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Intrauterine growth curves based on ultrasonically estimated foetal weights

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Available standard intrauterine growth curves based on birthweights underestimate foetal growth in preterm period. New growth curves are presented based on data from four Scandinavian centres for 759 ultrasonically estimated foetal weights in 86 uncomplicated pregnancies. Mean weight of boys exceeded that of girls by 2–3%. A uniform SD value of 12% of the mean weight was adopted for the standard curves as the true SD varied non-systematically between 9.1 and 12.4%. Applied to an unselected population of 8663 singleton births, before 210 days of gestation, 32% of birthweights were classified as small-for-gestational age (SGA; i.e. below mean −2 SD); the corresponding figures were 11.1% for gestational ages between 210 and 258 days, and 2.6% for ages of 259 days or longer. The new growth curves reveal better the true distribution of SGA foetuses and neonates, and are suggested for use in perinatological practice. □ *Foetal growth, foetus, gestational age, growth curve, neonate, pregnancy, ultrasound*

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Intrauterine development determines, to a certain extent, the future somatic and psychomotor development of an individual, and impaired growth *in utero* has an impact on perinatal morbidity. The evaluation of intrauterine growth is important for rational planning of possible obstetric intervention and for the neonate's proper management.

Paediatricians evaluated for many years the birthweight by comparison with the mean birthweight of gestational age-matched neonates and several growth curves based on birthweights have been published (1–4). Such birthweight curves do not necessarily represent the intrauterine population, especially not in the preterm period, and therefore it would be preferable to use weight curves depicting foetal growth continuing *in utero* until term. However, available curves of intrauterine growth, based on ultrasound estimation of foetal weight, have not been considered reliable, mainly because ultrasound provides an estimate of weight and not a precise measurement (5). Moreover, previously published curves have been based on relatively few observations (6, 7).

As the rapid development of ultrasound technique during the last two decades has enabled reliable estimates to be made of gestational age and foetal weight, it is now possible to evaluate individual intrauterine growth by serial foetometry. In the following, an intrauterine growth curve is presented that is based on ultrasound estimation of foetal weight in uncomplicated pregnancies at four perinatal centres in Sweden and Denmark. The curve can be used for evaluation of both foetal weight and birthweight.

Subjects and methods

Serial ultrasound foetometry was performed on singleton foetuses in uncomplicated pregnancies. The participants were scheduled for nine to 11 measurements during pregnancy, every 3 weeks in three perinatal centres (Linköping and Malmö, Sweden; Herlev, Denmark) and every 4 weeks in 1 centre (Gothenburg, Sweden). Owing to drop-outs ($n = 10$) and complications of pregnancy, e.g. preterm delivery ($n = 3$), pre-eclampsia ($n = 3$) and intrauterine growth retardation (birthweight below mean −2 SD of the Swedish standard charts; $n = 2$), only 86 women completed the whole series of measurements. On average, 3.4 (range 3–4) and 10.2 (range 7–11) measurements were performed per foetus in Gothenburg and the other three centres, respectively. The measurements were equally distributed between 76 and 286 days of gestation in 35 women from Herlev, 14 women from Linköping and 19 women from Malmö, and between 190 and 280 days in 18 women from Gothenburg.

The women participated voluntarily in the study after giving their informed consent. Forty-seven women

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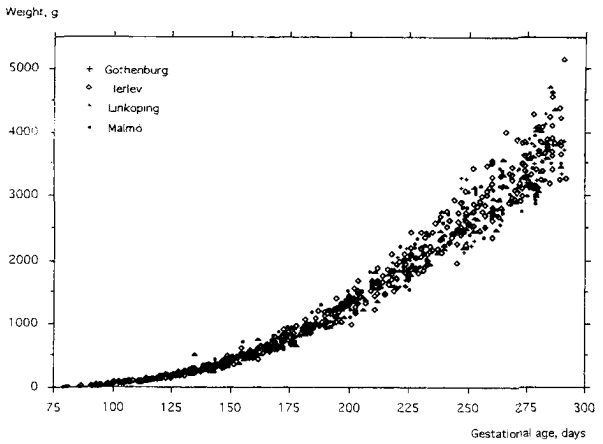

Fig. 1. Ultrasonically estimated foetal weights ($n = 759$) and birthweights ($n = 86$) versus gestational age (data from four Scandinavian centres).

