Neonatal Anthropometric Charts: The Italian Neonatal Study Compared With Other European Studies

*Enrico Bertino, †Elena Spada, *Luciana Occhi, *Alessandra Coscia, *Francesca Giuliani, ‡Luigi Gagliardi, *Giulio Gilli, §Gianni Bona, *Claudio Fabris, ||Mario De Curtis, and †Silvano Milani

ABSTRACT

Background and Objective: This was a nationwide prospective study carried out in Italy between 2005 and 2007, involving 34 centers with a neonatal intensive care unit. The study reports the Italian Neonatal Study charts for weight, length, and head circumference of singletons born between 23 and 42 gestational weeks, comparing them with previous Italian data and with the most recent data from European countries.

Patients and Methods: Single live born babies with ultrasound assessment of gestational age within the first trimester, and with both parents of Italian origin. Only fetal hydrops and major congenital anomalies diagnosed at birth were excluded. The reference set consists of 22,087 girls and 23,375 boys.

Results: At each gestational age, boys are heavier than girls by about 4%. Later-born neonates are heavier than firstborn neonates by about 3%. The effects of sex and birth order on length and head circumference are milder. No differences were observed between babies born in central-north Italy and southern Italy. A large variability emerged among European neonatal charts, resulting in huge differences in the percentage of Italian Neonatal Study neonates below the 10th centile, which is traditionally used to define small-for-gestational-age babies. In the last 2 decades prominent changes in the distribution of birth weight emerged in Italy and in the rest of Europe, in both term and preterm neonates.

Conclusions: The existing European neonatal charts, based on more or less recent data, were found to be inappropriate for Italy. Until an international standard is developed, the use of national updated reference charts is recommended.

Key Words: birth weight, growth, length and head circumference, neonatal anthropometric charts, small-for-gestational-age

(*JPGN* 2010;51: 353–361)

In clinical practice, a neonate is classified as small-for-gestational-age (SGA), appropriate-for-GA, or large-for-GA on the basis of threshold values derived from the distribution of a given anthropometric trait (eg, birth weight [BW]) in a population of neonates regarded either as standard or more often as a reference. A standard is based on highly restrictive criteria aimed at excluding all neonates exposed to any risk factor for fetal growth, thus describing ''how growth should be.'' In the absence of these exclusion criteria, a chart is considered a reference, which describes ''how growth actually is.'' At present, the large majority of neonatal charts in use are essentially references (1).

The heterogeneity of methods used to trace these charts, mainly in regard to the criteria adopted to select the neonates, results in wide differences between the threshold values, which do not necessarily reflect substantial differences between populations. The present trend is that each country produces or updates its own national charts (2). In Italy, the 6 charts based on data of babies born from 1979 to 2003 and published in the last decade (3–8) present large differences, mainly at low values of GA (eg, at 28 weeks the values of the 10th centile differ by up to 223 g in boys and 177 g in girls).

For this reason, the Italian Society of Neonatology, the Italian Society of Pediatric Endocrinology and Diabetology, and the Italian Society of Medical Statistics and Clinical Epidemiology promoted a multicenter survey with the aim to produce an Italian neonatal anthropometric reference fulfilling the set of criteria suggested in a previous study (9). The present study reports and discusses Italian Neonatal Study (INeS) charts for weight, length, and head circumference of singletons born between 23 and 42 gestational weeks, and compares them with previous Italian data and with the most recent data from European countries.

PATIENTS AND METHODS

Reference Set

The present study, which lasted from 2005 to 2007, involved 34 of the 125 Italian centers selected on a voluntary basis, having a neonatal intensive care unit, and trained to use standard instruments and measurement techniques. In the first year of the study, all of the neonates in participating centers were enrolled; in the second and third years, only preterm neonates were recruited to increase the number of babies born at low GAs. In accordance with the protocol of the study, single live-born babies delivered from 23 to 42 gestational weeks and with both parents of Italian origin were included in the reference set. GA, recorded in completed weeks plus days, was based on ultrasound assessment within the first trimester. Only 3% of neonates showed a discrepancy with the estimate derived from last menstrual period larger than 1 week; also in these cases the ultrasound assessment was used. Fetal hydrops and major congenital anomalies diagnosed at birth were excluded.

The reference set described above consists of 45,462 neonates: 22,087 girls and 23,375 boys (Table 1). The percentage of neonates coming from north-central Italy (72%) was slightly higher

Received October 28, 2009; accepted February 7, 2010.

From the *S.C.D.U. Neonatologia, Dipartimento di Scienze Pediatriche e dell'adolescenza, Università degli Studi di Torino, Torino, the †Statistica ica e Biometria ''GA Maccacaro'' Università degli Studi di Milano, Milano, the ‡Divisione di Neonatologia e Pediatria Ospedale Versilia, Lido di Camaiore, the §Clinica Pediatrica di Novara, Università del Piemonte Orientale ''A. Avogadro,'' Novara, and the ||Dipartimento di Pediatria, Università di Roma ''La Sapienza,'' Rome, Italy.

Address correspondence and reprint requests to Enrico Bertino, S.C.D.U. Neonatologia, Dipartimento di Scienze Pediatriche e dell'adolescenza, Università degli Studi di Torino, Via Ventimiglia 3, 10126 Torino, Italy (e-mail: enrico.bertino@unito.it).

The authors report no conflicts of interest.

DOI: 10.1097/MPG.0b013e3181da213e

TABLE 1. Number of Italian Neonatal Study babies by birth order, sex, and gestational age

	Firstborn neonates		Later-born neonates		
GA, wk	Girls	Boys	Girls	Boys	All
23	2	4	1	4	11
24	11	17	9	7	44
25	22	25	18	13	78
26	23	35	12	23	93
27	27	35	25	26	113
28	50	33	29	30	142
29	42	50	28	22	142
30	76	72	31	42	221
31	89	97	37	43	266
32	108	112	57	71	348
33	130	152	81	88	451
34	162	213	101	136	612
35	210	230	156	188	784
36	310	344	252	321	1227
37	574	695	717	797	2783
38	1477	1707	2047	2269	7500
39	2571	2667	2724	2785	10,747
40	3132	3113	2540	2540	11,325
41	2163	2211	1403	1441	7218
42	425	484	215	233	1357
All	11,604	12,296	10,483	11,079	45,462

in the reference set than in the Italian neonatal population (65%) in the same period (10). The percentage of firstborn neonates (53%) was close to that observed in Italy (51%) (11).

