

of the vena cava, and impaired venous return. This situation can be easily resolved by insertion of a venous cannula into the abdomen [2-3]. One should avoid the right upper quadrant in performing this procedure as the large neonatal liver can be injured. Cannula decompression of a tension pneumoperitoneum is a technique which can be performed as a life-saving measure by neonatologists, paediatricians and nursing staff involved in the care and transfer of neonates.

#### Further reading

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## Sex-differences in Apgar scores for full-term neonates

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#### Received

1 October 2008; revised 16 January 2009;  
accepted 20 January 2009.

DOI:10.1111/j.1651-2227.2009.01238.x

Male gender is overrepresented in several medical conditions and in complications during the perinatal period and infancy, although the origin of this sex-related vulnerability is not fully understood. Severe perinatal acidaemia and encephalopathy are examples of the statistically more frequent complications among boys (1). Similarly, sudden infant death syndrome (2), brain tumors (3), congenital hydrocephalus, neurodevelopmental malformations, epilepsy and cerebral palsy are more frequent in male than female infants, worldwide. Such increased vulnerability in male infants is not unique to humans, but seems to be universal among mammals. Even male rat pups have worse survival rates after perinatal asphyxia than females (4).

The Apgar scores, used to indicate newborn infants' adaptation to the extra-uterine life, also show sex-related differences. Premature male newborns, with very low birth-weight, were found to have lower Apgar scores than females (5,6) and in large-cohort studies low 5-min Apgar scores occurred less frequently in girls than in boys (7,8). Male fetuses' have a higher risk for preterm delivery as well (8,9). Mean Apgar scores correlate with gestational age (GA), and premature infants' 5-min mean Apgar scores are lower than those of full-term infants, and in general, Apgar scores are lower as the function of the GA (10). The interpretation of the significance of these results has been controversial, ranging from 'statistical rather than clinical interest', to the theory of the 'disadvantaged newborn male'. In full-term newborns such GA-related differences in the Apgar scores disappear between 37 and 40 gestational weeks

(10). The relationship between the male sex and lower Apgar scores thus, may be directly or indirectly related to the sex-related GA differences, instead of a direct sex-Apgar score link.

The current study examined the question whether full-term, healthy neonates show similar sex-related differences in their 1-, 5- and 10-min Apgar scores, or whether in the absence of such differences, the sex-related differences in the Apgar scores reflect increased vulnerability of high-risk, premature male neonates only.

At the Department of Obstetrics and Gynaecology of the University of Szeged, data from 709 healthy, full-term (born at 37-40 gestational weeks) singleton newborns (377 boys and 332 girls) were analyzed from the period of 2004-2007. None of the babies required perinatal intensive care. The delivery and the babies' first 72 postnatal hours were free of any medical complications. The total number of births in the clinic in this period was 8609. Mothers of full-term, singleton babies born in a randomly chosen 10-day period of each season, were asked for their consent to be included in the database. The study was reviewed and approved by the Ethical Committee of the University of Szeged.

The mean weight of the babies was 3402 g (SD = 419, range 2170-4660 g), and the mean GA was 38.90 weeks (SD = 0.94, 40 ≥ GA ≥ 37). Four hundred and five babies were born by caesarean section and 304 by vaginal delivery.

The prevalence of caesarean section in the clinic during this period was an average of 39%. Babies born with caesarean section were somewhat overrepresented in our

sample, because the mothers stayed an average a day longer in the hospital, and were more available for informed consent. There was no sex-related difference in the way of delivery [ $\chi^2 = 0.49$ , non-significant (n.s.)].

The weight of the boys was significantly larger (boys mean = 3457 g, SD = 423 g, girls mean = 3340 g, SD = 406,  $t_{2,705} = 3.74$ ,  $p < 0.001$ ), and boys were marginally overrepresented in the lower GA compared to girls ( $\chi^2 = 7.83$ ,  $p = 0.05$ , Table S1), thus both weight and GA were taken into account in the further analyses on the effect of sex on the Apgar scores.

Using a mixed design, repeated measures analysis of variance (ANOVA) with Apgar scores (Apgar 1-, 5- and 10-min) as within-subject, sex as between-subject factors and weight as a covariate, there was a significant main effect of the Apgar score changes (with Greenhouse–Geisser correction,  $F_{2,825.31} = 4.28$ ,  $p < 0.05$ ) and a significant Apgar\*sex interaction (with Greenhouse–Geisser correction,  $F_{2,825.31} = 4.79$ ,  $p < 0.01$ ). The Apgar\*Sex, Apgar\*GA, and Apgar\*Sex\*GA interactions were n.s.

