



# PEDIATRIC PATHOLOGY

*By*

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# Preface

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This is a work devoted to anatomic appearances with respect to diseases of childhood. That there is need for such a book is indicated by the great number of deaths occurring in this period, by the occurrence of some diseases almost entirely within the childhood years and, mainly, by the lack of any other such work in the field.

The absence of this type of book is explainable. A devotion to pathology is an affection that most pathologists succumb to very early in their careers in medicine, and their postgraduate training is devoted strictly to the furtherance of their knowledge in this field. Their clinical training in medical school is almost exclusively gained from contact with adult patients, and their exposure to pediatrics is usually brief and in many schools it is not compulsory. Furthermore, aside from neonatal deaths, pediatric material comprises only a small part of the general pathologist's material, for the usual varieties of disease requiring pathologic examination are rare in childhood and outside of children's hospitals are even less commonly encountered.

Pediatrics, although the broadest of all medical specialties, is a separate discipline and makes use of specialized concepts and terms of reference. The pathologist faced with the task of translating pediatric notation into his own terms is often unable to do so and, humanly enough, tends to relegate the problem to a position of secondary importance. That the most junior member of the pathology staff does the autopsies of the newly born is still the accepted order of things in many hospitals, and the autopsies of stillborn infants are not included in the total autopsy statistics when accreditation of a hospital as a training institution is being considered.

The unfamiliarity of the pathologist with the problems of pediatrics, and his inability to answer the questions of the pediatrician satisfactorily has, in turn, caused the pediatrician to "forget"

pathology. For example, biopsy is a technique that is resorted to rather infrequently in pediatrics as compared to its use in adult medicine. The less contact he has with the pediatrician the less the pathologist thinks of matters pediatric. This vicious cycle has led to a further and further separation of the two groups, and to a neglect of the field as a whole except by a small, truly devoted group.

The purpose of this work is to show that the pathology of children's diseases is in truth a valid subspecialty of pathology in general, and that the pathologist can be of assistance to the clinician in a great many problems.

This book deals primarily with pathology, and, to the greatest degree, was written with the hope that it would be of assistance to the pathologist. For this reason it is a specialized text and does require some background material. A certain amount of clinical data has been included, for I do not believe that morbid anatomy comprises all of pathology. Generally, emphasis has been laid upon the histologic aspects of various lesions, for I believe that gross lesions are usually apparent enough not to require lengthy descriptions.

The photomicrographs, for the most part, have been made from sections stained with hematoxylin and eosin. In some instances the lesions are not as clearly demarcated as they would have been with other stains, but since the hematoxylin and eosin stain technique is that most universally used, it is from slides stained in this manner that the pathologist formulates first opinions. Representation of the lesions as they appear in routine sections, therefore, appeared to be most desirable.

The book is replete with hypotheses, new terms, altered classifications, and unanswered questions. The existence of such material has been dictated by the nature of the subject, for many of the problems have not been dealt with specifically in other works; many have been lumped together

## PREFACE

with the consideration of similar conditions in adults, whereas in children they constitute clinically, if not morphologically, different problems; and, finally, some problems have not even previously been noted as such. I do not hold any of these ideas sacred or inviolable. They are merely ideas on subjects about which no ideas have been expressed or those hypotheses about which, largely derived from thoughts gained by observations on adults, do not fit the facts as seen in children. It may be said that to think is to be, and if these ideas arouse howls of disagreement or scorn, they still serve the purpose of showing the existence of problems which, up to the present, did not seem to exist.

Throughout the preparation of the work I have had the assistance of innumerable persons. First, the group of anonymous pathologists must be mentioned, both military and civilian, who labored to make the collection of the Armed Forces Institute of Pathology a source of material almost without limits. In the absence of such a background to supplement my previous experience, I would never have felt secure enough to undertake the task in the first place. To these professional workers must be added those others on the staff of the Institute who coded, arranged, filed, and prepared the material, and also made it instantly available in workable form.

Miss Margery Cork has given invaluable aid. She has prepared the sections from which many of the photographs were made, taken photographs, typed, read proof, edited, made suggestions on form and content, and kept the organization of the manuscript in order. Without her assistance the book never would have been finished.