Measurements

BW was measured within 1 hour from delivery with an electronic weighing scale and recorded to the nearest 5 g. Birth crown-heel length (BL), and head circumference (HC) were measured within 1 day from delivery with a Harpenden neonatometer and an inelastic tape, respectively, and recorded to the nearest millimeter. Measurements were taken by trained personnel according to the techniques described by Cameron (12).

Statistical Analysis

The raw nonparametric centiles of BW, BL, and HC distribution conditional on GA have highly irregular patterns. To draw smooth neonatal charts, we resorted to the extended mechanistic growth function (EMGF) method, an extension of the Healy et al (13) approach to the case of nonlinear functions (14). To trace smooth centiles, raw centiles were fitted with an ad hoc function, derived from the generalized logistic function as described in detail in the Appendix. The neonatal charts thus obtained are completely defined by 10 constants, which express the mean pattern of the relation of BW (or BL or HC) to GA according to a prefixed growth model, as well as the conditional standard deviation and skewness of the anthropometric trait distribution. The centiles estimated with EMGF can also be expressed in terms of smooth GA-specific curves L, M, and S, just as in the Cole and Green LMS (GC-LMS) model (15), which is regarded as the gold standard to trace anthropometric charts. The M and S curves correspond to the median and coefficient of variation of the auxometric trait at each GA, whereas the L curve allows for the GA-dependent skewness of the distribution of the same trait. The value (y) of a trait measured on a neonate of a given GA, sex, and birth order can be transformed into a standard deviation score (SDS):

$$SDS = \frac{(y/M)^L - 1}{S \times L} \quad (1)$$

Alternatively, the value of a centile can be computed from the L, M, and S values. For instance, for the 10th centile (whose SDS is -1.28) of BW of a 28-week female later-born neonate, we have $L = 1.022$, $M = 995$, and $S = 0.214$; therefore,

$$y(10^{th}) = 995 \times (1 - 1.28 \times 1.022 \times 0.214)^{1/1.022} = 722 \quad (2)$$

RESULTS

Tables 2 and 3 show the 3rd, 50th, and 97th centiles for weight, length, and head circumference of neonates conditional on GA, sex, and birth order. The tables also report the L (power) and S (coefficient of variation) values required to compute SDS. On average, boys are heavier than girls by about 4%, the difference in weight being 23 g (23 weeks), 43 g (28 weeks), and 152 g (42 weeks). Later-born neonates are heavier than firstborn neonates by about 3%, with the difference increasing from 17 g (23 weeks) to 32 g (28 weeks) and 115 g (42 weeks). The effects of sex and birth order on length and head circumference are milder. Males are longer than females by 1.6% (the difference increasing from 5 to 8 mm) and have larger heads by 1.8% (the difference increasing from 4 to 6 mm). Later-born neonates are longer and have larger heads than firstborn neonates by 0.8%, the difference ranging from 2 to 4 mm. No differences were observed between babies born in central-north Italy and southern Italy. The precision of the estimates, which is higher for BL and HC than for BW, increases from 23 to 40 weeks and then decreases slightly. As for BW, at 24 weeks, 95% confidence limits of the 10th centile are 7.4 and 13.2 centiles, whereas they are 9.0 to 11.0 at 28 weeks and 9.5 to 10.5 at 40 weeks.

Table 4 reports the percentage of Italian neonates whose BW, BL, and HC values fall below the 10th centile of some European charts published after 1999. The percentage of INeS babies below the 10th centile of Scottish (16) and 2007 French charts (17) is close to the expected value of 10% but is by far higher when Norwegian (18) and Swedish (19) charts are considered. With respect to 2008 French (20), northwest Italian (5), and Spanish (21) charts there is an excess of preterm neonates and a shortage of term neonates below the 10th centile of BW and BL distribution (when available). In all of the charts, these percentages decrease with increasing GA.

Table 5 shows the temporal trend in birth weight expressed as increase or decrease of selected centiles of the weight (g/y) distribution of the more recent neonatal European charts with respect to charts based on data collected in the 1980s. As for term babies, median weight increased by 3.5 to 5.5 g/y and the lower centile by 5 to 10.5 g/y; the temporal trend of the higher centile is negative only in Italy. As for preterm babies born in France and Italy, weight decreased in the median and, to a larger extent, in the higher centile. The lower centile increased by 0.5 to 10.5 g/y.

DISCUSSION

The INeS charts meet all of the characteristics suggested to produce reliable neonatal charts (9). They are a descriptive reference, based on a preplanned multicenter ad hoc study. The target population consists of all singletons with both parents of Italian

TABLE 2. Italian Neonatal Study charts: 3rd, 50th, and 97th centiles and S and L functions of BW, BL, and HC distribution in firstborn neonates

Girls

GA	Weight					Length					Head circumference				
wk	3rd	50th	97th	S	L	3rd	50th	97th	S	L	3rd	50th	97th	S	L
23	348	508	666	0.166	1.035	25.2	29.2	33.0	0.0707	1.320	18.3	20.7	23.1	0.0621	1.166
24	371	578	783	0.189	1.027	26.3	30.4	34.3	0.0697	1.333	19.0	21.5	24.0	0.0613	1.175
25	402	657	909	0.205	1.023	27.4	31.6	35.6	0.0687	1.349	19.8	22.4	24.9	0.0605	1.187
26	443	746	1047	0.215	1.021	28.5	32.8	36.9	0.0675	1.369	20.7	23.3	25.9	0.0597	1.203
27	495	848	1198	0.220	1.020	29.7	34.1	38.3	0.0663	1.396	21.5	24.2	26.8	0.0587	1.226
28	561	963	1362	0.221	1.021	31.0	35.5	39.7	0.0650	1.432	22.3	25.1	27.8	0.0576	1.258
29	643	1094	1541	0.218	1.022	32.3	36.8	41.1	0.0636	1.482	23.3	26.1	28.8	0.0564	1.305
30	739	1242	1740	0.214	1.025	33.6	38.2	42.5	0.0619	1.552	24.1	27.0	29.7	0.0551	1.372
31	854	1409	1957	0.208	1.031	35.0	39.7	44.0	0.0601	1.651	25.1	28.0	30.8	0.0535	1.467
32	991	1597	2194	0.200	1.040	36.4	41.1	45.4	0.0580	1.789	26.1	29.0	31.7	0.0516	1.595
33	1149	1806	2449	0.191	1.057	37.8	42.5	46.7	0.0555	1.978	27.0	29.9	32.6	0.0494	1.762
34	1330	2035	2719	0.181	1.087	39.3	43.9	48.0	0.0526	2.229	28.0	30.8	33.4	0.0469	1.962
35	1532	2279	2994	0.170	1.135	40.7	45.3	49.2	0.0494	2.539	28.8	31.6	34.1	0.0442	2.174
36	1750	2529	3260	0.158	1.207	42.1	46.5	50.2	0.0460	2.889	29.6	32.3	34.7	0.0415	2.359
37	1979	2770	3499	0.145	1.294	43.3	47.5	51.0	0.0425	3.228	30.3	32.9	35.2	0.0389	2.467
38	2197	2984	3700	0.133	1.371	44.4	48.4	51.7	0.0392	3.475	31.0	33.4	35.6	0.0367	2.458
39	2379	3155	3861	0.124	1.396	45.4	49.1	52.2	0.0363	3.551	31.5	33.8	35.9	0.0351	2.328
40	2519	3279	3982	0.118	1.350	46.2	49.7	52.7	0.0341	3.413	31.7	34.0	36.1	0.0339	2.111
41	2612	3362	4071	0.115	1.259	46.8	50.1	53.0	0.0326	3.091	32.0	34.2	36.3	0.0333	1.862
42	2661	3414	4140	0.115	1.166	47.2	50.4	53.3	0.0317	2.669	32.2	34.4	36.5	0.0331	1.629