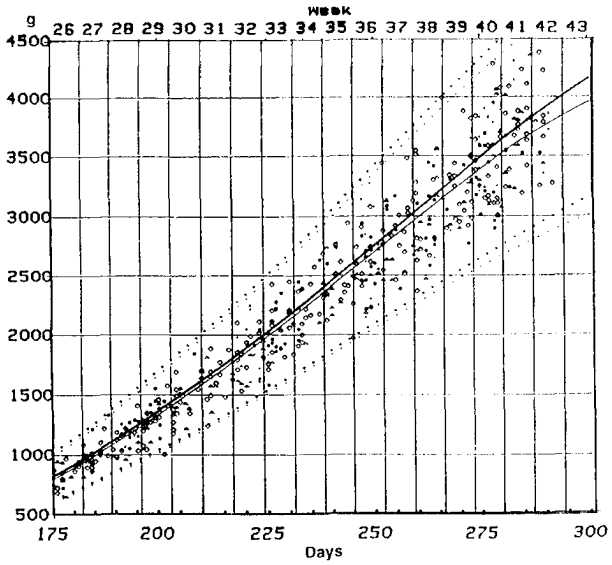

Fig. 2. Sex-specific intrauterine growth curves fitted to the plotted foetal weights and birthweights according to fourth degree polynomial functions. The solid lines give mean weights and the dotted lines mean ±2 SD (1 SD = 12% of the mean). Gestational age is given both in weeks (upper part) and days (lower part). Thick rule, boys; thin rule, girls.

(55%) were nulliparae and 21 (24%) were smokers (10 cigarettes or less per day). All women gave birth at term and the perinatal outcome was normal in all cases (Apgar score greater than 7 at 5 min, uneventful neonatal period). In 53 male neonates, mean gestational age at birth was 279.8 days (SD 8.5) and mean birthweight 3580 g (SD 519). The corresponding figures for 33 female neonates were 279.7 days (SD 8.6) and 3529 g (SD 508).

The ultrasound measurements were performed by experienced operators, using modern, commercially available real-time scanners. In all cases, the date of last menstrual period was known and gestational age was confirmed by ultrasound measurements of foetal biparietal diameter (BPD) in the early second trimester ($n = 72$) or of crown-rump length (CRL) in the first trimester ($n = 14$). In no case did ultrasound correction of gestational age exceed 7 d.

The following foetal variables were measured on each occasion: BPD (measured from the outer to the inner border of the echo complexes representing the anterior and posterior foetal skull bones) (8), abdominal diameter (AD) (the mean of the anterio-posterior and transverse diameters measured in the plane perpendicular to foetal spine at the level of intraabdominal umbilical vein from the outer to the outer outline of the abdominal wall echoes) (9) and femur length (FL) (10).

Foetal weight was calculated according to the formula developed by Persson and Weldner (6):

$$\text{Foetal weight} = \text{BPD}^{0.972} \times \text{AD}^{1.743} \times \text{FL}^{0.367} \times 10^{-2.646}$$

The best fit of the data for 759 foetal weights, supplemented by the 86 birthweights, was found using a fourth degree polynomial equation. Curves were calculated for the series as a whole, for each centre and for male and female subgroups. The SD was calculated cross-sectionally for each week of gestation. Some of the data have been published in other contexts (6, 7).

The growth curves based on the intrauterine ultrasound measurements were compared with the recently published Swedish growth curves based on birthweights (11). Furthermore, the birthweights of an unselected population of 8663 live singleton neonates, born in Malmö during the years 1989–1991, were plotted on the new intrauterine growth curves.

Table 1. Fourth degree polynomial equations fitted to the data for boys and girls, and for the series as a whole.