Doctor George Fetterman deserves special thanks. It was through his urging that the writing of this book was undertaken in the first place, and he has made numerous and invaluable suggestions throughout.

Doctor Leo Geppert read the manuscript from

the disquieting point of view, for me, of the clinician, and, I am sure, has not only corrected many of my mistakes, but has made many clinico-pathologic correlations clearer.

Miss Lucile D. Matteo, and the Mrs. Margaret Bolton, Evelyn Cralle and Stella Reeves typed the manuscript, a task, in view of my handwriting, of no mean proportions.

Mrs. Ruth Haynes and Mr. Herbert Kluge, the custodians of the photography files at the Armed Forces Institute of Pathology, were extremely gracious and helpful in making available thousands of illustrations from which I was able to select many of those used in this book.

Mr. Robert Nye made many of the original photomicrographs. Mr. Julius Halsman gave advice on the reproducibility of the photographs, and he reprinted and otherwise improved the originals. The illustrations themselves speak for the excellence of their work.

Miss Ethel Hicks has, for many years, been in charge of the continuous statistical analyses of the cases in the Registry of Pediatric Pathology. The Appendix of this volume is largely made possible through her efforts.

*Photographs.* Unless otherwise indicated all of the photographic material was obtained from the Medical Illustration Division of the Armed Forces Institute of Pathology, Washington 25, D. C.

Many of the photographs used in the chapter on the central nervous system were made from the slides of the Scholz Collections of Neuropathology which are housed at the Institute.

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# Growth and Development

## Normal Growth and Development

Growth and development are essentially synonymous terms that describe the series of changes an organism goes through to attain maturity. In practice, the term "growth" has come to signify the increase in size attendant upon maturation, whereas "development" is used to indicate the increase in functional capacities. Both are qualities unique to children, and, if justification for the speciality of pediatrics is needed, these changes provide that justification. It is largely because the child is still growing and developing that the manifestations of disease are frequently so different from those seen in adults. An understanding of the processes, rates, and forms of the growth and development is essential to the evaluation of any pediatric problem. For the clinician the problem is relatively simple, because he can make a series of observations over a period of time. Time, of course, is the critical factor, for both growth and development are dynamic functions. The pathologist, however, is severely limited in his ability to evaluate these fundamental attributes, because, by and large, he is limited to a single static observation. It becomes necessary, therefore, to compare the anatomic observations in respect to any single child against an average or norm. Several tables and figures which embody average measurements of height, weight, head circumference, time of appearance of ossification centers, and organ size in relation to age are given for this purpose (Table 1-6, Figs. 1-5). It is essential to understand that these tables represent average figures. The rates of growth and variations in bodily size are greater than those seen in adults, and deviations from these values cannot

be assumed to be significant, although they may be of considerable magnitude.

For instance, in studies of normal weights by Potter and Adair (Table 4), the average weight for the heart in infants weighing between 750 and 1250 gm. was 7.6 gm. The actual observations ranged from 3.5 gm. to 20 gm., and all the hearts were without any obvious manifestations of disease. This difficulty is circumvented to some degree by the utilization of the percentile graphs such as those illustrated for evaluation of length, weight, and head circumference, but, at present no such studies on weights of organs are available. Nevertheless, the data of Potter and Adair (Table IV) are of great value in the estimation of the relative status of growth of an individual child. By comparison of their findings with our own observations of organ weights in over 20,000 infants and children, we found a high degree of correlation.

For the most part, Tables 1-6 need no comment. Appreciation of proportional as well as total growth must also be borne in mind. In the antenatal period, as indicated in Table 1, both crown-rump and crown-heel lengths are given. In the neonatal period, the sitting height of the child is about 70 per cent of the total height. The proportions for older children are shown in Table 5.

Changes in the proportions of the cranial vault and jaws are still more marked. Tables indicating these values are not given, however, although such measurements are possible. The technique of measuring is subject to wide variation, especially when done by different observers, and, hence, it loses some of its value.