Boys

GA	Weight					Length					Head circumference				
wk	3rd	50th	97th	S	L	3rd	50th	97th	S	L	3rd	50th	97th	S	L
23	370	531	690	0.160	1.037	25.7	29.7	33.5	0.0695	1.332	18.7	21.1	23.5	0.0610	1.172
24	395	603	808	0.182	1.029	26.8	30.9	34.8	0.0685	1.345	19.4	21.9	24.4	0.0603	1.181
25	431	686	939	0.197	1.024	27.9	32.1	36.1	0.0675	1.362	20.2	22.8	25.3	0.0595	1.193
26	474	779	1081	0.207	1.022	29.1	33.4	37.5	0.0663	1.383	21.1	23.7	26.3	0.0586	1.210
27	532	885	1235	0.211	1.022	30.3	34.7	38.8	0.0651	1.411	21.9	24.6	27.2	0.0577	1.234
28	603	1006	1406	0.212	1.022	31.6	36.0	40.2	0.0638	1.448	22.8	25.6	28.3	0.0566	1.268
29	688	1142	1591	0.210	1.024	32.9	37.4	41.7	0.0624	1.500	23.8	26.6	29.3	0.0554	1.316
30	791	1297	1797	0.206	1.027	34.3	38.9	43.2	0.0608	1.573	24.6	27.5	30.2	0.0541	1.386
31	914	1472	2023	0.200	1.033	35.6	40.3	44.6	0.0590	1.675	25.6	28.5	31.3	0.0525	1.484
32	1060	1668	2266	0.192	1.044	37.1	41.8	46.1	0.0569	1.819	26.6	29.5	32.2	0.0506	1.618
33	1225	1886	2532	0.184	1.062	38.5	43.2	47.4	0.0544	2.017	27.6	30.5	33.2	0.0484	1.793
34	1417	2125	2811	0.174	1.094	40.1	44.7	48.8	0.0516	2.280	28.6	31.4	34.0	0.0459	2.002
35	1631	2380	3095	0.163	1.146	41.5	46.0	49.9	0.0484	2.607	29.4	32.2	34.7	0.0432	2.226
36	1864	2642	3371	0.151	1.224	42.8	47.2	50.9	0.0449	2.979	30.2	32.9	35.3	0.0405	2.423
37	2099	2893	3621	0.139	1.321	44.1	48.3	51.8	0.0414	3.341	31.0	33.5	35.8	0.0380	2.541
38	2329	3116	3829	0.127	1.407	45.3	49.2	52.4	0.0381	3.613	31.6	34.0	36.2	0.0358	2.537
39	2522	3295	3995	0.118	1.437	46.2	49.9	53.0	0.0353	3.705	32.1	34.4	36.5	0.0341	2.404
40	2670	3425	4120	0.112	1.389	47.1	50.5	53.4	0.0331	3.570	32.5	34.7	36.8	0.0329	2.177
41	2768	3512	4213	0.109	1.290	47.7	50.9	53.7	0.0315	3.236	32.7	34.9	37.0	0.0323	1.915
42	2819	3566	4284	0.109	1.187	48.1	51.2	54.0	0.0306	2.790	32.8	35.0	37.1	0.0321	1.669

The values of L and S are required to compute standard deviation scores (SDS) with the expression $SDS = [(y/M)^L - 1]/(L \times S)$, y being the value of the anthropometric trait and M the value of the 50th centile. BL = Birth crown-heel length; BW = birth weight; GA = gestational age; HC = head circumference. GA is approximated to the nearest week.

TABLE 3. Italian Neonatal Study charts: 3rd, 50th, and 97th centiles and S and L functions of BW, BL, and HC distribution in later-born neonates