	Polynomial regression equation[a]
Boys	$f(x) = -1.907345\text{E}{-6} * x^4 + 1.140644\text{E}{-3} * x^3 + -1.336265\text{E}{-1} * x^2 + 1.976961\text{E} + 0 * x + 2.410053\text{E} + 2$
Girls	$f(x) = -2.761948\text{E}{-6} * x^4 + 1.744841\text{E}{-3} * x^3 + -2.893626\text{E}{-1} * x^2 + 1.891197\text{E} + 1 * x + -4.135122\text{E} + 2$
Total material	$f(x) = -2.278843\text{E}{-6} * x^4 + 1.402168\text{E}{-3} * x^3 + -2.008726\text{E}{-1} * x^2 + 9.284121\text{E} + 0 * x + -4.125956\text{E} + 1$

[a] $f(x)$, foetal weight (in g); x, gestational age (in days).

Results

Figure 1 shows all 759 estimated foetal weights and 86 birthweights plotted against gestational age. The fourth degree equations for the data are presented in Table 1. Equations based on 759 intrauterine observations

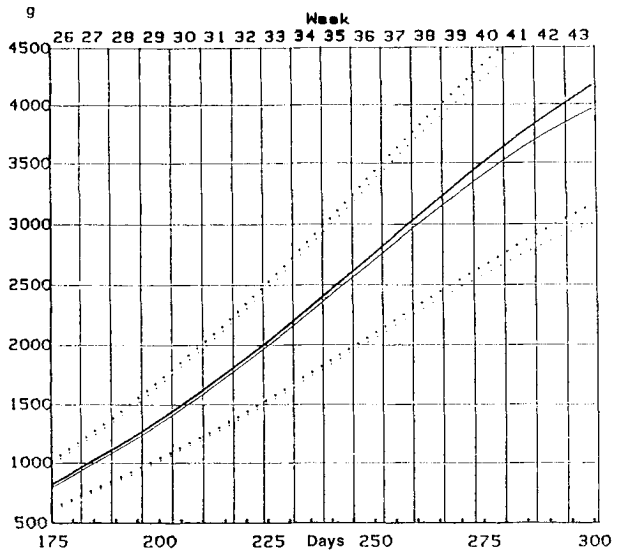

Fig. 3. Intrauterine growth curves for boys and girls. Mean ±2 SD. Thick rule, boys; thin rule, girls.

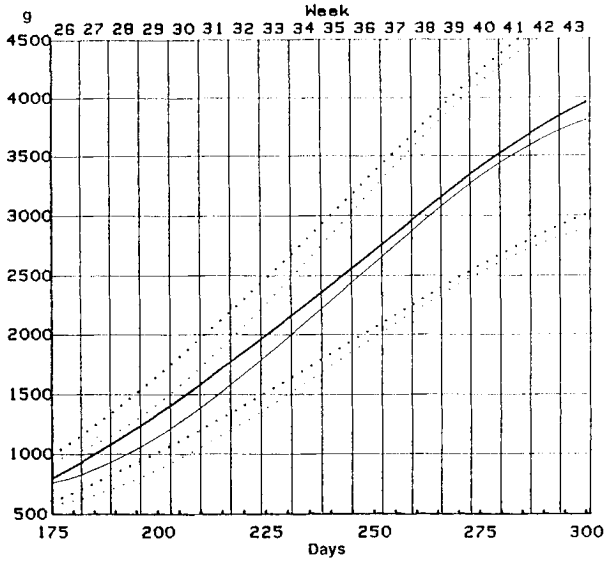

Fig. 5. Comparison of intrauterine (thick rule) and postnatal (thin rule) growth curves for girls. Postnatal growth curve according to Källén et al. (11). Mean ±2 SD.

alone, excluding the birthweights, did not differ significantly from the curves for the series as a whole nor did the equations of four centres differ from each other.

The fitted curves for boys and girls are shown in Fig. 2. The relative weight differences in percent between the curves according to foetal sex were: before 190 days of gestation, 3%; between 190 and 270 days, 2%; and, thereafter, 3% of the mean estimated weight for boys.

