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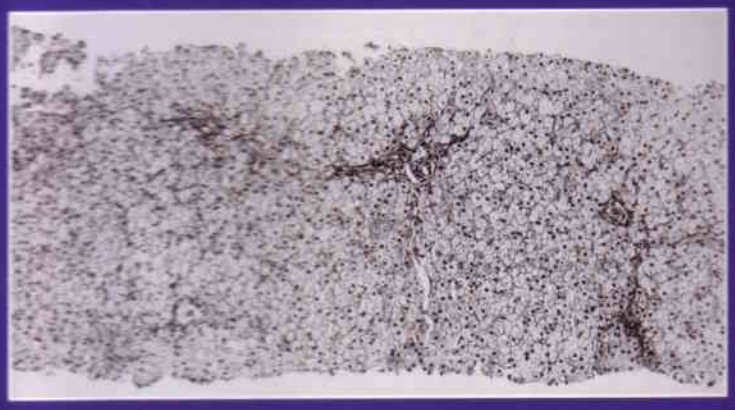

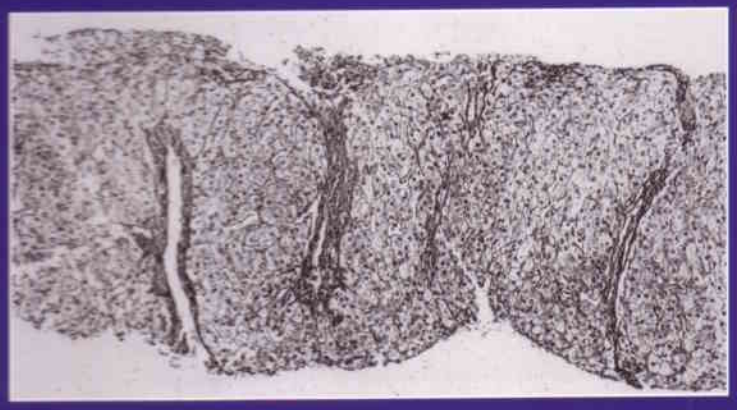

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Organ Weights in Human Fetuses after Formalin Fixation: Standards by Gestational Age and Body Weight

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ABSTRACT

This study provides new standards of fetal organ weights (brain, heart, liver, pancreas, spleen, lungs, kidneys, adrenals, thymus, and thyroid) and body dimensions (crown–heel and crown–rump lengths, head circumference, and foot length). Subjects came from a large dataset including more than 4000 fetuses autopsied in fetopathology units of pediatric hospitals in Paris between 1986 and 2001. From this dataset, 673 subjects were carefully selected by exclusion of multiple pregnancies, macerated and malformed fetuses, subjects with abnormal karyotypes, and those with severe infections. Fetal age ranged from 9 to 42 gestational weeks, with a very large sample of fetuses in the first half of gestation. Each organ was weighed after fixation in formalin. The standards were computed in relation to age and body weight. The mathematical models used to fit the percentile growth curves were carefully selected for each organ or dimension. This study, based on reliable methodology, affords a whole set of accurate growth standards useful for pathologists.

Key words: fetal biometry, fetal growth, formalin fixation, growth standards, human, organ weights

INTRODUCTION

Accurate standards of viscera growth are indispensable to define the exact pathology of autopsied fetuses. Previous studies have provided weight standards for various fetal organs. Most standards are old and concern only fetuses in the viable age range [1–7]. Some studies deal with smaller fetuses, weighing less than 1500 g [8–10]. Only one study [11] has given standards of organ weights for the whole gestational period (50–4000 g fetuses). In all these papers, weights of organs are recorded in tables and/or gathered in charts or growth curves. Nevertheless, the information base is dispersed from one paper to another: none of these studies has given complete standards, including tables and charts, for each organ in relation to age and body weight, for the whole gestational period. Most of these studies were based on cohorts whose gestational age was estimated from the duration of maternal amenorrhea, and do not benefit from progress achieved with the widespread use of early ultrasound definition of gestational age. Furthermore, published standards concern fresh organ weights, in conformity with pathology practice in numerous countries (especially in North America), whereas other places (mainly in Europe) use fixed organ weights.

Therefore, the aim of the present study is to provide accurate weight standards of the main organs, after formalin fixation, set out in a practical way for the pathologist. Our goal was to report weight standards by age interval and body weight interval for each organ studied (brain, heart, liver,

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pancreas, spleen, right and left lungs, right and left kidneys, right and left adrenals, thymus, and thyroid) in user-friendly tables and corresponding percentile charts.

METHODS

Selection of the sample

Subjects came from a large dataset including more than 4000 fetuses autopsied in fetopathologic units of pediatric hospitals in Paris between 1986 and 2001. From these data, 673 subjects were carefully selected according to several criteria. We excluded the following:

- Multiple pregnancies
- Macerated fetuses
- Fetuses with any malformation or macroscopic dysruptive lesion (except minor malformations, e.g., polydactyly, single umbilical artery, or Meckel diverticulum)
- Fetuses with chromosomal abnormalities
- Fetuses from diabetic mothers
- Fetuses with severe septicemia, toxoplasmosis, listeriosis, or cytomegalic inclusion disease, since it is well known that such diseases have a major effect on fetal growth and organ structure.

However, subjects with minor pulmonary infections related to recent chorioamnionitis were retained in the study.

To assess the impact of such infections on growth, the organ weights of both infected (defined by the presence of at least some polymorphonuclear cells in the pulmonary tree), and noninfected fetuses were plotted on the same diagrams in relation to age: only the adrenals exhibited a visible shift of the data in second-trimester infected fetuses. Nevertheless, statistically significant differences in mean weights were also found for other organs, mainly the spleen between 17 and 26 gestational weeks (GW), the lungs between 19 and 26 GW, and the pancreas between 21 and 34 GW (Mann-Whitney U test).

Although inflammatory processes induced by infections might lead to a weight increase of several organs (mainly the lungs, the spleen, and the adrenals), we chose to include these fetuses since they constitute more than one-third of our cohort of normal fetuses. Such fetuses may be considered a common component of an autopsied population of fetuses, and must be included for the calculation of growth standards.

Cytogenetic studies were performed at autopsy, when phenotypic abnormalities were visible, or as part of the routine program of trisomy 21 screening. Among the 673 subjects selected according to the other criteria, 10% have been karyotyped, and are undoubtedly free from any chromosomal abnormality. Concerning the other fetuses, the rigorous selection and obstetrical content of the sample (high level of maternal infectious pathologies) let us assume a high probability of normal karyotypes.

The age of each subject was calculated in weeks from the beginning of the last menstrual period (gestational weeks [GW]), fine-tuned or corrected by the first-trimester ultrasound crown–rump length measurement and confirmed at autopsy by the estimation of organ maturation [12]. When there was a discrepancy of more than 2 weeks between the two estimations of fetal age, the subject was excluded from the study. Fetal age ranged from 9 to 42 GW, with a prevalence of fetuses in the first half of gestation. The distribution of subjects by organ and age interval is reported in Table 1.

Data record and statistical processing

Fetal examinations and measurements were all performed by one medical team (F.M., A.L.D.), according to the same procedure. Visceral dissection was undertaken in two steps: "monoblock" evisceration was performed as soon as the fetus arrived in the laboratory and the viscera were immersed in 4% formalin for 24 to 48 h. In case of spontaneous abortion, a small piece of right lung (< 1 g) was cut off for bacteriological analysis. Organs were then dissected and weighed. The brain, heart, liver, pancreas, spleen, right and left lungs, right and left kidneys, right and left adrenals, thymus, and thyroid were weighed with a precision of 1 dg, the body weight with a precision of 1 g.

To provide a whole set of biometric standards for fetopathologists, the main linear dimensions of the fetus (crown–heel length, crown–rump length, head circumference and foot length) were also recorded.