TABLE 1\*  
Length of fetus in relation to age

Lunar Month	Crown-Rump Length		Crown-Heel Length	
	Streeter	Scammon and Calkins	Dietrich	Scammon and Calkins
	cm.	cm.	cm.	cm.
Second.....	2.3		3.0	
Third.....	7.4	5.1	9.8	7.0
Fourth.....	11.6	10.7	18.0	15.5
Fifth.....	16.4	15.5	25.0	22.7
Sixth.....	20.8	19.7	31.5	29.2
Seventh.....	24.7	23.6	37.1	35.0
Eighth.....	28.3	27.1	42.5	40.4
Ninth.....	32.1	30.5	47.0	45.4
Tenth.....	36.2	33.6	50.0	50.2

\* From G. L. Streeter, *Contributions to Embryology*, Nos. 55 and 274, 1921; courtesy of the Carnegie Institution of Washington, Washington, D. C. Also from R. E. Scammon and L. A. Calkins, *The Development and Growth of the External Dimensions of the Human Body*, 1929; courtesy of the University of Minnesota Press, Minneapolis. As published in E. L. Potter, *Pathology of the Fetus and the Newborn*, 1952; courtesy of Year Book Publishers, Chicago.

All of these measurements have been, for the most part, based on observations upon Caucasian children. Certain racial differences have been noted. Negro and Oriental babies tend to be smaller than Caucasian babies at birth and at various times in gestation, but the rates of growth and development are the same.

It would be desirable at this point to be able

TABLE 2\*  
Weight of fetus in relation to age

Lunar Month	Streeter	Scammon and Calkins
	cm.	cm.
Second.....	1.1	3.5
Third.....	14.2	14.3
Fourth.....	108.0	86.8
Fifth.....	316.0	260.9
Sixth.....	630.0	551.6
Seventh.....	1,045.0	971.4
Eighth.....	1,680.0	1,519.0
Ninth.....	2,378.0	2,196.1
Tenth.....	3,405.0	2,998.8

\* From G. L. Streeter, *Contributions to Embryology*, Nos. 55 and 274, 1921; courtesy of the Carnegie Institution of Washington, Washington, D. C. Also from R. E. Scammon and L. A. Calkins, *The Development and Growth of the External Dimensions of the Human Body*, 1929; courtesy of the University of Minnesota Press, Minneapolis. As published in E. L. Potter, *Pathology of the Fetus and the Newborn*, 1952; courtesy of Year Book Publishers, Chicago.

to discuss intelligently the factors influencing physical growth. However, although a great deal of work has been done on the subject, we are still essentially in ignorance. The results of most studies, both experimental and clinical, have been of negative value to a large extent. It is known, for instance, that there is little relation between the size of the infant at birth and the size of the mother. It is further known that only in the instance of the most extreme lack of nutritional

TABLE 3\*  
Calculated values of length of extremities at close of each fetal month

Portion of Extremity Measured	Fetal Months							
	3	4	5	6	7	8	9	10
	mm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.
Length of lower extremity.....	23.4	59.8	91.0	118.6	143.7	166.8	188.5	208.9
Thigh length (trochanter to knee)....	11.5	27.5	41.3	53.5	64.6	74.8	84.4	93.4
Leg length (knee to lateral malleolus)...	9.7	26.6	41.1	53.9	65.6	76.4	86.4	95.9
Foot length.....	4.8	18.4	30.0	40.2	49.6	58.2	66.3	73.8
Length of upper extremity.....	24.3	58.2	87.2	112.8	136.2	157.7	177.9	196.8
Arm length (acromion to elbow).....	10.2	23.6	34.8	44.8	53.8	62.2	70.0	77.3
Forearm length.....	7.7	18.7	28.1	36.5	44.1	51.1	57.6	63.8
Hand length.....	3.5	15.6	24.3	32.0	39.1	45.5	51.6	57.2

\* From R. E. Scammon and L. A. Calkins, *Growth in the Fetal Period*, 1929; courtesy of University of Minnesota Press, Minneapolis. As published in E. L. Potter, *Pathology of the Fetus and the Newborn*, 1952; courtesy of Year Book Publishers, Chicago.