The weights were normally distributed, and, for the period of gestation between 175 and 286 days, the SD varied non-systematically from week to week between 9.1 and 12.3% of the mean weight for boys, and between 9.7 and 12.4% for girls. In the presentation of reference curves (Figs 2 and 3), we have adopted a uniform SD value of 12 % for both boys and girls in all weeks.

The present intrauterine growth curves are compared with the birthweight based growth curves by Källén (11) in Figs 4 and 5 for boys and girls, respectively.

In Fig. 6, the birthweights of 8663 live singleton

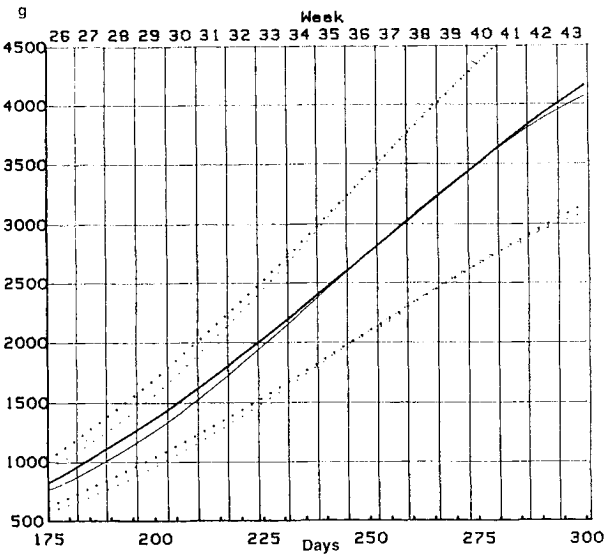

Fig. 4. Comparison of intrauterine (thick rule) and postnatal (thin rule) growth curves for boys. Postnatal growth curve according to Källén et al. (11). Mean ±2 SD.

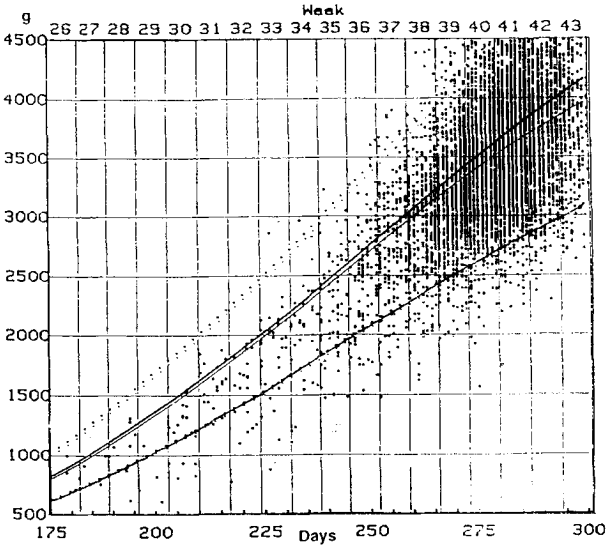

Fig. 6. Intrauterine growth curves and birthweights of 8663 live singleton newborns delivered in Malmö during 1989–1991. Thick rule, boys; thin rule, girls.

Table 2. Percentage of small-for-gestational age neonates according to the intrauterine and postnatal growth curve, respectively (small-for-gestational age: birthweight below mean −2 SD).

	Gestational age (days)		
Growth curve	175–209	210–258	259–294
Intrauterine[a]	32.0	11.1	2.6
Postnatal[b]	21.0	8.9	2.4

[a]Present study.
[b]Källén (11).

newborns are plotted on the new intrauterine growth curves. The birthweights of babies born before 259 days of gestation (preterm births) were negatively skewed. Between 175 and 209 days, 32.0%, and between 210 and 258 days, 11.1% of birthweights fell below the mean intrauterine weight −2 SD. At term (259 days or longer), the corresponding figure was 2.6% (Table 2).