Table 1. Sample size for each organ by age interval (GW)

GW	Body weight	Adrenal (R)	Adrenal (L)	Brain	Heart	Kidney (R)	Kidney (L)	Liver	Lung (R)	Lung (L)	Pancreas	Spleen	Thymus	Thyroid
9–10	1	0	0	0	0	0	0	0	0	0	0	0	0	0
11–12	6	0	0	0	2	0	0	2	2	2	1	0	0	0
13–14	20	18	16	16	18	19	19	19	19	20	14	11	11	2
15–16	60	61	61	52	59	60	60	59	59	60	58	50	51	19
17–18	81	80	81	77	78	82	79	80	82	83	81	76	73	46
19–20	79	78	78	74	77	78	79	77	77	78	76	74	74	52
21–22	113	111	111	107	110	109	110	109	111	111	109	108	111	80
23–24	109	109	109	100	105	109	107	107	107	106	107	104	106	86
25–26	58	57	58	56	56	58	58	56	56	57	58	58	58	48
27–28	24	25	25	22	25	23	24	25	25	25	24	25	25	21
29–30	11	11	11	11	11	10	10	11	11	10	9	11	10	6
31–32	12	12	12	11	11	12	12	12	12	12	12	12	11	6
33–34	10	10	10	8	10	10	10	9	10	10	9	10	10	7
35–36	10	10	10	9	9	10	10	10	10	10	10	10	10	8
37–38	18	18	18	17	18	18	18	17	18	18	16	18	17	12
39–40	35	33	33	33	32	33	33	33	33	33	33	32	33	26
41–42	14	13	13	12	14	14	14	14	14	14	14	13	14	12
Total	661	646	646	605	635	645	643	640	646	649	631	612	614	431

GW, gestational weeks; R, right; L, left.

The subjects were grouped in intervals of 2 weeks and in intervals of 200 g of body weight. Considering the small sample size in some intervals, we did not calculate distinct standards for males and females.

The large inequality of sample size from one interval to another complicated the calculation of the standards. The mean value was rather stable, regardless of the sample size, but the parameters of dispersion of the distribution (as percentiles) were very dependent on the sample size.

To avoid this problem, we did not compute directly the percentiles in each age (or body weight) interval, but we partially applied the parametric method recommended by Altman and Chitty [13]. Mean organ weights were computed by age interval and body weight interval. The mean growth curves in relation to age and body weight were then smoothed by fitting mathematical models. The choice of the adequate mathematical model was based partly on its statistical significance (high coefficient of determination r^2), and partly on the visual appreciation of the goodness of fit. Linear and polynomial regression models (degrees 2 to 5), as well as a power model were tested and selected for each organ according to the guidelines defined above.

The same process was applied to the values of the standard deviation (SD) calculated by age and body weight interval. The SD curves in relation to age or body weight were smoothed by fitting regression or power models.

Generally, the degrees of the polynomials fitting the standard deviation curves were lower than those fitting the mean curves. Power fitting was only satisfactory for spleen, thymus, and thyroid organs.

Assuming that the distribution of data in each interval was normal, the 5th and 95th percentiles of the distributions were calculated as follows:

- 5th centile = fitted mean − 1.645 fitted SD
- 95th centile = fitted mean + 1.645 fitted SD
- the value of 1.645 coming from the theoretical normal distribution.

RESULTS

The mean, SD, 5th and 95th percentiles of each organ by age interval are given in Table 2, and by body weight interval in Table 3. The growth standards of body dimensions by age interval are given in Table 4. We have also provided the charts for the right lung (Figs. 7 and 17), despite the underestimation of weight due to bacteriological sampling.

The corresponding charts of growth of each organ in relation to gestational age are shown in Figures 1–11, and in relation to body weight in Figures 12–21. The charts of body dimensions are given in Figures 22–25.

DISCUSSION

The most debated question about the reliability of fetal growth standards concerns the definition of the reference population. The subjects used for computing growth standards are implicitly considered "normal" or "healthy" and "representative" of a large population. If studied cohorts concern autopsied subjects, the question of "normality" is irrelevant. The sample should be built by selection of subjects with the least pathology possible, by exclusion of fetuses on several criteria. However, there is no general agreement about these criteria of exclusion, so that the composition of the samples used to compute growth standards is often different from one study to another. Generally, multiple births, macerated fetuses, and infants surviving more than 3 days are excluded. Exclusion of other pathologies is inconstant in the literature. In most studies [1,3,4,8–11], important malformations are excluded, but the limits are differently defined from one paper to another. For example, in the study of Schulz et al. [7], only the malformed organ(s) is (are) left out of the standards; the other organs of the same fetus are included. Other criteria of exclusion, e.g., abnormal karyotypes, maternal diabetes, congenital infections (rubella, listeriosis, etc.), are considered diversely from one study to another. In the present work, numerous criteria of exclusion based on macroscopic or histological examinations were applied. Therefore, the subsequent sample looks almost like a sample of "normal" fetuses.

In spite of quite strict criteria of selection, we were able to gather a large dataset, particularly before 16 GW. Such standards of growth for early gestation are rare in the literature. However, they are of great interest: today, prenatal diagnosis of

Table 2. Mean, standard deviation, and 5th and 95th percentiles of organ weight in relation to gestational age

Age interval (GW)	Mean	SD	5th percentile	95th percentile
Body weight				
11–12	9.1	7.9	−3.8	22.0
13–14	55.8	14.4	32.2	79.4
15–16	108.6	24.7	68.0	149.3
17–18	176.1	39.0	112.0	240.3
19–20	267.7	57.1	173.7	361.7
21–22	392.7	79.2	262.5	522.9
23–24	559.6	105.1	386.7	732.5
25–26	773.9	134.9	552.0	995.8
27–28	1038.2	168.6	760.9	1315.5
29–30	1350.4	206.1	1011.3	1689.5
31–32	1702.5	247.6	1295.2	2109.7
33–34	2080.2	292.9	1598.3	2562.0
35–36	2460.8	342.1	1898.0	3023.7
37–38	2813.1	395.3	2162.9	3463.3
39–40	3095.1	452.2	2351.2	3839.1
41–42	3254.9	513.1	2410.9	4099.0
Brain				
13–14	9.09	2.49	5.00	13.18
15–16	18.98	4.60	11.42	26.54
17–18	31.37	7.11	19.67	43.06
19–20	47.93	10.03	31.43	64.43
21–22	69.90	13.35	47.93	91.87
23–24	97.98	17.08	69.88	126.08
25–26	132.43	21.21	97.53	167.33
27–28	172.98	25.75	130.62	215.34
29–30	218.89	30.69	168.41	269.38
31–32	268.95	36.04	209.67	328.23
33–34	321.43	41.79	252.69	390.17
35–36	374.13	47.94	295.27	453.00
37–38	424.37	54.50	334.72	514.02
39–40	468.96	61.46	367.85	570.07
41–42	504.23	68.83	391.01	617.46
Heart				
13–14	0.24	0.13	0.02	0.46
15–16	0.82	0.23	0.45	1.20
17–18	1.44	0.37	0.83	2.05
19–20	2.21	0.56	1.29	3.12
21–22	3.23	0.79	1.93	4.52
23–24	4.55	1.07	2.79	6.30
25–26	6.21	1.39	3.92	8.49
27–28	8.20	1.76	5.31	11.09
29–30	10.48	2.17	6.90	14.05
31–32	12.98	2.63	8.65	17.31
33–34	15.60	3.14	10.44	20.76

(*continued*)

Table 2. (*Continued*)

Age interval (GW)	Mean	SD	5th percentile	95th percentile
35–36	18.21	3.69	**12.15**	24.27
37–38	20.63	4.28	**13.59**	27.67
39–40	22.68	4.92	**14.58**	30.77
41–42	24.49	5.58	**15.31**	33.67
Liver				
13–14	3.09	0.27	**2.64**	3.54
15–16	5.81	1.71	**3.00**	8.62
17–18	9.39	3.33	**3.91**	14.87
19–20	14.33	5.15	**5.87**	22.80
21–22	21.00	7.15	**9.23**	32.77
23–24	29.63	9.35	**14.24**	45.02
25–26	40.27	11.75	**20.95**	59.60
27–28	52.89	14.33	**29.32**	76.46
29–30	67.29	17.10	**39.15**	95.42
31–32	83.10	20.07	**50.09**	116.12
33–34	99.87	23.23	**61.67**	138.08
35–36	116.97	26.58	**73.25**	160.69
37–38	133.64	30.12	**84.10**	183.18
39–40	148.97	33.85	**93.29**	204.66
41–42	161.94	37.78	**99.80**	224.08
Pancreas				
13–14	0.09	0.01	**0.08**	0.11
15–16	0.28	0.08	**0.15**	0.41
17–18	0.42	0.16	**0.16**	0.68
19–20	0.57	0.24	**0.17**	0.98
21–22	0.78	0.34	**0.22**	1.35
23–24	1.08	0.45	**0.33**	1.82
25–26	1.47	0.57	**0.54**	2.41
27–28	1.98	0.70	**0.83**	3.13
29–30	2.58	0.84	**1.21**	3.96
31–32	3.26	0.98	**1.64**	4.87
33–34	3.97	1.14	**2.09**	5.84
35–36	4.66	1.31	**2.50**	6.81
37–38	5.26	1.49	**2.82**	7.71
39–40	5.71	1.67	**2.96**	8.46
41–42	5.90	1.87	**2.82**	8.97
Spleen				
13–14	0.06	0.04	**−0.01**	0.14
15–16	0.12	0.08	**−0.00**	0.25
17–18	0.23	0.13	**0.02**	0.44
19–20	0.38	0.20	**0.06**	0.71
21–22	0.62	0.29	**0.14**	1.11
23–24	0.96	0.42	**0.27**	1.66
25–26	1.44	0.59	**0.48**	2.41
27–28	2.09	0.80	**0.78**	3.41
29–30	2.95	1.06	**1.21**	4.70