	Girls															Boys														
GA	Weight					Length					Head circumference					Weight					Length					Head circumference				
wk	3rd	50th	97th	S	L	3rd	50th	97th	S	L	3rd	50th	97th	S	L	3rd	50th	97th	S	L	3rd	50th	97th	S	L	3rd	50th	97th	S	L
23	366	526	684	0.161	1.037	25.5	29.5	33.3	0.0701	1.326	18.5	20.9	23.3	0.0616	1.169	386	548	708	0.156	1.039	25.9	29.9	33.7	0.0689	1.338	18.9	21.3	23.7	0.0605	1.175
24	389	597	803	0.184	1.028	26.5	30.6	34.5	0.0691	1.339	19.2	21.7	24.2	0.0608	1.178	414	623	829	0.177	1.030	27.0	31.1	35.0	0.0679	1.351	19.6	22.1	24.6	0.0598	1.184
25	424	679	932	0.199	1.024	27.6	31.8	35.8	0.0680	1.356	20.0	22.6	25.1	0.0601	1.190	451	708	963	0.192	1.026	28.2	32.4	36.4	0.0668	1.368	20.4	23.0	25.5	0.0590	1.196
26	466	771	1073	0.209	1.022	28.8	33.1	37.2	0.0669	1.376	20.9	23.5	26.1	0.0592	1.206	498	804	1107	0.201	1.024	29.3	33.6	37.7	0.0657	1.390	21.3	23.9	26.5	0.0582	1.213
27	523	876	1226	0.213	1.021	30.0	34.4	38.6	0.0657	1.404	21.7	24.4	27.0	0.0582	1.229	558	914	1267	0.206	1.023	30.6	35.0	39.1	0.0645	1.418	22.1	24.8	27.4	0.0572	1.238
28	592	995	1394	0.214	1.022	31.3	35.8	40.0	0.0644	1.440	22.5	25.3	28.0	0.0572	1.263	634	1038	1439	0.206	1.024	31.9	36.3	40.5	0.0633	1.456	23.0	25.8	28.5	0.0562	1.272
29	677	1131	1580	0.212	1.024	32.6	37.1	41.4	0.0630	1.491	23.5	26.3	29.0	0.0560	1.310	724	1179	1629	0.204	1.025	33.2	37.7	42.0	0.0618	1.509	24.0	26.8	29.5	0.0550	1.322
30	779	1284	1784	0.208	1.027	34.0	38.6	42.9	0.0614	1.563	24.4	27.3	30.1	0.0546	1.378	832	1339	1840	0.200	1.029	34.6	39.2	43.5	0.0602	1.583	24.9	27.8	30.6	0.0536	1.392
31	899	1456	2006	0.202	1.033	35.3	40.0	44.3	0.0595	1.663	25.4	28.3	31.1	0.0530	1.475	961	1519	2070	0.194	1.035	36.0	40.7	45.0	0.0584	1.688	25.9	28.8	31.6	0.0520	1.492
32	1042	1650	2248	0.194	1.043	36.8	41.5	45.8	0.0574	1.804	26.3	29.2	31.9	0.0511	1.606	1110	1721	2322	0.187	1.046	37.4	42.1	46.4	0.0563	1.835	26.9	29.8	32.5	0.0502	1.629
33	1209	1866	2509	0.185	1.061	38.2	42.9	47.1	0.0549	1.998	27.3	30.2	32.9	0.0489	1.776	1283	1947	2596	0.179	1.066	38.9	43.6	47.8	0.0539	2.038	27.8	30.7	33.4	0.0480	1.806
34	1395	2103	2790	0.176	1.092	39.7	44.3	48.4	0.0521	2.255	28.3	31.1	33.7	0.0464	1.979	1484	2194	2882	0.169	1.099	40.4	45.0	49.1	0.0510	2.307	28.8	31.6	34.2	0.0455	2.020
35	1606	2356	3073	0.165	1.144	41.1	45.6	49.5	0.0489	2.574	29.1	31.9	34.4	0.0438	2.197	1702	2457	3177	0.159	1.155	41.9	46.4	50.3	0.0478	2.643	29.7	32.5	35.0	0.0428	2.249
36	1835	2615	3346	0.153	1.220	42.5	46.9	50.6	0.0454	2.935	29.9	32.6	35.0	0.0410	2.387	1944	2727	3459	0.147	1.238	43.2	47.6	51.3	0.0444	3.026	30.5	33.2	35.6	0.0401	2.452
37	2073	2864	3591	0.140	1.315	43.7	47.9	51.4	0.0419	3.286	30.7	33.2	35.5	0.0385	2.500	2190	2987	3716	0.135	1.342	44.5	48.7	52.1	0.0409	3.402	31.3	33.8	36.1	0.0375	2.575
38	2293	3084	3801	0.129	1.398	44.9	48.8	52.1	0.0386	3.545	31.3	33.7	35.9	0.0363	2.493	2429	3217	3928	0.123	1.435	45.7	49.6	52.8	0.0376	3.686	31.9	34.3	36.5	0.0354	2.573
39	2490	3261	3960	0.119	1.427	45.8	49.5	52.6	0.0358	3.629	31.7	34.0	36.1	0.0346	2.361	2630	3402	4099	0.114	1.470	46.7	50.3	53.3	0.0347	3.788	32.4	34.7	36.8	0.0337	2.439
40	2636	3390	4085	0.113	1.379	46.6	50.1	53.0	0.0336	3.493	32.1	34.3	36.4	0.0335	2.140	2790	3536	4221	0.107	1.421	47.5	50.9	53.8	0.0325	3.655	32.7	34.9	37.0	0.0325	2.208
41	2733	3476	4176	0.110	1.282	47.2	50.5	53.4	0.0320	3.164	32.3	34.5	36.6	0.0328	1.885	2891	3625	4314	0.104	1.314	48.1	51.3	54.1	0.0310	3.314	32.9	35.1	37.1	0.0319	1.940
42	2777	3529	4253	0.111	1.182	47.7	50.8	53.6	0.0311	2.730	32.4	34.6	36.7	0.0326	1.647	2938	3681	4395	0.105	1.203	48.5	51.6	54.4	0.0300	2.856	33.2	35.3	37.4	0.0316	1.688

The values of L and S are required to compute standard deviation scores (SDS) with the expression $SDS = [(y/M)^L - 1]/(L \times S)$, y being the value of the anthropometric trait and M the value of the 50th centile. BL = Birth crown-heel length; BW = birth weight; GA = gestational age; HC = head circumference. GA is approximated to the nearest week.

TABLE 4. Percentage of Italian Neonatal Study babies below the 10th centile of some recent European charts

Country (GA wk)*	23–31 wk	32–36 wk	37–42 wk
Weight			
Norway (23–42)	29.2	25.4	18.4
Sweden (24–40)	52.0	32.3	20.5
Scotland (24–43)	11.6	11.8	10.1
2007 France (25–42)	12.4	11.9	10.0
2008 France (28–42)	23.5	14.0	6.9
NW Italy (26–42)	15.3	11.7	4.6
Spain (24–42)	19.4	18.4	6.4
Length			
Sweden (24–40)	57.4	33.0	23.4
2007 France (25–42)	9.9	7.9	8.6
NW Italy (26–42)	19.7	14.2	7.0
Spain (24–42)	26.7	15.7	7.3
Head circumference			
Sweden (24–40)	30.2	18.8	20.7
NW Italy (26–42)	15.1	12.5	8.8
Spain (24–42)	22.5	25.7	19.2

GA = gestational age; NW = northwest.
*Range of GA considered in study.

origin born between 2005 and 2007, the only exclusion being stillbirths and major congenital anomalies. Twins have been excluded from the target population because they have a specific pattern of growth and need separate reference charts. For the same reason, the charts for firstborn and later-born neonates are presented separately.