Discussion

There are two ways of compiling standard reference curves for intrauterine growth. One method is based on cross-sectional observations of birthweights obtained from babies subgrouped according to gestational age at birth, expressed in weeks. This is a practical method that allows large nationwide data to be collected. However, there are doubts about the representativeness of these cross-sectional curves regarding true intrauterine growth because, except for the term period, they are based on abnormal deliveries, either pre- or post-term, or on deliveries at gestational weeks that have been difficult to verify objectively. The construction of cross-sectional birthweight curves that are claimed to represent the intrauterine growth is thus always subject to more or less sophisticated statistical elaborations and exclusions, in order to obtain data representative of the intrauterine population.

In this presentation, we have used a different approach, i.e. the ultrasound estimation of intrauterine weight. This method is laborious and therefore the number of subjects that can be included is limited. Accordingly, intrauterine curves are often the subject of discussion regarding their relevancy for a larger population. Furthermore, the precision of the weight estimating algorithm and the accuracy of gestational age estimations are sometimes questioned.

Although still relatively small (86 foetuses), the present series is one of the largest longitudinal series yet published. For practical reasons, recruitment could not be done randomly. In longitudinal series, an increasing number of participants drop out successively as they are delivered. To obtain the true shape of the curves towards term, we considered it necessary to include the birthweight as the final data point on the curve. This procedure could have influenced the shape of the curve if there was systematic under- or overestimation of foetal weight with the formula used. However, no difference in the shape was noted between curves with versus without birthweights.

The present foetal weight estimation formula (6), was developed using a stratified sample of 10 pregnancies in each 500 g weight class: below 500, 501–1000, 1001–1500 g, etc., up to 5000 g. BPD, AD and FL were measured in 89 uneventful pregnancies, within 48 h of delivery or legal termination of pregnancy. To test the reliability of the formula and to ascertain the estimation error, the formula was used to estimate foetal weight in another 135 pregnancies within 48 h of delivery. The slope of the regression line between the estimated and the true weight was identical in the test group and in the stratified group. The estimation error was 7.1% (SD) (6). The foetal weight estimation error has been also tested in a large unselected series examined within 48 h of delivery in a routine clinical program at the Ultrasound Unit in Malmö (Molin, pers. comm.). For foetuses born at a gestational age of less than 34 weeks, there was a mean difference between the estimated and true birthweight of +1.43% with an SD of 8.4% ($n = 48$), for deliveries at 34–36 weeks, the SD was 8.3% ($n = 106$), at 37–39 weeks 7.9% ($n = 250$) and greater than 39 weeks 8.5% ($n = 163$). For these births, there was no significant under- or overestimation of the true weight. This indicates that the formula works as well for a small foetus as it does for a large foetus and that there is no systematic error related to gestational age. The efficacy ot the weight estimation formula has been tested over a 10 year period in clinical practice with repeated product controls. Nevertheless, due to the difficulty in collecting sufficient number of comparisons in very preterm foetuses, some degree of uncertainty exists regarding the reliability of foetal weight estimation in the late second trimester.

Using ultrasound foetometry to estimate gestational age, the estimation error (SD) is less than 2.8 d (12, 13). However, the method of using BPD and FL to estimate gestational age has a small but significant built-in error. The BPD (and, to a much lesser extent, the FL) may already in the second trimester differ between boys and girls, and between genetically light and heavy babies. This error *per se* does not affect clinical management, but it does influence the actual difference between the growth curves for boys and girls. A female foetus of the same true age as a male foetus will be judged younger at birth than the (on average) heavier male. For instance, in the population of Malmö, the difference in mean gestational age at birth between boys and girls is 0.7 d (Persson, unpublished), which might be attributed to systematic error in the estimation of gestational age. Because of this, the present curves of boys and girls are somewhat closer than they ought to be. We estimate that our method diminishes the inter-sex weight difference by about 20 g at

term. For the new intrauterine curves, the mean difference between the sexes was found to be 120 g at 40 weeks, which according to the above discussion is about 20 g less than in reality.

When comparing the present longitudinal intrauterine growth curves with the cross-sectional curves based on a background data for about half million births in Sweden during a 6 year period (11), perfect agreement was found between the postnatal and intrauterine growth curves for boys at gestational ages of 235–290 days (Figs 4 and 5). Before 34 weeks, the intrauterine curve shows values almost 100 g above those of the postnatal curve. For girls, the intrauterine curve is similar in shape to the postnatal one, but shows higher values, the difference being 60 g in the term period and 170 g in the preterm period. This difference between the curves for girls cannot be fully explained by the above mentioned conditions.