TABLE 4\*

*Organ weight in relation to body weight in newborn infants (Potter and Adair)*

	Body Weight (Gm.)								
	250-750	750-1250	1250-1750	1750-2250	2250-2750	2750-3250	3250-3750	3750-4250	Over 4250
No. of Cases (1,144).....	168	193	172	121	94	168	125	70	33
Organ	Arithmetical Mean (Gm.)								
Thyroid.....	0.5	1.1	1.3	1.4	1.8	1.8	2.4	2.4	2.9
Thymus.....	1.4	3.1	5.1	8.5	9.9	9.3	10.8	15.3	12.8
Heart.....	4.6	7.6	10.8	14.5	20.1	17.9	21.7	25.4	29.3
Lungs.....	15.0	25.2	33.7	44.2	54.7	49.5	59.4	64.0	77.9
Liver.....	31.5	49.2	66.3	87.9	140.4	105.8	151.5	185.1	229.0
Spleen.....	1.0	2.1	4.0	5.8	9.7	7.6	11.1	12.2	13.0
Pancreas.....	0.6	1.2	1.6	2.1	3.4	2.8	3.6	3.9	4.6
Kidneys.....	5.3	9.7	13.6	18.3	23.6	21.1	26.6	29.3	32.2
Adrenals.....	2.5	3.3	4.3	5.3	7.6	6.9	9.3	10.5	12.5
Brain.....	82.8	160.6	226.8	289.2	390.9	332.6	429.6	402.9	456.0
Mean body weight.	555.0	999.0	1477.0	2006.0	3005.0	2508.0	3439.0	3945.0	4662.0
	Length (Cm.)								
Crown-heel.....	30.6	36.5	41.5	45.7	48.4	50.9	52.6	54.0	55.3
Crown-rump.....	21.0	24.7	27.9	30.9	32.9	34.8	36.3	37.3	39.0
Days.....	Interval between 1st Day of Last Menstrual Period and Delivery								
	167	195	217	248	258	272	279	277	291

\* From E. L. Potter, *Pathology of the Fetus and the Newborn*, 1952; courtesy of Year Book Publishers, Chicago.

balance in the mother is there an effect on the size and well-being of the infant. Moreover, it is evident that maternal stores of various substances may be seriously depleted in order to supply the needs of the growing fetus. Congenital malformations *per se* do not appear to affect the growth of the body as a whole, for even severely malformed infants are frequently of average length and weight for their gestational age, although they often are born prematurely. In some instances, such as in anencephaly, malformed infants who survive until term appear to be somewhat larger than the average. According to the history, in a series of 100 infants born at term with anencephaly, the average weight at birth was 3700 gm., as compared to the average of about 3200 gm. as determined at autopsy for the newborn population, as a whole. In the postnatal period this is not true, however, and not only severe congenital malformations,

TABLE 5\*

*Average circumferences of the head and thorax in the first five years of life*

	Head		Thorax	
	inches	cm.	inches	cm.
Birth.....	13.7	35	13.7	35
2 months.....	15.8	40	15.4	39
4 months.....	16.8	43	16.7	42
6 months.....	17.4	44	17.2	44
1 year.....	18.4	47	18.3	46
2 years.....	19.2	49	19.4	49
3 years.....	19.6	50	20.3	52
4 years.....	20.0	51	21.0	53
5 years.....	20.3	52	21.7	55

\* From Waldo E. Nelson (Editor), *Mitchell-Nelson Textbook of Pediatrics*, Ed. 5, 1950; courtesy of W. B. Saunders Co., Philadelphia.

but any variety of grave illness, severely compromises physical growth.