(*continued*)

Table 2. (*Continued*)

Age interval (GW)	Mean	SD	5th percentile	95th percentile
31–32	4.08	1.39	1.80	6.36
33–34	5.53	1.78	2.59	8.46
35–36	7.35	2.25	3.64	11.06
37–38	9.63	2.82	4.99	14.26
39–40	12.43	3.48	6.71	18.16
41–42	15.85	4.25	8.86	22.85
Thymus				
13–14	0.09	0.07	–	0.20
15–16	0.17	0.12	–	0.37
17–18	0.31	0.19	–	0.63
19–20	0.53	0.30	0.04	1.03
21–22	0.87	0.45	0.13	1.60
23–24	1.35	0.64	0.29	2.40
25–26	2.01	0.89	0.55	3.48
27–28	2.92	1.21	0.93	4.92
29–30	4.14	1.61	1.49	6.79
31–32	5.72	2.10	2.26	9.18
33–34	7.75	2.70	3.31	12.20
35–36	10.33	3.42	4.71	15.95
37–38	13.54	4.27	6.52	20.56
39–40	17.50	5.27	8.84	26.17
41–42	22.34	6.44	11.75	32.93
Thyroid				
15–16	0.13	0.08	−0.00	0.27
17–18	0.19	0.10	0.02	0.36
19–20	0.25	0.13	0.04	0.46
21–22	0.33	0.16	0.08	0.59
23–24	0.42	0.18	0.12	0.73
25–26	0.53	0.22	0.18	0.89
27–28	0.66	0.25	0.24	1.07
29–30	0.80	0.29	0.32	1.27
31–32	0.95	0.33	0.42	1.49
33–34	1.13	0.37	0.53	1.73
35–36	1.33	0.41	0.65	2.00
37–38	1.54	0.46	0.79	2.30
39–40	1.78	0.51	0.95	2.61
41–42	2.04	0.56	1.13	2.96

Age interval (GW)	Left				Right			
	Mean	SD	5th percentile	95th percentile	Mean	SD	5th percentile	95th percentile
Adrenals								
13–14	0.13	0.03	0.08	0.17	0.16	0.08	0.03	0.29
15–16	0.28	0.10	0.12	0.45	0.28	0.09	0.13	0.43
17–18	0.47	0.18	0.18	0.76	0.44	0.13	0.22	0.66
19–20	0.69	0.26	0.27	1.11	0.63	0.20	0.30	0.96
21–22	0.93	0.34	0.38	1.48	0.86	0.29	0.38	1.33

(continued)

Table 2. (*Continued*)

Age interval (GW)	Left				Right			
	Mean	SD	5th percentile	95th percentile	Mean	SD	5th percentile	95th percentile
23–24	1.21	0.42	0.51	1.90	1.12	0.39	0.47	1.76
25–26	1.51	0.51	0.67	2.34	1.41	0.50	0.58	2.24
27–28	1.84	0.60	0.86	2.82	1.73	0.62	0.71	2.76
29–30	2.21	0.69	1.07	3.34	**2.09**	**0.74**	0.88	3.31
31–32	2.60	0.78	1.31	3.89	**2.48**	**0.85**	1.09	3.88
33–34	3.02	0.88	1.57	4.47	2.91	**0.95**	1.34	4.47
35–36	3.47	0.98	1.86	5.09	3.36	**1.03**	1.66	5.06
37–38	3.95	1.08	2.17	5.74	3.84	**1.10**	2.04	5.65
39–40	4.47	1.19	2.51	6.42	4.36	1.14	2.49	6.23
41–42	5.01	1.30	2.87	7.14	4.91	1.15	3.02	6.79
Kidneys								
13–14	0.19	0.12	−0.01	0.39	0.22	0.10	0.05	0.38
15–16	0.37	0.18	0.08	0.66	0.34	0.17	0.05	0.62
17–18	0.71	0.26	0.28	1.13	0.67	0.27	0.22	1.11
19–20	1.21	0.37	0.60	1.83	1.20	0.39	0.55	1.85
21–22	1.91	0.51	1.07	2.75	1.93	0.54	1.03	2.82
23–24	2.81	0.68	1.69	3.92	2.83	0.72	1.65	4.01
25–26	3.89	0.87	2.45	5.32	3.89	0.92	2.38	5.40
27–28	5.14	1.09	3.34	6.94	5.08	1.15	3.20	6.97
29–30	6.52	1.34	4.31	8.73	6.38	1.40	4.07	8.68
31–32	7.99	1.62	5.32	10.65	7.74	1.68	4.98	10.51
33–34	9.48	1.93	6.32	12.65	9.14	1.99	5.87	12.40
35–36	10.94	2.26	7.22	14.65	10.52	2.32	6.71	14.33
37–38	12.27	2.62	7.96	16.58	11.85	2.67	7.45	16.25
39–40	13.38	3.01	8.43	18.33	13.07	3.06	8.04	18.10
41–42	14.16	3.42	8.53	19.79	14.12	3.47	8.42	19.82
Lungs								
13–14	0.70	0.25	0.29	1.12	0.56	0.25	0.15	0.97
15–16	1.52	0.55	0.62	2.42	1.47	0.53	0.59	2.35
17–18	2.42	0.88	0.97	3.87	2.67	0.93	1.13	4.20
19–20	3.53	1.26	1.46	5.59	4.15	1.42	1.81	6.49
21–22	4.92	1.67	2.18	7.67	5.92	2.00	2.64	9.20
23–24	6.67	2.12	3.19	10.15	7.98	2.63	3.65	12.31
25–26	8.77	2.60	4.48	13.05	10.32	3.32	4.87	15.78
27–28	11.20	3.13	6.05	16.35	12.95	4.03	6.32	19.59
29–30	13.92	3.70	7.84	20.00	15.87	4.77	8.03	23.71
31–32	16.82	4.30	9.75	23.90	19.08	5.50	10.02	28.13
33–34	19.79	4.94	11.66	27.91	22.57	6.23	12.33	32.81
35–36	22.64	5.62	13.39	31.88	26.34	6.92	14.97	37.72
37–38	25.18	6.34	14.75	35.61	30.41	7.56	17.97	42.85
39–40	27.18	7.10	15.51	38.85	34.76	8.15	21.36	48.16
41–42	28.36	7.89	15.38	41.33	39.24	8.66	25.00	53.47

Table 3. Mean, standard deviation, and 5th and 95th percentiles of organ weight in relation to body weight