The distribution of foetal weights, calculated cross-sectionally and expressed in SD, varied non-systematically between different gestational weeks from 9.1 to 12.4% of the mean weight. For graphic presentation of the reference curve we adopted a smoothed SD value of 12% of mean weight for all gestational weeks. In another larger cross-sectional series of ultrasonically dated pregnancies, the SD was found to be 11.5% of the mean birthweight (14). For the new postnatal growth curve, Källén also found weight dispersion of around 12% (11). Initially, we considered to estimate the variation of present data by calculating individual regression lines. However, such an approach would give a falsely narrow distribution. Recently, it has been pointed out that such a method is incorrect and that longitudinal data are more suited to describe the growth than to give the distribution of weight (15). Therefore, in agreement with the two above mentioned cross-sectional studies (11, 14), we decided to use ±24% (± 2 SD) as the upper and lower reference limits, enclosing most of the present data (Fig. 2).

The difference between the postnatal and the intrauterine curves is negligible during the term period, but not during the preterm period. It is reasonable to suppose the difference to be due to the already discussed fact that the postnatal data are not representative of the preterm intrauterine population. The choice of curve will therefore have some important clinical implications. In Fig. 6 we have plotted birthweights of all 8663 liveborn singleton babies delivered during a 3 year period in Malmö. It is obvious that the majority of preterm born babies' birthweights fall below the mean gestational age-related intrauterine weight. In Table 2, the proportions of newborns classifable as small-for-gestational age (SGA; birthweight below mean −2 SD) using the intrauterine and the postnatal reference curves are compared.

As discussed above, the present intrauterine curves are by no means the ultimate solution to the problem of describing the intrauterine growth. Nevertheless, it is our hope that the use of intrauterine growth curves for evaluation of both foetal weights and birthweights in clinical perinatological practice might facilitate the management of growth retarded foetuses and neonates. The choice of reference curve, postnatal or intrauterine, depends on the purposes for which it is required by the obstetrician or the neonatologist. When using the present intrauterine growth curves [and, to some extent, also when using the postnatal curves of Källén (11)], many more neonates will be classified as SGA in the preterm period; babies previously classified as being below the mean −2 SD will now fall below the mean weight −4 SD, and some babies previously classified as 'near-SGA' will now be classified as SGA, which probably will better reflect the increased perinatal morbidity of this group. With the intrauterine growth curves there will be better correspondence between the magnitude of deviation in newborns' size in the preterm and term period. Paediatricians might find it suitable to quantify the degree of SGA in a newborn by adopting the method used by obstetricians for foetuses and to express the deviation from the expected weight value in multiples of the SD.

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Announcements

11th Congress of the International Society for Prevention of Child Abuse and Neglect (ISPCAN) will take place in Dublin on 18–21 August 1996. Further information may be obtained from the Congress Chairperson, Dr Imelda Ryan, Our Lady's Hospital, Crumlin, Dublin 12, Ireland. Tel: +353 1 455 8221. Fax: +353 1 661 2073.

Hand in hand with Rett Syndrome. World Congress on Rett Syndrome will be held in Göteborg, Sweden on 30 August to 1 September 1996. Information may be obtained from Professor Emeritus Bengt Hagberg, Neuropaediatric Section, Children's Clinic, East Hospital, S-41 685 Göteborg, Sweden. Fax: +46 31 257 960.

6th International Conference on Osteogenesis Imperfecta will be held on 19–21 September 1996 at the Woudschoten Conference Center in Zeist, The Netherlands. Further information may be obtained from: Mrs E. J. Breslau-Siderius, Clinical Genetics Center Utrecht, PO Box 18009, NL-3501 Utrecht, The Netherlands. Tel: +31 30 320 210. Fax: +31 30 320 383.