Effect of Sex, Birth Order, and Geographical Area on Neonatal Size

The difference in birth weight between sexes and between birth orders increases with GA in absolute terms but is constant in relative terms. Boys are heavier than girls by about 4%; later-born are heavier than firstborn babies by about 3%. Only 6% of later-born neonates are below the 10th centile of the birth weight distribution of firstborns; thus, birth order should always be taken into account when neonatal charts are used to detect SGA. Literature reports the substantial invariance of the relative difference between sexes (22,23) and between birth orders (16,22). Differences in median weight ranging from 100 to 200 g between term babies born to primiparous and multiparous women are reported (23–26). The geographical area, which in Italy is associated with the size of children, adolescents, and young adults (14), does not seem to be related to neonatal size.

Methodological Heterogeneity

The INeS charts differ from the Italian and European charts published in the past decade in that they are based on data recorded in registries or on admission or discharge forms, without an ad hoc protocol (3–8,16–19), and were often carried out on regional basis. Stillbirths (3,16), twins (6,7), and, as for Italy, children of non-Italian parents are included (3,6,7). Cesarean sections are excluded (18,19); these deliveries were included in the INeS charts (which are a reference and not a standard) because they represent more than one third of all deliveries in Italy. The effect of birth order is considered only in Scottish charts (16); INeS data demonstrate that this effect is not negligible. The assessment of GA is not uniformly based on ultrasound scans (3,6,7,17,18); measuring techniques and instruments are described in only 2 studies (5,21): the reliability of a neonatal chart, which rests upon the accuracy of GA assessments and the quality of anthropometric measurements, cannot be evaluated when methods used to determine GA and neonatal size are not reported. GAs <26 (4,5) or >36 weeks are not considered (6): clinically useful charts should apply to preterm and term neonates and include also very low GAs because of the increasing number of severely preterm liveborn neonates. Some studies report only charts for birth weight (3,6–8,16,20) and are not suitable for a comprehensive evaluation of neonatal body proportions.

Detecting SGA

The methodological differences described above result in a large variability of the 10th centile (which is traditionally used to define SGA babies) among European neonatal charts, even when charts refer to the same country and time period (17,20). The 10th centile of the INeS charts for BW is lower than the 10th centile of Swedish (19) (by 250 g) and Norwegian (18) (by 150 g) charts at 28 weeks of gestation and by about 200 g at 40 weeks. The difference between the 10th centile of Swedish and INeS charts decreases from 5 cm (at 28 weeks) to 3 cm (at 40 weeks) as for BL, whereas it is about 1 cm for HC at each GA. This determines huge differences in the percentage of INeS neonates below the 10th centile of the other European charts (Table 4). The exclusion of babies delivered by cesarean section (Sweden and Norway) and born to women with diseases such as urinary infections, kidney diseases, epilepsy, asthma, ulcerative colitis, systemic lupus erythematosus had a likely role in determining such a wide difference. The differences between charts decrease consistently with increasing GA, likely because the criteria used to define the reference populations act mainly at low GA, where the prevalence of fetal growth restriction among neonates is higher (27).

TABLE 5. Temporal trends (g/y) of birth weight distribution in 3 European countries

Country	Lower centile*		Median		Higher centile†	
	Preterm‡	Term§	Preterm‡	Term§	Preterm‡	Term§
Sweden (19,29) (1991–1999 vs 1977–1981)	+21.0	+10.5	+11.5	+5.5	+2.0	+6.0
France (17,28) (2002–2005 vs 1984–1988)	+5.5	+5.0	−2.0	+3.5	−14.5	+0.5
Italy (5) (2005–2007 vs 1982–1997)	+0.5	+10.0	−4.0	+4.5	−9.5	−4.0

*3rd (Italy and Sweden) or 5th (France) centile.
†97th (Italy and Sweden) or 95th (France) centile.
‡36 weeks or less.
§37 weeks or more.

Temporal Trends

Prominent changes in the distribution of birth weight emerged in Europe in the last 2 decades in both term and preterm neonates. As for term neonates (≥37 weeks), the median increase of 4.5 g/y observed in Italy between 1982 to 1997 (5) and 2005 to 2007 (Table 5) is in good agreement with findings reported in other European countries (17,19,28,29). A positive temporal trend in birth weight has also been reported for Scotland (16) and Norway (18). The increase in median birth weight values is likely due to the enhancement of maternal care before and during pregnancy (30). An even larger increase in lower centiles (1.5–2 times the median increase) was observed in Italy as well as in the other countries examined here. The larger increase in lower centiles may also reflect the present trend in obstetrical care to bring forward the delivery date in the presence of fetal growth restriction and the consequent decrease in the prevalence of small babies at term (18,31). The 97th centile of Italian charts decreased by 4 g/y. By contrast, an increase in higher centiles is reported in Sweden (19,29), France (17,28), and Scotland (16). We have no explanation for these differences. A number of epidemiological studies suggest that both high and low birth weights are associated with a higher risk of overweight in childhood and adult life (32). If it were so, we could expect that the narrowing of birth weight distribution observed in Italy would result in lower prevalence of obesity in later life. The extent of positive temporal trend of median and lower centiles of birth weight distribution in Italy lessens with decreasing GA and vanishes at 37 weeks.

As for preterm babies (≤36 weeks) a negative trend of 4 g/y in median birth weight and 9.5 g/y in the 97th centile occurred in Italy. An analogous trend is reported in France (17) and, for the 97th centile only, in Scotland (16). This decrease at lower GA reflects the higher prevalence of small babies among liveborn preterm neonates, as a consequence of the increasing occurrence of induced deliveries in case of poor fetal growth. The decrease in the 97th centile is larger than that in the median; this is ascribable to the decrement of cases with severely underestimated GA, which affects mainly the higher centiles. Surprisingly, by comparison of data reported by Niklasson et al in 1991 (29) and Niklasson and Albertsson in 2008 (19), a positive trend emerges for the whole birth weight distribution in Swedish preterm neonates; this is likely due to the exclusion of cesarean sections from the latter cohort but not from the former.