Body weight (g)	Mean	SD	5th percentile	95th percentile
Brain				
1–200	25.2	7.9	12.3	38.1
201–400	55.0	11.2	36.5	73.5
401–600	85.6	14.6	61.5	109.7
601–800	117.0	18.0	87.3	146.6
801–1000	149.0	21.4	113.8	184.2
1001–1200	181.4	24.8	140.7	222.2
1201–1400	214.1	28.2	167.8	260.5
1401–1600	246.9	31.6	195.0	298.8
1601–1800	279.4	34.9	221.9	336.8
1801–2000	311.2	38.3	248.2	374.2
2001–2200	342.1	41.7	273.5	410.7
2201–2400	371.5	45.1	297.3	445.7
2401–2600	399.1	48.5	319.3	478.8
2601–2800	424.3	51.9	338.9	509.6
2801–3000	446.5	55.2	355.6	537.4
3001–3200	465.2	58.6	368.8	561.6
3201–3400	479.7	62.0	377.7	581.7
3401–3600	489.4	65.4	381.8	597.0
3601–3800	496.9	68.8	383.7	610.0
3801–4000	504.4	72.2	385.7	623.1
4001–4200	511.9	75.6	387.6	636.1
Heart				
1–200	9.4	5.1	1.0	17.8
201–400	25.3	7.1	13.6	37.1
401–600	41.0	9.2	26.0	56.1
601–800	56.5	11.1	38.2	74.8
801–1000	71.8	13.0	50.4	93.3
1001–1200	86.9	14.9	62.3	111.4
1201–1400	101.8	16.8	74.2	129.3
1401–1600	116.4	18.6	85.9	146.9
1601–1800	130.8	20.3	97.4	164.2
1801–2000	145.1	22.0	108.8	181.3
2001–2200	159.1	23.7	120.1	198.0
2201–2400	172.8	25.3	131.2	214.5
2401–2600	186.4	26.9	142.2	230.6
2601–2800	199.8	28.4	153.0	246.5
2801–3000	212.9	29.9	163.7	262.1
3001–3200	225.9	31.4	174.3	277.4
3201–3400	238.6	32.8	184.7	292.5
3401–3600	251.1	34.1	195.0	307.2
3601–3800	263.4	35.4	205.1	321.7
3801–4000	275.5	36.7	215.1	335.8
4001–4200	287.3	37.9	224.9	349.7

(*continued*)

Table 3. (*Continued*)

Body weight (g)	Mean	SD	5th percentile	95th percentile
Liver				
1–200	8.2	4.0	1.7	14.8
201–400	17.7	5.5	8.6	26.8
401–600	27.2	7.1	15.6	38.8
601–800	36.6	8.6	22.5	50.8
801–1000	46.1	10.1	29.5	62.7
1001–1200	55.6	11.6	36.5	74.7
1201–1400	65.1	13.2	43.4	86.7
1401–1600	74.5	14.7	50.4	98.7
1601–1800	84.0	16.2	57.3	110.7
1801–2000	93.5	17.7	64.3	122.6
2001–2200	102.9	19.3	71.3	134.6
2201–2400	112.4	20.8	78.2	146.6
2401–2600	121.9	22.3	85.2	158.6
2601–2800	131.3	23.8	92.1	170.6
2801–3000	140.8	25.4	99.1	182.5
3001–3200	150.3	26.9	106.1	194.5
3201–3400	159.8	28.4	113.0	206.5
3401–3600	169.2	29.9	120.0	218.5
3601–3800	178.7	31.5	126.9	230.5
3801–4000	188.2	33.0	133.9	242.4
4001–4200	197.6	34.5	140.9	254.4
Pancreas				
1–200	0.32	0.11	0.14	0.50
201–400	0.67	0.21	0.34	1.01
401–600	1.03	0.30	0.53	1.53
601–800	1.38	0.40	0.72	2.04
801–1000	1.73	0.50	0.92	2.55
1001–1200	2.09	0.59	1.11	3.06
1201–1400	2.44	0.69	1.31	3.58
1401–1600	2.79	0.79	1.50	4.09
1601–1800	3.15	0.88	1.69	4.60
1801–2000	3.50	0.98	1.89	5.11
2001–2200	3.85	1.08	2.08	5.63
2201–2400	4.21	1.17	2.28	6.14
2401–2600	4.56	1.27	2.47	6.65
2601–2800	4.91	1.37	2.66	7.16
2801–3000	5.27	1.46	2.86	7.68
3001–3200	5.62	1.56	3.05	8.19
3201–3400	5.97	1.66	3.25	8.70
3401–3600	6.33	1.75	3.44	9.22
3601–3800	6.68	1.85	3.64	9.73
3801–4000	7.04	1.95	3.83	10.24
4001–4200	7.39	2.05	4.02	10.75

(*continued*)

Table 3. (*Continued*)

Body weight (g)	Mean	SD	5th percentile	95th percentile
Spleen				
1–200	0.10	0.07	−0.02	0.22
201–400	0.46	0.24	0.07	0.86
401–600	0.93	0.42	0.25	1.61
601–800	1.47	0.60	0.49	2.45
801–1000	2.07	0.78	0.79	3.36
1001–1200	2.73	0.97	1.13	4.32
1201–1400	3.43	1.16	1.52	5.34
1401–1600	4.17	1.35	1.94	6.40
1601–1800	4.95	1.55	2.40	7.50
1801–2000	5.76	1.75	2.89	8.63
2001–2200	6.60	1.94	3.41	9.80
2201–2400	7.48	2.14	3.95	11.00
2401–2600	8.38	2.35	4.52	12.24
2601–2800	9.31	2.55	5.12	13.50
2801–3000	10.26	2.75	5.74	14.79
3001–3200	11.24	2.96	6.38	16.11
3201–3400	12.25	3.16	7.05	17.45
3401–3600	13.27	3.37	7.73	18.81
3601–3800	14.32	3.58	8.44	20.20
3801–4000	15.38	3.78	9.15	21.60
4001–4200	16.43	3.99	9.86	23.00
Thymus				
1–200	0.18	0.12	−0.01	0.38
201–400	0.73	0.36	0.14	1.32
401–600	1.39	0.60	0.40	2.37
601–800	2.12	0.84	0.74	3.51
801–1000	2.91	1.09	1.13	4.70
1001–1200	3.75	1.33	1.57	5.94
1201–1400	4.64	1.57	2.05	7.23
1401–1600	5.55	1.82	2.56	8.55
1601–1800	6.51	2.06	3.11	9.90
1801–2000	7.49	2.31	3.69	11.29
2001–2200	8.49	2.56	4.29	12.70
2201–2400	9.53	2.80	4.92	14.14
2401–2600	10.59	3.05	5.57	15.60
2601–2800	11.67	3.29	6.25	17.08
2801–3000	12.77	3.54	6.94	18.59
3001–3200	13.89	3.79	7.66	20.12
3201–3400	15.03	4.04	8.39	21.67
3401–3600	16.19	4.28	9.14	23.23
3601–3800	17.36	4.53	9.91	24.82
3801–4000	18.55	4.78	10.69	26.41
4001–4200	19.73	5.02	11.46	28.00

(*continued*)

Table 3. (*Continued*)

Body weight (g)	Mean	SD	5th percentile	95th percentile
Thyroid				
1–200	0.16	0.11	−0.03	0.35
201–400	0.27	0.14	0.05	0.50
401–600	0.38	0.16	0.12	0.64
601–800	0.49	0.18	0.20	0.79
801–1000	0.60	0.20	0.26	0.93
1001–1200	0.70	0.23	0.33	1.07
1201–1400	0.80	0.25	0.39	1.21
1401–1600	0.90	0.27	0.45	1.34
1601–1800	0.99	0.29	0.51	1.47
1801–2000	1.08	0.31	0.56	1.60
2001–2200	1.17	0.34	0.62	1.73
2201–2400	1.26	0.36	0.67	1.85
2401–2600	1.34	0.38	0.71	1.97
2601–2800	1.42	0.40	0.75	2.08
2801–3000	1.50	0.43	0.79	2.20
3001–3200	1.57	0.45	0.83	2.31
3201–3400	1.64	0.47	0.87	2.42
3401–3600	1.71	0.49	0.90	2.52
3601–3800	1.78	0.52	0.93	2.63
3801–4000	1.84	0.54	0.96	2.73
4001–4200	1.91	0.56	0.98	2.83

