial hypoplasia, VSD, IUGR	Advanced maternal age; TOP at 20 weeks, 210 g