

*Invited Comment*  
**Introductory Comments Special Section:  
Trisomy 18**

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Received 14 March 2006; Accepted 15 March 2006

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**How to cite this article: Carey JC. 2006. Introductory comments special section: Trisomy 18. Am J Med Genet Part A 140A:935–936.**

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Trisomy 18, Edwards syndrome, is the third most common chromosome disorder in liveborn infants after the Down and 22q deletion syndromes. This condition occurs in about 1 in 6,000 live births, and if we include stillborn infants in the estimation of occurrence, the prevalence-at-birth rises considerably and makes it one of the most common multiple congenital anomaly syndromes among total births. Not counting the parents who receive a prenatal diagnosis of trisomy 18 and choose pregnancy termination, about 1,000 families per year in the US alone experience the birth of a baby with the syndrome and have to mobilize to cope with the implications. The impact of trisomy 18 (and the related chromosome condition, trisomy 13), is familiar to all medical geneticists and genetic counselors: High frequency of medically important congenital malformations, increased neonatal and infant mortality, and, in older children, a significant psychomotor disability. There are many unanswered questions that could provide the foundation for a research agenda for the study of trisomy 18. So why is it that this common, important, serious condition has received so little attention in both the genetics and pediatrics literature? Even more notably: why have the complex (and sometimes controversial) issues surrounding management and care of infants with trisomy 18 (and trisomy 13) received little dialogue in the bioethics literature?

In this Special Section of the Journal, we feature several papers dealing with some of the important themes surrounding the genetic and medical aspects of trisomy 18. In a novel study, Koskosho et al. [2006] from Nagano, Japan provide the clinical details on 24 newborns with trisomy 18 who receive intensive treatment. To my knowledge, this is the first series, which attempts to address the question of what happens to outcome if a more “hands-on” approach

to the newborn care of infants with trisomy 18 is applied. Mean survival time in this series of 24 patients is just over 5 months, compared to published population studies which have median survival time of 3–6 days [Rasmussen et al., 2003]. Survival rate at 1 month is over 83%, compared to literature series where survival after 1 week is less than 50%. Survival after 1 year was 6 of 24 babies or 25%, compared to recent population studies where 1-year survival is 5%–10%. While the numbers are small in relation to the larger population series, this investigation provides unique information. Of note, only two children of the 24 survived past 2 years.

Two other papers in this Special Section also deal with survival figures in different ascertainment groups: Niedrist et al. [2006] examine the outcome from Switzerland in cases ascertained through cytogenetic laboratories. While this is different than a population-based epidemiologic study, the number of cases analyzed is the largest of any previously published study. Linhy et al. [2006] from Taiwan examine the clinical characteristics and survival of a hospital-based series in that nation.

The remaining papers in this Special Section address other important issues in trisomy 18. Lebel et al. [2006] composed a letter in response to the paper by Kelly et al. [2002] and raise interesting points about care and the language we use in discussing management. Also stimulated by the same paper of Kelly et al., Shanske [2006] provides follow up on one of the original patients with trisomy 18

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DOI 10.1002/ajmg.a.31251

who developed Wilms tumor. This young lady also represents one of the older patients reported with trisomy 18. Lastly, Chen [2006] summarizes experience with newborns who have trisomy 18 and specific structural anomalies, orofacial clefts, and preaxial limb defects.

These papers begin to address some of the unanswered questions in the analysis and study of this important condition which impacts so many families throughout the world. What are the issues that comprise what I will label as a research agenda for trisomy 18? I suggest the following:

1. The outcome of children older than 1 year of age. There are very little data and in the population studies, there are less than 16 children beyond a year of age; these small numbers do not allow accurate survival figures past 12 months.
2. The unique presentation of Wilms tumor in children with trisomy 18. The average age is 5 years, with a much wider range of presentation than in typical Wilms tumor. The biology of Wilms tumor in trisomy 18 is certainly unique [Carey, 2005].
3. The ethical issues surrounding the care of fetuses, newborns, and older children with trisomy 18. Certainly the issue surrounding the option of Cesarean during labor management, the care of the newborn, and decisions surrounding surgery at any time have rarely been discussed in dialogues—still to me a surprising point.
4. The critical region of the 18 chromosome necessary to produce the full Edwards phenotype. This still remains an incompletely answered question [Carey, 2005].
5. The equal occurrence of the nondisjunctional event causing trisomy 18 in meiosis I and II compared to the predominance of meiosis I in trisomy 21 and 13. This observation may be a clue for a unique origin in trisomy 18.

One potential resource for investigation of some of these issues is the patient registry maintained and developed by the Support Organization For Trisomy 18, 13, and Related Disorders (SOFT) ([www.trisomy.org](http://www.trisomy.org)). As an example, a perusal of this database demonstrates that there are five times as many children with full trisomy 18 reported to the Registry

over the age of 10 years than are in the entire medical literature. At last count, the SOFT Registry contains 51 children over age 10 years, and 15 persons (all women) over age 20 years. I am currently attempting to address the issue of survival past 1 year by ascertaining children who entered the Registry before 1 year of age and then following their outcome from that point until the present.

In regards to ethical issues surrounding management, I could envision the orchestration of a multidisciplinary conference designed to address these complex issues. From my own experience in meeting families who have a prenatal diagnosis of trisomy 18 (or trisomy 13) and who continue their pregnancies, development of a care plan that involves the obstetric practitioners and the newborn nursery staff provides a mechanism to foster communication in a non-urgent way, prior to both labor and neonatal management. I could envision such care plans being a component of routine prenatal management for the many families who receive a later prenatal diagnosis of trisomy 18 or those who elect continuation.

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