Body weight (g)	Right				Left			
	Mean	SD	5th percentile	95th percentile	Mean	SD	5th percentile	95th percentile
Adrenals								
1–200	0.41	0.26	−0.02	0.83	0.43	0.26	0.00	0.86
201–400	0.68	0.32	0.15	1.20	0.71	0.32	0.19	1.23
401–600	0.94	0.38	0.32	1.57	0.99	0.37	0.38	1.60
601–800	1.21	0.44	0.49	1.93	1.27	0.42	0.58	1.97
801–1000	1.48	0.50	0.67	2.30	1.55	0.48	0.77	2.34
1001–1200	1.75	0.56	0.84	2.67	1.83	0.53	0.96	2.71
1201–1400	2.02	0.62	1.01	3.04	2.11	0.59	1.15	3.08
1401–1600	2.29	0.68	1.18	3.40	2.40	0.64	1.34	3.45
1601–1800	2.56	0.73	1.35	3.77	2.68	0.69	1.53	3.82
1801–2000	2.83	0.79	1.52	4.14	2.96	0.75	1.73	4.19
2001–2200	3.10	0.85	1.70	4.50	3.24	0.80	1.92	4.56
2201–2400	3.37	0.91	1.87	4.87	3.52	0.86	2.11	4.93
2401–2600	3.64	0.97	2.04	5.24	3.80	0.91	2.30	5.30
2601–2800	3.91	1.03	2.21	5.60	4.08	0.96	2.49	5.67
2801–3000	4.18	1.09	2.38	5.97	4.36	1.02	2.68	6.04
3001–3200	4.44	1.15	2.55	6.34	4.64	1.07	2.88	6.40
3201–3400	4.71	1.21	2.73	6.70	4.92	1.13	3.07	6.77
3401–3600	4.98	1.27	2.90	7.07	5.20	1.18	3.26	7.14
3601–3800	5.25	1.33	3.07	7.44	5.48	1.24	3.45	7.51
3801–4000	5.52	1.39	3.24	7.80	5.76	1.29	3.64	7.88
4001–4200	5.79	1.45	3.41	8.17	6.04	1.34	3.83	8.25

(*continued*)

Table 3. (*Continued*)

Body weight (g)	Right				Left			
	Mean	SD	5th percentile	95th percentile	Mean	SD	5th percentile	95th percentile
Kidneys								
1–200	0.66	0.28	0.20	1.12	0.56	0.31	0.05	1.08
201–400	1.58	0.43	0.87	2.28	1.55	0.46	0.80	2.30
401–600	2.48	0.58	1.53	3.43	2.52	0.60	1.53	3.51
601–800	3.37	0.73	2.18	4.57	3.47	0.74	2.25	4.69
801–1000	4.26	0.87	2.82	5.70	4.41	0.89	2.95	5.86
1001–1200	5.14	1.02	3.46	6.82	5.32	1.03	3.63	7.02
1201–1400	6.00	1.17	4.08	7.93	6.22	1.17	4.30	8.15
1401–1600	6.86	1.32	4.69	9.03	7.11	1.31	4.94	9.27
1601–1800	7.71	1.47	5.30	10.13	7.97	1.46	5.58	10.37
1801–2000	8.55	1.62	5.89	11.21	8.82	1.60	6.19	11.45
2001–2200	9.38	1.76	6.48	12.29	9.65	1.74	6.78	12.52
2201–2400	10.20	1.91	7.06	13.35	10.47	1.89	7.36	13.57
2401–2600	11.02	2.06	7.62	14.41	11.26	2.03	7.92	14.60
2601–2800	11.82	2.21	8.18	15.46	12.04	2.17	8.47	15.62
2801–3000	12.61	2.36	8.73	16.49	12.80	2.32	8.99	16.61
3001–3200	13.40	2.51	9.27	17.52	13.55	2.46	9.50	17.59
3201–3400	14.18	2.66	9.81	18.54	14.27	2.60	9.99	18.55
3401–3600	14.94	2.80	10.33	19.56	14.98	2.75	10.47	19.50
3601–3800	15.70	2.95	10.84	20.56	15.68	2.89	10.92	20.43
3801–4000	16.45	3.10	11.35	21.56	16.36	3.03	11.37	21.35
4001–4200	17.21	3.25	11.86	22.56	17.05	3.17	11.82	22.27
Lungs								
1–200	2.76	1.49	0.32	5.21	1.45	0.78	0.16	2.73
201–400	4.87	1.88	1.78	7.96	3.87	1.15	1.98	5.75
401–600	6.98	2.27	3.24	10.72	6.18	1.51	3.70	8.67
601–800	9.08	2.67	4.70	13.47	8.39	1.88	5.30	11.47
801–1000	11.19	3.06	6.15	16.23	10.49	2.24	6.80	14.17
1001–1200	13.30	3.46	7.61	18.98	12.47	2.61	8.19	16.76
1201–1400	15.40	3.85	9.07	21.73	14.35	2.97	9.47	19.24
1401–1600	17.51	4.24	10.53	24.49	16.12	3.33	10.64	21.61
1601–1800	19.62	4.64	11.99	27.24	17.78	3.70	11.70	23.87
1801–2000	21.72	5.03	13.45	30.00	19.34	4.06	12.65	26.02
2001–2200	23.83	5.42	14.90	32.75	20.78	4.43	13.49	28.06
2201–2400	25.93	5.82	16.36	35.51	22.11	4.79	14.23	30.00
2401–2600	28.04	6.21	17.82	38.26	23.34	5.16	14.85	32.82
2601–2800	30.15	6.61	19.28	41.01	24.45	5.52	15.37	33.54
2801–3000	32.25	7.00	20.74	43.77	25.46	5.89	15.78	35.15
3001–3200	34.36	7.39	22.20	46.52	26.36	6.25	16.08	36.64
3201–3400	36.47	7.79	23.66	49.28	27.15	6.62	16.27	38.03
3401–3600	38.57	8.18	25.11	52.03	27.83	6.98	16.35	39.32
3601–3800	40.68	8.58	26.57	54.79	28.47	7.35	16.38	40.55
3801–4000	42.79	8.97	28.03	57.54	29.10	7.71	16.42	41.79
4001–4200	44.89	9.36	29.49	60.29	29.74	8.08	16.45	43.02

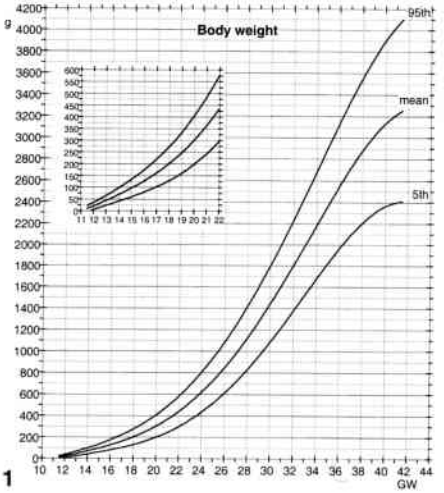
Table 4. Mean, standard deviation, and 5th and 95th percentiles of body dimensions (mm) in relation to gestational age

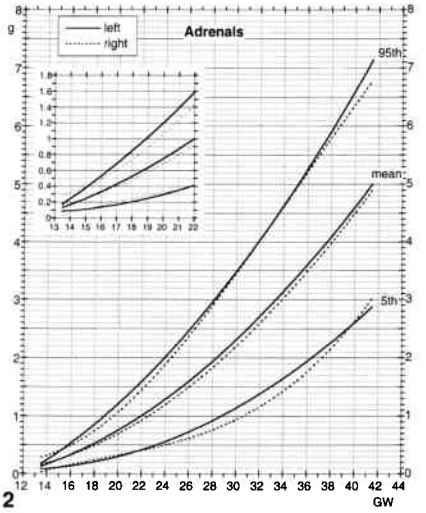
Age interval (GW)	Mean	SD	5th percentile	95th percentil
Crown–heel length				
11–12	91.7	14.6	67.6	115.8
13–14	131.8	15.4	106.4	157.2
15–16	170.4	16.2	143.7	197.1
17–18	207.4	17.0	179.4	235.4
19–20	242.9	17.8	213.6	272.2
21–22	276.8	18.6	246.2	307.4
23–24	309.2	19.4	277.3	341.1
25–26	340.0	20.2	306.8	373.2
27–28	369.3	21.0	334.8	403.8
29–30	397.0	21.8	361.2	432.8
31–32	423.2	22.6	386.1	460.3
33–34	447.8	23.4	409.4	486.3
35–36	470.9	24.2	431.2	510.7
37–38	492.5	24.9	451.4	533.5
39–40	512.5	25.7	470.1	554.8
41–42	530.9	26.5	487.3	574.6
Crown–rump length				
11–12	62.1	11.2	43.6	80.5
13–14	89.6	11.7	70.4	108.9
15–16	116.2	12.2	96.1	136.2
17–18	141.7	12.7	120.9	162.5
19–20	166.2	13.1	144.6	187.9
21–22	189.8	13.6	167.4	212.2
23–24	212.3	14.1	189.1	235.5
25–26	233.8	14.6	209.9	257.8
27–28	254.4	15.1	229.6	279.1
29–30	273.9	15.5	248.3	299.5
31–32	292.4	16.0	266.1	318.8
33–34	309.9	16.5	282.8	337.1
35–36	326.5	17.0	298.5	354.4
37–38	342.0	17.5	313.3	370.7
39–40	356.5	17.9	327.0	386.0
41–42	370.0	18.4	339.7	400.3
Foot length				
11–12	8.9	2.8	4.3	13.0
13–14	14.0	2.9	9.0	19.0
15–16	19.0	3.0	14.0	24.0
17–18	25.0	3.2	19.0	30.0
19–20	30.0	3.3	25.0	36.0
21–22	36.0	3.5	30.0	42.0
23–24	42.0	3.6	36.0	48.0
25–26	48.0	3.8	41.0	54.0
27–28	53.0	3.9	47.0	59.0
29–30	58.0	4.1	51.0	65.0
31–32	63.0	4.2	56.0	70.0
33–34	67.0	4.4	60.0	74.0
35–36	71.0	4.6	63.0	78.0
37–38	74.0	4.7	66.0	82.0
39–40	76.0	4.9	68.0	84.0
41–42	77.0	5.1	69.0	86.0