CONCLUSIONS

The INeS charts are an updated national reference having the properties that a chart should be of both epidemiologic and clinical use (9). They allow for sex and birth order and apply to all single-born neonates with GA between 23 and 42 weeks of gestation. Last and most important, the INeS charts are summarized through the LMS parametrization that enables the user to express anthropometric traits as SDS, even in the case of skewed distribution. This parametrization, which at present is the most common form to represent cross-sectional growth charts for children and adolescents, is expected to become in the future increasingly used in the neonatal field, thus extending this flexible method to this branch of auxology.

The differences observed with other European charts are partly due to methodological discrepancies, but a role of differences among populations, such as diet, environment, and prevalence of risk factors, cannot be excluded. Therefore, caution should be used against the extension of any national chart to other countries. Until an international standard is developed, we would recommend the use of updated national reference charts constructed according to an accurate methodology.

APPENDIX 1

The raw centiles conditional on GA (t), sex (females: $x_g = 0$, males: $x_g = 1$) and birth order (firstborn neonates: $x_p = 0$, later-born neonates $x_p = 1$) were fitted with the following EMGF:

$$E(y(t, z, x_g, x_p)) = \gamma_0 z(t - \tau_0)(t > \tau_0) + \frac{\kappa(1 + \gamma_1 z)(1 + \vartheta_g x_g + \vartheta_p x_p)}{\left[1 + \alpha \exp\left(-\frac{4\beta}{\kappa}(t - \tau_1 - \tau_2 z)\right)\right]^{1/\alpha}} \quad (2)$$

where $E(y(t, z, x_g, x_p))$ is the expected value of the centile whose normal deviate is z (eg, the z of the 10th centile of normal distribution is −1.28). The generalized logistic function that models the median includes 6 constants: κ (upper asymptote), τ_1 (GA at the occurrence of maximum median increase), β (the median increase at GA = τ_1), α (the constant that controls the symmetry of the curve with respect to τ_1), ϑ_g (effect of sex), and ϑ_p (effect of birth order). The extraconstants γ_0, γ_1, and τ_0 control the distance between centiles modeling skewness, whereas τ_2 allows each centile to have its own inflection point. Therefore, the median curves for sex and birth order differ only for a multiplicative constant, whereas the distance between centiles is determined by both an additive and a multiplicative constant. Least-squares estimates of the smooth centiles were obtained with Marquardt algorithm, resorting to SAS PROC NLIN version 9.1.3 (SAS Institute, Cary, NC). The same procedure was used to derive the values of L and S from the values of the 9 centiles (3rd, 5th, 10th, 25th, 50th, 75th, 90th, 95th, 97th) predicted by the EMGF model: the differences between the centiles computed from the L and S values thus obtained and those directly predicted by the EMGF model were negligible, the higher percent differences regarding the 25th and 75th centiles and being always lower than 0.10% (BW), 0.05% (BL) and 0.03% (HC).

With the aim of comparing the EMGF model with the CG-LMS model (15), regarded as a criterion standard, the latter was used to fit INeS data. According to the criteria suggested in the LMS program, for each sex and birth order a model with 4 (L), 9 (M), and 7 (S) equivalent degrees of freedom was found to fit birth weight satisfactorily.

Figure A compares EMGF with CG-LMS birth weight charts (left) and the corresponding L and S functions (right), as regards firstborn boys. The 2 models largely differ in the shape of the L function and only slightly in the location of the peak value of the S function. Nonetheless, the EMGF and CG-LMS centiles generally overlap, the largest differences occurring before the 26th week (median and higher centiles), after the 39th week (extreme centiles), and from the 39th to 41st week (median). Table A shows the percentage of severely preterm, preterm, and term INeS babies classified as SGA, appropriate for GA, and large for GA on the basis of the centiles computed with the EMGF and CG-LMS models. In most of the cases the observed percentages are similar to those expected, and the CG-LMS models, which required 20 equivalent degrees of freedom for each sex and birth order, do not appear to fit BW distribution better than the EMGF model, which required the estimate of only 10 parameters.

APPENDIX 2: PARTICIPATING HOSPITALS

- Cattedra di Neonatologia, Università di Torino—Azienda Sanitaria Ospedaliera OIRM—S.Anna: Bertino E, Occhi L
- Neonatologia ASL TO2, Ospedale Maria Vittoria Torino: Caroni G; Savant Levet P

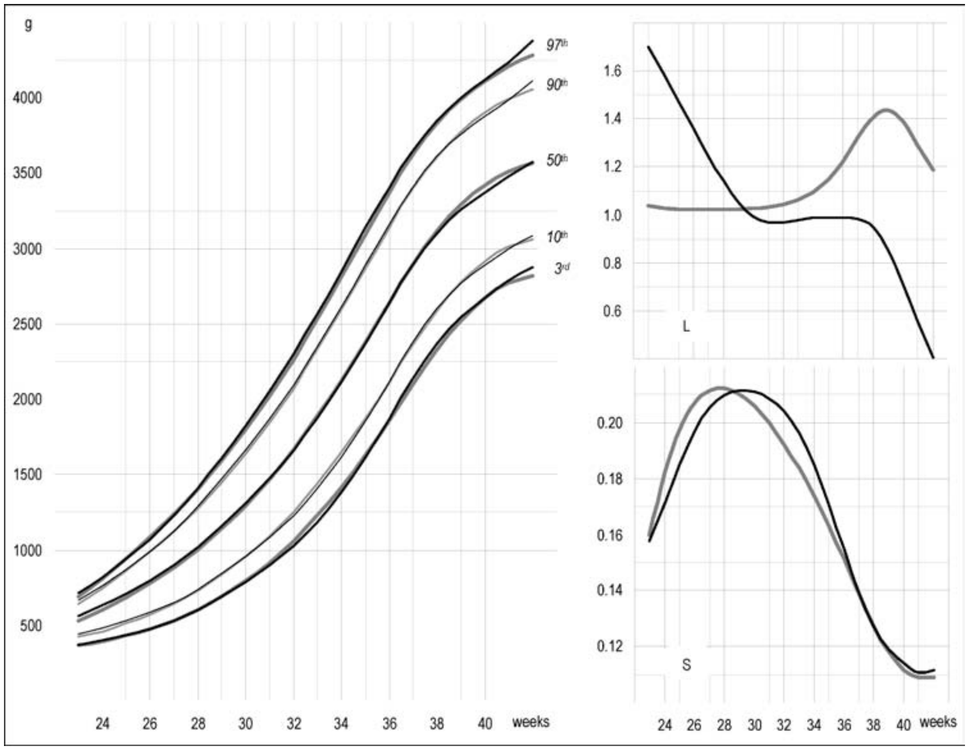

FIGURE A. Comparison between extended mechanistic growth function and CG-LMS birth weight charts, as regards firstborn boys. On the right the corresponding L (skewness) and S (coefficient of variation) functions are shown.