Post-hoc analysis of the main effect of Apgar scores showed, as expected, that the Apgar scores significantly increased over time (mean Apgar 1 = 9.36, mean Apgar 5 = 9.83, mean Apgar 10 = 9.97, pairwise comparisons were significant at  $p < 0.001$  level for Apgar 1–5, Apgar 1–10, Apgar 5–10).

Post-hoc analysis of the significant sex\*Apgar interaction showed that boys had significantly lower scores at 1-min (Boys = 9.25, SD = 1.32, girls = 9.48, SD = 0.97,  $t = -2.54$ ,  $p < 0.05$ ) and at 5 min (Boys = 9.79, SD = 0.65, girls = 9.89, SD = 0.38,  $t = -2.22$ ,  $p < 0.05$ ) Apgar scores, but by 10 min the Apgar scores were not significantly different between the sexes (Boys = 9.96, SD = 0.22, girls = 9.98, SD = 0.12,  $t = -1.65$ ,  $p = 0.10$ ).

Considering Apgar scores  $\leq 7$  as low (according to the practice of the clinic (11)), male newborns were significantly overrepresented in the lower 1-min Apgar scores than females ( $\chi^2 = 3.84$ ,  $p < 0.05$ ), and were overrepresented in the lower 5-min Apgar scores ( $\chi^2 = 10.19$ ,  $p = 0.01$ ). By 10 min all newborns were above Apgar score 7. [See Table S2 for odd ratio (OR) and confidential interval (CI)].

The lower Apgar scores of full-term, healthy male, compared to female newborns reported in this study suggest: i) that similar earlier results, including those with premature and very-low-birth-weight newborns, are more than of purely 'statistical rather than clinical interest', and ii) that not only high-risk, but also full-term, healthy, male neonates; thus male newborns in general score lower on a measure evaluating vital signs and extra-uterine adjustment, when compared to females. The Apgar score has been found to be related to the sympathoadrenal activity, to the level of catecholamines in the umbilical artery, in the neonate (12). Term infants produce higher levels of catecholamines at birth, than preterm infants do, without sex-related differences (13). Preterm female infants, however, especially after asphyxia, produce relatively higher levels of catecholamines than preterm males after asphyxia (12). If Apgar score is regarded an indicator of the vitality of the neonate, that is

related to the activity of the sympathoadrenal system (13), the results from our study and the above papers point to girls' increased adaptation to adverse circumstances at birth.

Such sex-related differences in their adjustment to the environment are observable even at the behavioural level in newborns and young infants. Social stress, such as depression of the mother in the first months, affects boys' later emotional and cognitive development more severely (14) than of the girls. Not only human, but also male rhesus infants (15) react to early social deprivation more severely on both physiological and behavioural levels, than females do. Sackett (15) in his 'buffered females' theory, suggested that females are able to adapt more flexibly to the changing environment by quickly inhibiting previously adaptive behaviours that became maladaptive in a new, changed environment. Nagy et al. (16) suggested that the presence of complex psychophysiological and metabolic differences between male and female neonates lead to a potential gender paradox in their psychobiological adjustment. The larger absolute and relative size of male newborns' heads may reflect a disproportionately higher energy consumption of the newborn male brain, and along with their lower baseline heart rate, lower baseline body temperature, higher cardiovascular reactivity, and their increased sensitivity to socio-environmental challenges, may result in the males' increased socio-biological vulnerability in this early developmental period. Such differential vulnerability however, could represent an evolutionary heightened responsivity, in the form of differential susceptibility, or differential sensitivity to biological context. This means that male infants in a more prolonged window of early development are not merely more vulnerable, but may also be more susceptible to positive interventions as well. This hypothesis however, requires further investigation. In summary, although the lower Apgar scores of full-term, healthy male newborns *per se* are not direct indicators of individual vulnerability, it is likely to be a part of a wider onto- and phylo-genetically determined pattern of sex-related developmental differences.

#### ACKNOWLEDGEMENTS

The authors thank Jozsefne Varga and Dezsone Nagy for their help in the data management, and the Reviewers and the Editor for their help in improving the paper.

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#### SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Table S1** Number (and %) of boys and girls in the sample at gestational ages 37–40.

**Table S2** Number (and %) of boys and girls with low Apgar 1- and Apgar 5-min scores.

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