4th International Conference of the European Society for Pediatric Otorhinolaryngology will take place in Siena, Italy on 2–5 October 1996. For further information please contact the General Secretary, Bellussi Luisa, Universita degli Studi di Siena, Servizio Congressi, Banchi di Sotto 46, I-53100 Siena, Italy. Tel: +39 577 298129. Fax: +39 577 298134.

The Changing Scope of Lung Disease in Infancy. This Conference, arranged by the Boerhaave Committee for Postgraduate Medical Education, will be held on 11 October 1996 in Leiden, The Netherlands. Further information may be obtained from the Office of the Boerhaave Committee, PO Box 2084, 2301 CB Leiden, The Netherlands. Tel: +31 71 527 5293.

3rd International Meeting of the International Society for Neonatal Screening will be held in Boston, Massachusetts, USA on October 21–24, 1996. For registration and information – By *mail: ISNS/Travel Vision, 49 River Street, Waltham, MA* 02154, USA. By fax: +1 617 894 6454.

9th Asian Congress of Paediatrics will be held on 23 to 27 March 1997 at the Hong Kong Convention and Exhibition Centre. The Congress theme will be "Paediatric Priorities in the 21st Century". For further information, please contact the Congress Secretariat by Tel: 852 2660 4447 or by Fax: 852 2667 6927.

5th Congress of the Asian Pan Pacific Society of Pediatric Gastroenterology and Nutrition will be held in Taipei on 10–13 April 1997. Call for Papers. Further information may be obtained from The Secretariat, c/o K&A International Co., Ltd., PO Box 55, 1143 Taipei, Taiwan. Tel: +886 2 516 3952. Fax: +886 2 516 2512.

3rd London International Conference on Eating Disorders will take place on 15–17 April 1997 in the New Connaught Rooms, Great Queen Street, London WC2B. Early booking discount up to 10th September 1996. For further information and registration form, please contact the Conference Manager, Eating Disorders '97, Mark Allen International Conferences Ltd, Croxted Mews, 286A-288 Croxted Road, London SE24 9BY. Tel: +44 181 671 7521. Fax: +44 181 671 7327.

16th Congress of the ESPHI (European Society for Paediatric Haematology and Immunology) will be held in Thessaloniki, Greece on 14–17 May 1997. Further information may be obtained from The Secretariat, Mrs Fotoula Cotsis, 4, Filellinon Street, 105 57 Athens, Greece. Tel: +30 1 3224 368/3229 151/3230 380 1. Fax: +30 1 3219 296/3245 049.

7th International Congress of Inborn Errors of Metabolism will take place on 21–25 May 1997 in Vienna, Austria. For information please contact Mondial Congress, Faulmanngasse 4, A-1040 Vienna, Austria. Tel: +43 1 58 8040. Fax: +43 1 586 9185.

16th International Congress of Nutrition will be held in Montréal, QC, Canada on 27 July until 1 August 1997. For further information, please contact: Congress Secretariat, IUNS '97, National Research Council Canada, Building M-19, Montreal Road, Ottawa, ON, Canada K1A 0R6. Tel: 613 993 7271. Fax: 613 993 7260.

The Fate of the Jewish and Politically Persecuted German Pediatricians after 1983. At their 91st annual meeting in 1995 the board and the general assembly of the German Society of Pediatrics (Deutsche Gesellschaft für Kinderheilkunde) resolved that a documentary report be drawn up about those pediatricians who were persecuted for racial or political reasons in Nazi Germany after 1933. With this documentary report, the Society intends to honour their memory. The Historical Commission of the Society is asking all colleagues to collaborate. Those who had been affected, their relatives, colleagues and friends are being cordially invited to contribute any data, facts and material they still may have to this project. In addition, the Austrian pediatricians so affected after 1938 will also be included.

German Society of Pediatrics: *President* E. Schmidt, Düsseldorf. Historical Commission, Th. Lennert, Berlin. Contact address: Prof. Eduard Seidler, MD, Institute for the History of Medicine of the Albert-Ludwigs-University, Stefan-Meier-Straße 26, D-70104 Freiburg im Breisgau. Phone: + +761/203-5033. Fax: + +761/203-5039.