TABLE A. Percentage of severely preterm, preterm, and term Italian Neonatal Study babies classified as small for gestational age, appropriate for gestational age, and large for gestational age on the basis of the centiles computed with the EMGF and CG-LMS models

	Girls				Boys			
	23–31 wk	32–36 wk	37–42 wk	All	23–31 wk	32–36 wk	37–42 wk	All
Firstborn neonates								
LGA								
EMGF	7.2	10.6	8.9	9.0	12.8	9.8	10.0	10.1
CG-LMS	9.2	9.2	10.2	10.1	10.4	8.6	10.3	10.1
AGA								
EMGF	80.0	77.9	82.3	81.9	77.5	78.4	80.6	80.3
CG-LMS	81.3	79.9	80.9	80.8	79.9	79.8	81.0	80.9
SGA								
EMGF	12.8	11.5	8.8	9.1	9.7	11.8	9.4	9.6
CG-LMS	9.5	10.9	8.9	9.1	9.7	11.6	8.7	9.0
Later-born neonates								
LGA								
EMGF	10.5	9.9	8.8	8.9	9.7	10.0	9.7	9.7
CG-LMS	9.5	9.4	10.1	10.0	10.6	9.1	10.1	10.0
AGA								
EMGF	81.0	79.8	82.4	82.2	79.7	81.0	79.8	79.9
CG-LMS	80.0	79.5	81.2	81.1	76.0	81.3	80.9	80.7
SGA								
EMGF	8.5	10.3	8.8	8.9	10.6	9.0	10.5	10.4
CG-LMS	10.5	11.1	8.7	8.9	13.4	9.6	9.2	9.3

The expected percentage of small for gestational age and large for gestational age neonates in a reference population is 10%. EMGF = extended mechanistic growth function.

– Struttura Complessa Neonatologia Ospedaliera S. Anna Torino: Leonessa M, Farina D
– Sezione Neonatale SOC di Pediatria Ospedale ''Cardinal Massaia'' di Asti: Savina C, Debenedetti E
– ASL To5 Regione Piemonte, Ospedale S. Croce di Moncalieri; SC di Pediatria e Neonatologia, SS di Neonatologia-TIN: de Vonderweid U; Marra A
– Clinica Pediatrica di Novara, Università del Piemonte Orientale ''A. Avogadro,'' Novara: Bona G, Zaffaroni M
– Presidio Ospedaliero Macedonio Melloni. S.C. di Neonatologia—Patologia Neonatale—Terapia Intensiva Neonatale, Milano: Arslanoglu S. Moro GE
– Istituto di Pediatria e Neonatologia, Fondazione IRCCS Ospedale Maggiore Policlinico Mangiagalli e Regina Elena Università di Milano: Mosca F, Roggero P
– Reparto di Terapia Intensiva Neonatale e Neonatologia Ospedale di Rho—Milano: Coppa I, Micanti M
– Patologia Neonatale e Terapia Intensiva Neonatale Ospedale Manzoni di Lecco: De Poli S, Bellù R
– Ospedali Riuniti di Bergamo, Azienda Ospedaliera: Rossi F, Mangili G
– UO Patologia Neonatale e Terapia Intensiva. IRCCS Policlinico San Matteo. Pavia: Bozzola E, Ferrari G
– Ospedale di Trento—Presidio Ospedaliero S. Chiara UO di Neonatologia—Terapia Intensiva Neonatale: De Nisi G, Franco E
– Azienda Ospedaliero-Universitaria ''Santa Maria della Misericordia'' Udine; Struttura Operativa Complessa ''Neonatologia'' del Dipartimento Materno-Infantile: Da Riol R, Furlan R
– UC di Neonatologia e Terapia Intensiva Neonatale. IRCCS Burlo Garofolo. Trieste: Forleo V, Demarini S
– Terapia Intensiva Neonatale e Neonatologia, Università degli Studi di Ferrara: Vigi V, Fanaro S
– AUSL Cesena Ospedale M. Bufalini, Cesena (FC): Mariani S, Biasini A
– Neonatologia e Terapia Intensiva Neonatale, Ospedale Maggiore, Bologna: Sandri F, Alati S
– UO di Pediatria e Neonatologia, Ospedale Versilia, USL 12 Viareggio: Gagliardi L; Merusi I
– UO Neonatologia e Terapia Intensiva Neonatale, Dipartimento di Medicina della Procreazione e dell'Età Evolutiva. Azienda Ospedaliero-Universitaria Pisana: Ghirri P, Bartoli A
– Fatebenefratelli Ospedale San Pietro. Dipartimento Materno-Infantile. UOC Terapia Intensiva Neonatale e Patologia Neonatale, Roma: Finocchi M, Pacella M
– Dipartimento di Scienze Ginecologiche, Perinatologia e Puericultura. Università ''La Sapienza''—Roma: Lucchini R, Marciano A
– UOC di Neonatologia—Università Cattolica del Sacro Cuore—Roma: Romagnoli C, Maggio L
– Neonatologia Ospedale Santa Maria del Popolo degli Incurabili ASL NA1, Napoli: Saporito M, Esposito L
– Ospedale Buon Consiglio Fatebenefratelli, Napoli: Salvia G, Fonterico V
– Ospedale Sacro Cuore di Gesù—Fatebenefratelli, Benevento: Vetrano G, Rabuano R
– ''Ospedali Riuniti''—Azienda Ospedaliero-Universitaria di Foggia. SC di Neonatologia e Terapia Intensiva: Di Gianni AM, Cella AVP
– UO Pediatria e TIN Dipartimento Materno Infantile, Università di Palermo: Corsello G, Piro E
– Casa di Cura Candela SpA, Palermo: Cinquegrani MR, Birriolo Piazza E
– UOC Neonatologia-TIN AO S. Antonio Abate di Trapani: Galia A, Porsio A
– Terapia Intensiva Neonatale, Puericultura e Nido. Università degli Studi di Cagliari: Fanos V, Costa L
– Azienda Ospedaliera-Universitaria ''G. Martino'' Patologia neonatale e TIN, Messina: Arco A, Pagano G
– Terapia Intensiva Neonatale—Neonatologia ASO S. Croce e Carle, Cuneo: Gancia P, Bellagamba O
– IRCCS Giannina Gaslini, Genova: Traggiai C, Di Battista E