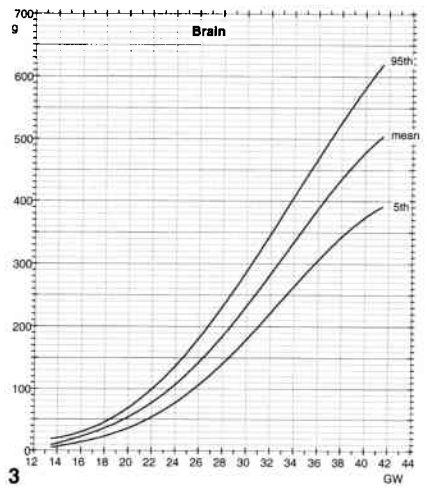
(continu

Table 4. (*Continued*)

Age interval (GW)	Mean	SD	5th percentile	95th percentile
Head circumference				
11–12	60.3	11.5	41.4	79.2
13–14	89.2	11.8	69.7	108.7
15–16	116.7	12.2	96.6	136.8
17–18	142.8	12.6	122.1	163.5
19–20	167.5	12.9	146.2	188.8
21–22	190.9	13.3	169.0	212.8
23–24	212.8	13.7	190.3	235.3
25–26	233.4	14.0	210.3	256.5
27–28	252.7	14.4	229.0	276.4
29–30	270.5	14.8	246.2	294.8
31–32	287.0	15.1	262.1	311.9
33–34	302.1	15.5	276.5	327.6
35–36	315.8	15.9	289.7	341.9
37–38	328.1	16.2	301.4	354.8
39–40	339.1	16.6	311.7	366.4
41–42	348.6	17.0	320.7	376.6







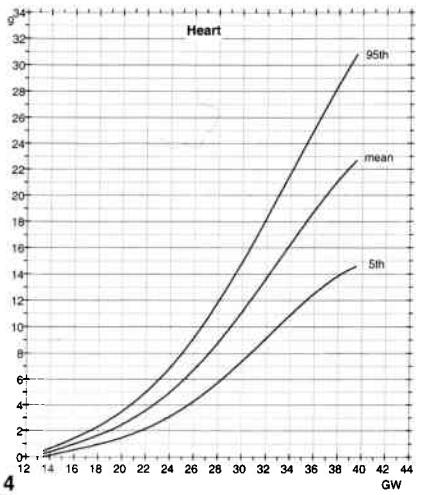
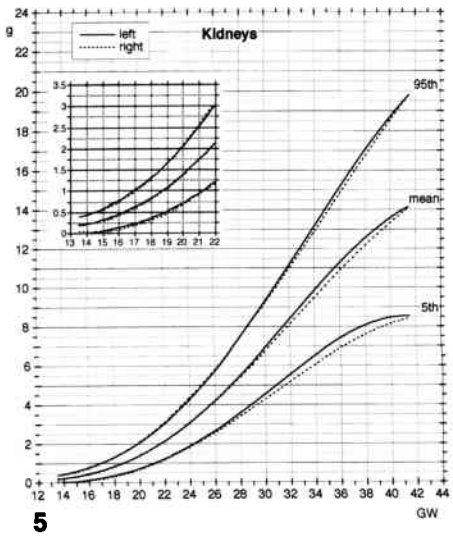


Figure 1. Body weight (BW) by gestational week (GW). **Inset:** detail of the chart for ages below 22 GW.
Figure 2. Adrenal weights by GW. **Inset:** detail of the chart for ages below 22 GW.
Figure 3. Brain weight by GW.
Figure 4. Heart weight by GW.



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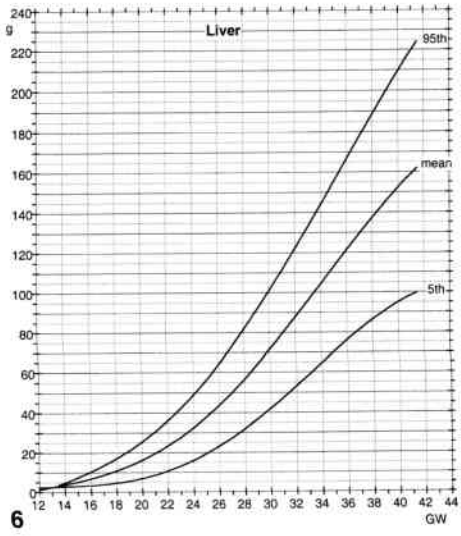

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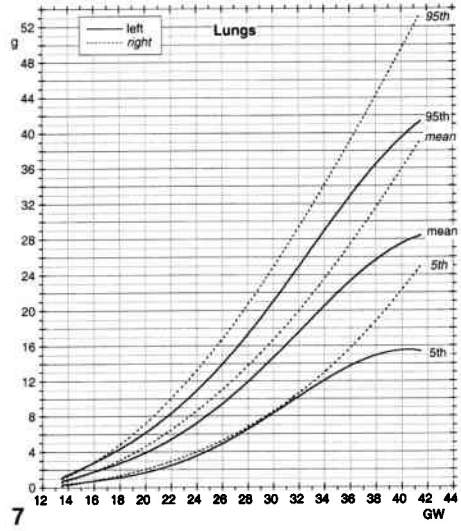

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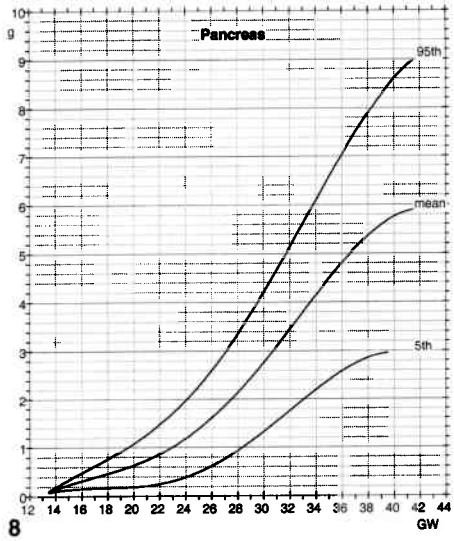

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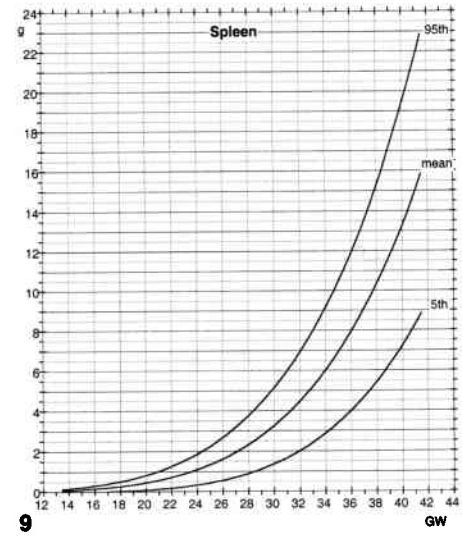

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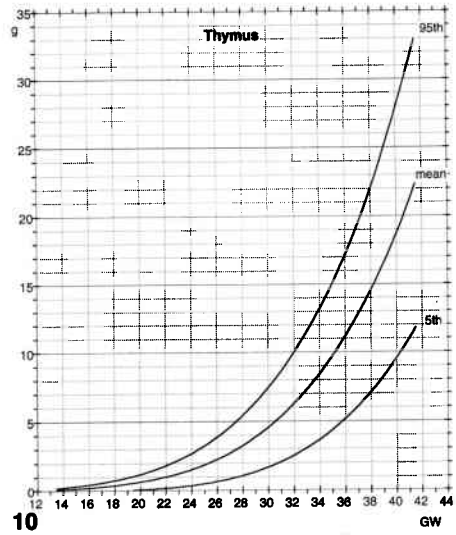

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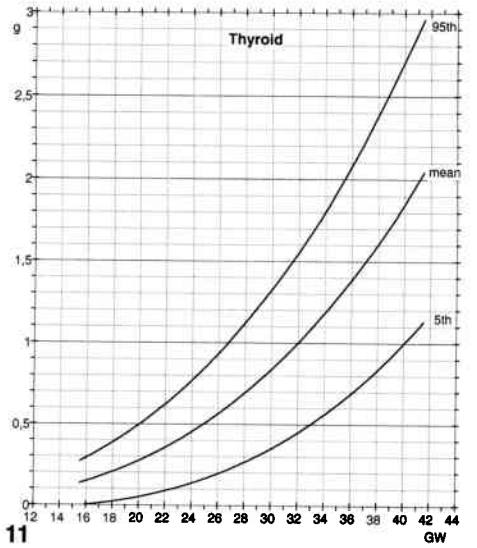
Figure 5. Kidney weights by GW. **Inset:** detail of the chart for ages below 22 GW.
Figure 6. Liver weight by GW.
Figure 7. Lung weights by GW. Standards for right lung should be used with caution, owing to the bacteriological sampling made in some fetuses.
Figure 8. Pancreas weight by GW.
Figure 9. Spleen weight by GW.
Figure 10. Thymus weight by GW.



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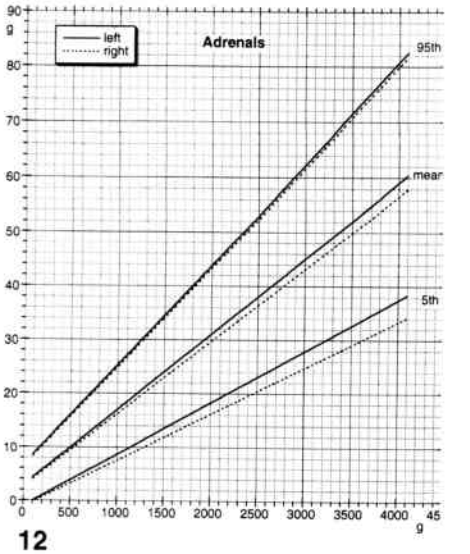

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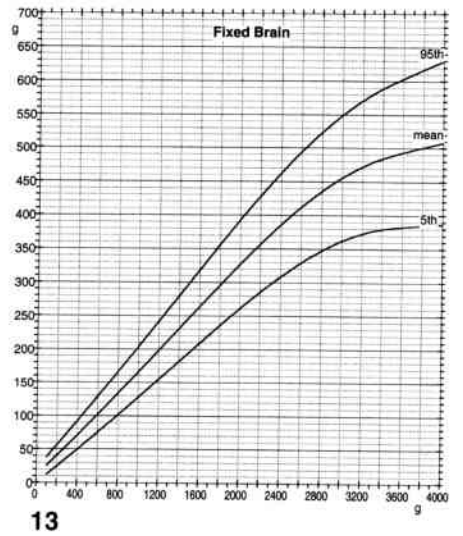

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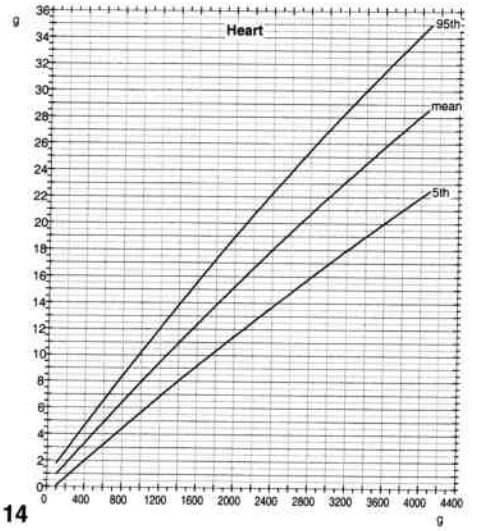

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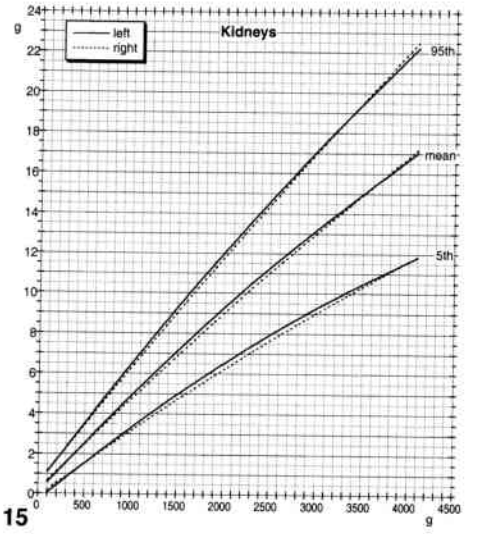

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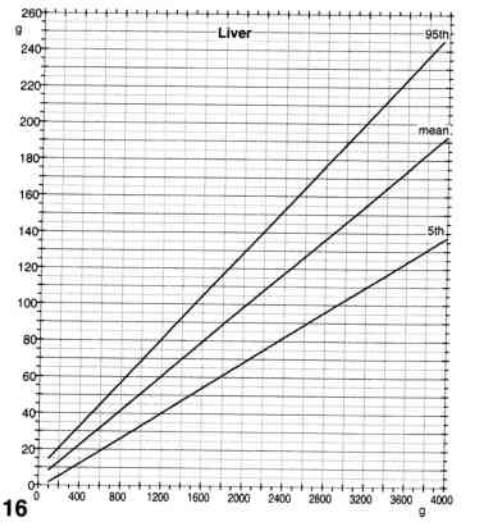

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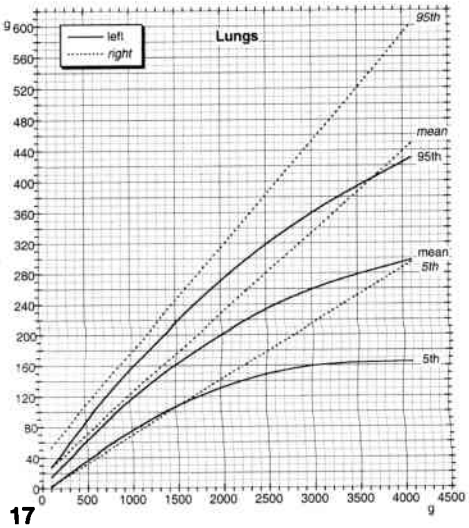
Figure 11. Thyroid weight by GW.
Figure 12. Adrenal weights by BW.
Figure 13. Brain weight by BW.
Figure 14. Heart weight by BW.
Figure 15. Kidney weights by BW.
Figure 16. Liver weight by BW.



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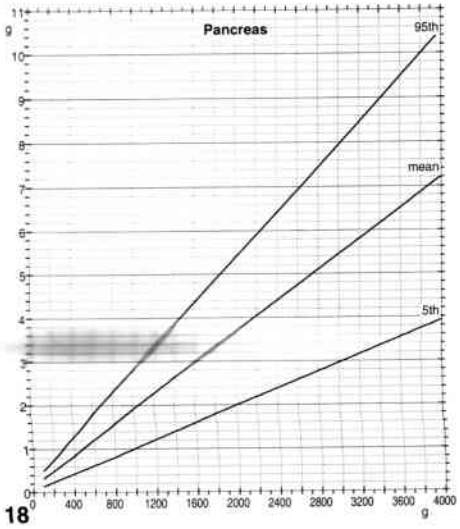

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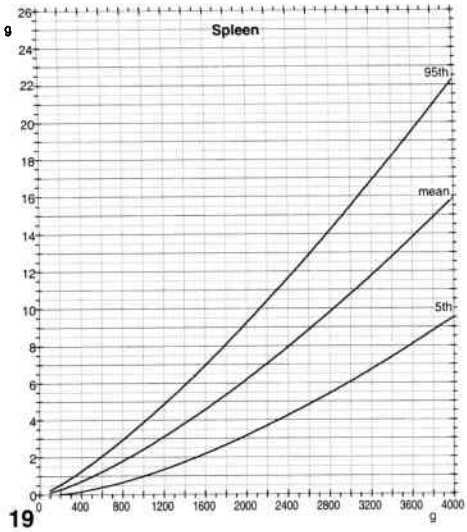