REFERENCES

1. Bertino E, Giuliani F, Occhi L, et al. Benchmarking neonatal anthropometric charts published in the last decade. *Arch Dis Child Fetal Neonatal Ed* 2009;94:F233.
2. Karlberg J, Cheung YB, Luo ZC. An update on the update of growth charts. *Acta Paediatr* 1999;88:797–802.
3. Parazzini F, Cortinovis I, Bortolus R, et al. Birth weight of infants born between the 23rd and 42nd gestational week in Italy. *Pediatr Med Chir* 1998;20:93–7.
4. Gagliardi L, Macagno F, Pedrotti D, et al. Weight, length, and head circumference at birth of a North-eastern Italian population. Report of the ad hoc committee of the Italian Society of Neonatology. *Riv Ital Pediatr* 1999;25:159–69.
5. Bertino E, Murru P, Bagna R, et al. Anthropometric neonatal standards based on a north-west Italian population. *Riv Ital Pediatr* 1999; 25:899–906.
6. Vergara G, Carpentieri M, Colavita C. Birthweight centiles in preterm infants. A new approach. *Minerva Pediatr* 2002;54:221–5.
7. Festini F, Procopio E, Taccetti G, et al. Birth weight for gestational age centiles for Italian neonates. *J Matern Fetal Neonatal Med* 2004; 15:411–7.
8. Polo A, Pezzotti P, Spinelli A, et al. Comparison of two methods for constructing birth weight charts in an Italian region: years 2000–2003. *Epidemiol Prev* 2007;31:261–9.
9. Bertino E, Milani S, Fabris C, et al. Neonatal anthropometric charts: what they are, what they are not. *Arch Dis Child Fetal Neonatal* 2007;92:F7–10.
10. Nati vivi legittimi e naturali per sesso e regione, 2007. Istituto Nazionale di Statistica (ISTAT). Rome: Annuario Statistico Italiano; 2008.
11. Avere un figlio in Italia, 2002. Rome: Istituto Nazionale di Statistica (ISTAT), 2006.
12. Cameron N. Measuring techniques and instruments. In: Nicoletti I, Benso L, Gilli G, eds. *Physiological and Pathological Auxology.* Firenze: Edizioni Centro Studi Auxologici; 2004:117–159.
13. Healy MJR, Rasbash J, Yang M. Distribution-free estimation of age related centiles. *Ann Hum Biol* 1988;15:17–22.
14. Cacciari E, Milani S, Balsamo A, et al. Italian cross-sectional growth charts for height, weight and BMI (2 to 20 yr). *J Endocrinol Invest* 2006;29:581–93.
15. Cole TJ, Green PJ. Smoothing reference centile curves: the LMS method and penalized likelihood. *Stat Med* 1992;11:1305–19.
16. Bonellie S, Chalmers J, Gray R, et al. Centile charts for birthweight for gestational age for Scottish singleton births. *BMC Pregnancy Childbirth* 2008;8:5.
17. Salomon LJ, Bernard JP, de Stavola B, et al. Birth weight and size: charts and equations. *J Gynecol Obstet Biol Reprod (Paris)* 2007;36:50–6.
18. Skjaerven R, Gjessing HK, Bakketeig LS. Birthweight by gestational age in Norway. *Acta Obstet Gynecol Scand* 2000;79:440–9.
19. Niklasson A, Albertsson-Wikland K. Continuous growth reference from 24th week of gestation to 24 months by gender. *BMC Pediatr* 2008;8:8.
20. Rousseau T, Ferdynus C, Quantin C, et al. Liveborn birth-weight of single and uncomplicated pregnancies between 28 and 42 weeks of gestation from Burgundy perinatal network. *J Gynecol Obstet Biol Reprod (Paris)* 2008;37:589–96.

21. Carrascosa A, Yeste D, Copil A, et al. Anthropometric growth patterns of preterm and full-term newborns (24-42 weeks' gestational age) at the Hospital Materno-Infantil Vall d'Hebron (Barcelona) (1997–2002). *An Pediatr (Barc)* 2004;60:406–16.
22. Tin W, Wariyar UK, Hey EN. Selection biases invalidate current low birthweight weight-for-gestation standards. The Northern Neonatal Network. *Br J Obstet Gynaecol* 1997;104:180–5.
23. Hemming K, Hutton JL, Glinianaia SV, et al. Differences between European birthweight standards: impact on classification of ''small for gestational age.'' *Dev Med Child Neurol* 2006;48:906–12.
24. Ong KK, Preece MA, Emmett PM, et al. Size at birth and early childhood growth in relation to maternal smoking, parity and infant breast-feeding: longitudinal birth cohort study and analysis. *Pediatr Res* 2002;52:863–7.
25. Oken E, Kleinman KP, Rich-Edwards J, et al. A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatr* 2003;3:6.
26. Ogunyemi D, Manigat-Wilson B, Bazargan M, et al. Birth weight for gestational age patterns by ethnicity, gender, and parity in an urban population. *South Med J* 2007;100:615–6.
27. Zaw W, Gagnon R, da Silva O. The risks of adverse neonatal outcome among preterm small for gestational age infants according to neonatal versus fetal growth standards. *Pediatrics* 2003;111: 1273–7.
28. Mamelle N, Munoz F, Grandjean H. Fetal growth from the AUDIPOG study. I. Establishment of reference curves. *J Gynecol Obstet Biol Reprod (Paris)* 1996;25:61–70.
29. Niklasson A, Ericson A, Fryer JG, et al. An update of the Swedish reference standards for weight, length and head circumference at birth for given gestational age (1977–1981). *Acta Paediatr Scand* 1991; 80:756–62.
30. Ehrenkranz RA. Estimated fetal weights versus birth weights: should the reference intrauterine growth curves based on birth weights be retired? *Arch Dis Child Fetal Neonatal Ed* 2007;92:F161–2.
31. Kramer MS. Maternal nutrition and adverse pregnancy outcomes: lessons from epidemiology. *Nestle Nutr Workshop Ser Pediatr Program* 2005;55:1–10.
32. Simmons R. Perinatal programming of obesity. *Semin Perinatol* 2008;32:371–4.