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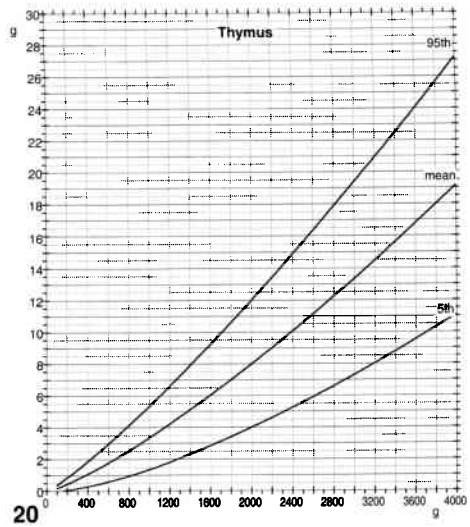

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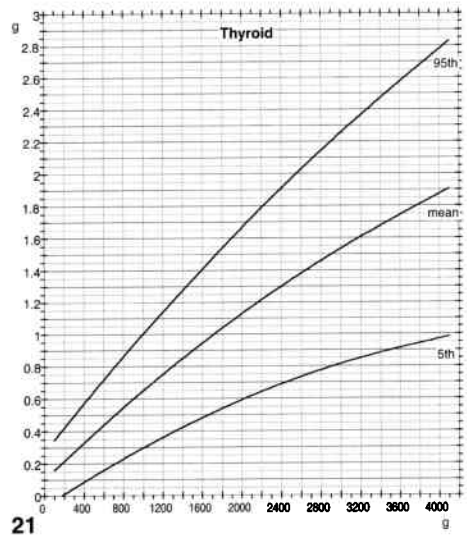

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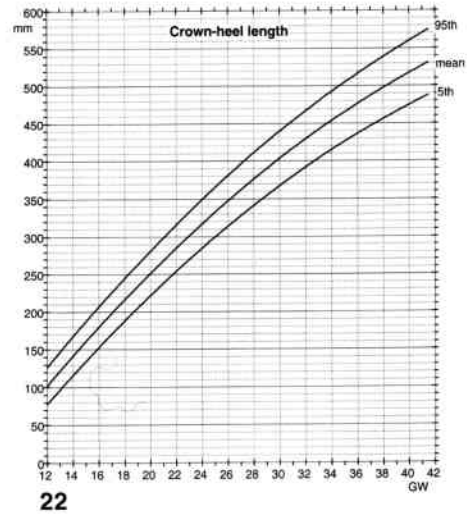

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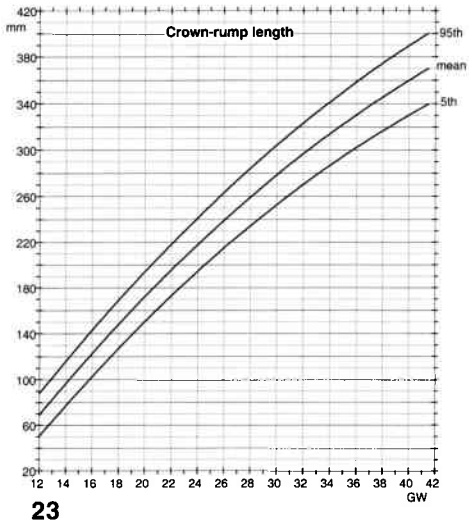
Figure 17. Lung weights by BW. Standards for right lung should be used with caution, owing to the bacteriological sampling made in some fetuses.
Figure 18. Pancreas weight by BW.
Figure 19. Spleen weight by BW.
Figure 20. Thymus weight by BW.
Figure 21. Thyroid weight by BW.
Figure 22. Crown–heel length by GW.



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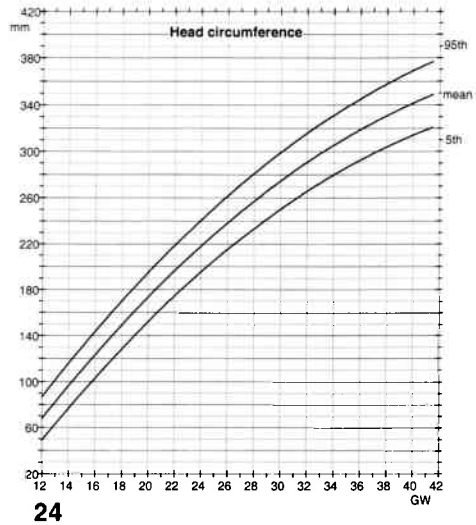

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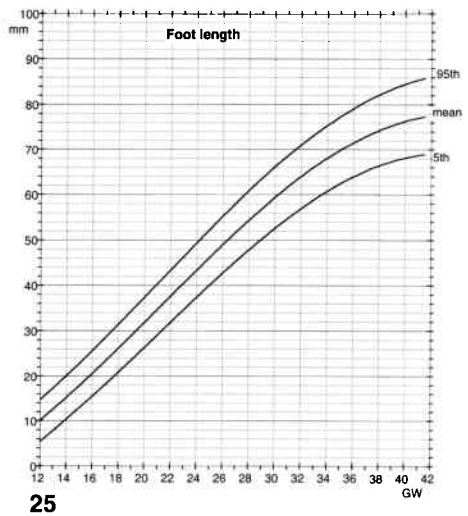

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Figure 23. Crown–rump length by GW.

Figure 24. Head circumference by GW.

Figure 25. Foot length by GW.

malformations is usually made at the 11 GW ultrasound examination, leading to early termination of pregnancy. So, it becomes essential for the pathologist to have accurate fetal measurement standards corresponding to early phases of development.

Another difficulty in the definition of reference populations remains the accurate estimation of gestational age of the fetuses. Our method, combining (1) amenorrhea age, (2) ultrasound age, and (3) macroscopic, radiologic, and histologic criteria of fetal maturation, probably represents the most reliable estimation of the true developmental age of the subjects.

Bearing in mind these differences in sample composition between the published standards of organ weights, it may be hazardous to compare them. Furthermore, there is a great diversity in the choice of the mathematical models fitting row data, which enhances the discrepancies between the smoothed values of organ weight standards. This disparity in methodological choices may partly explain the differences observed between organ growth standards. As observed by Barr et al. [11], there is no important difference in mean organ weights between the studies, but a significant one in extreme percentiles. Furthermore, differences between standards may come from mathematical processing of the data. In the present study several mathematical models were tested and visually assessed for the mean and the SD of each organ in relation to age and body weight. In our opinion, this careful treatment of the raw data as well as the scrupulous selection of subjects included in the sample make these organ weight standards very reliable.

An interesting characteristic of the curves we established was that they concerned formalin-fixed organs, whereas the other publications concerned fresh dissected viscera. Fixation certainly modifies organ weights. Larroche [12] has estimated the weight gain of the brain during fixation: it may reach up to 15% to 20% of the initial weight. With regard to the other viscera, we attempted to estimate the effect of fixation by comparing our results with the tables of Singer et al. [14]. As an example, we found no significant differences in heart, brain, and liver weights at 20 GW. Thereafter, the weight increase varies from 10% to 12% for the brain to

20% to 25% for the heart and liver. Nevertheless, these differences in organ weights are comparable to the differences in body weight observed between the two studies. The mean body weight in our study is similar to that of Singer's stillborns at 20 GW, but is 20% higher in the oldest fetuses. Therefore, the higher organ weights observed in our study could be due not only to fixation but also to a bias of selection of the heaviest fetuses. Consequently, it seems difficult to accurately compare standards of fresh and fixed organ weights from distinct populations. Therefore, our results give specifically appropriate references for laboratories using postfixation weighing.

In most publications, combined weight (right + left) has been given for pair organs (adrenals, lungs, kidneys). This study seems the first to give both charts and standard values for the left and right organs. It is noteworthy that significant differences of growth can be observed between symmetrical organs, so distinct models may occasionally be necessary to fit the respective left and right data (see the growth curves of the lungs and kidneys).

In conclusion, this study, based on careful methodology, provides the most complete and accurate set of standards for formalin-fixed organs, useful for pathologists.

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