# PEDIATRIC PATHOLOGY

TABLE 6\*

*Organ weights in relation to age and body length*

Age	Body Length	Heart	Lungs		Spleen	Liver	Kidneys		Brain
			Right	Left			Right	Left	
	cm.	gm.	gm.	gm.	gm.	gm.	gm.	gm.	gm.
Birth to 3 days.....	49	17	21	18	8	78	13	14	335
3 to 7 days.....	49	18	24	22	9	96	14	14	358
1 to 3 weeks.....	52	19	29	26	10	123	15	15	382
3 to 5 weeks.....	52	20	31	27	12	127	16	16	413
5 to 7 weeks.....	53	21	32	28	13	133	19	18	422
7 to 9 weeks.....	55	23	32	29	13	136	19	18	489
9 to 3 months.....	56	23	35	30	14	140	20	19	516
4 months.....	59	27	37	33	16	160	22	21	540
5 months.....	61	29	38	35	16	188	25	25	644
6 months.....	62	31	42	39	17	200	26	25	660
7 months.....	65	34	49	41	19	227	30	30	691
8 months.....	65	37	52	45	20	254	31	30	714
9 months.....	67	37	53	47	20	260	31	30	750
10 months.....	69	39	54	51	22	274	32	31	809
11 months.....	70	40	59	53	25	277	34	33	852
12 months.....	73	44	64	57	26	288	36	35	925
14 months.....	74	45	66	60	26	304	36	35	944
16 months.....	77	48	72	64	28	331	39	39	1010
18 months.....	78	52	72	65	30	345	40	43	1042
20 months.....	79	56	83	74	30	370	43	44	1050
22 months.....	82	56	80	75	33	380	44	44	1059
24 months.....	84	56	88	76	33	394	47	46	1064
3 years.....	88	59	89	77	37	413	48	49	1141
4 years.....	99	73	90	85	39	516	58	56	1191
5 years.....	106	85	107	104	47	596	65	64	1237
6 years.....	109	94	121	122	58	642	68	67	1243
7 years.....	113	100	130	123	66	680	69	70	1263
8 years.....	119	110	150	140	69	736	74	75	1273
9 years.....	125	115	174	152	73	756	82	83	1275
10 years.....	130	116	177	166	85	852	92	95	1290
11 years.....	135	122	201	190	87	909	94	95	1320
12 years.....	139	124			93	936	95	96	1351

\* From J. M. Coppelletta and S. B. Wolbach, *Body Length and Organ Weights of Infants and Children*, American Journal of Pathology, 9: 55, 1933; courtesy of American Journal of Pathologists, Cincinnati.

## Disturbances of Physical Growth

**Dwarfism.** A dwarf is any man of less than 130 cm. in height or any woman of less than 122 cm. In most instances, the failure to achieve normal stature is secondary to some more basic disorder. This is apparent from the following classification:

### Classification of Dwarfism

- I. Primary (true, essential, ateleiotic) dwarfs.
- II. Dwarfism secondary to endocrine disorders:
  - A. Pituitary:

1. Without lesions of the gland (functional).
2. With destructive lesions of the pituitary gland.
- B. Hypothyroidism:
- C. Gonadal dysgenesis (ovarian agenesis, Turner's Syndrome):
  1. Pseudohypoparathyroidism (Albright's Syndrome):
- D. Adrenal dysgenesis:
  1. Adrenal hypoplasia.
  2. Mixed adrenal disease (adrenal hyperplasia).

- III. Renal dwarfism:
  - A. deToni-Fanconi disease.
  - B. Nephrocalcinosis with rickets and dwarfism.
  - C. Congenital malformations of the kidney or urinary tract.
  - D. Chronic primary renal disease.
- IV. Metabolic disorders associated with dwarfism:
  - A. Rickets.
  - B. Malnutrition.
  - C. Inborn errors of metabolism:
    - 1. Cystinosis.
    - 2. Glycogen storage disease.
    - 3. Gargoylism.
    - 4. Cystic fibrosis of the pancreas.
- V. Skeletal disorders associated with dwarfism:
  - A. Achondroplasia.
  - B. Chondrodystrophies.
  - C. Osteogenesis imperfecta.
- VI. Infectious diseases associated with dwarfism:
  - A. Congenital syphilis.
  - B. Tuberculosis, especially of the vertebrae.
  - C. Chronic debilitating disease in infancy and childhood.
  - D. Toxoplasmosis.
- VII. Miscellaneous conditions associated with dwarfism:
  - A. Leprechaunism.
  - B. Lawrence-Moon-Biedel Syndrome.
  - C. Progeria.
  - D. Various other congenital malformations.
  - E. Congenital heart disease.
  - F. Chondroectodermal dysplasia (Ellis-van Creveld's Syndrome).

Dwarfism associated with specific lesions of various organs, or with known functional disorders, is discussed in the specific sections of this book devoted to these disorders.

**Primary Dwarfism.** The cause of primary dwarfism is unknown, but the supposition that it is of genetic origin is indicated by a strong familial tendency. Frequently, several siblings are affected and the condition may occur in several consecutive generations. The true dwarf can usually be recognized at birth by his diminutive stature; however, some are of normal size. Some manifest genital infantilism, but in others,

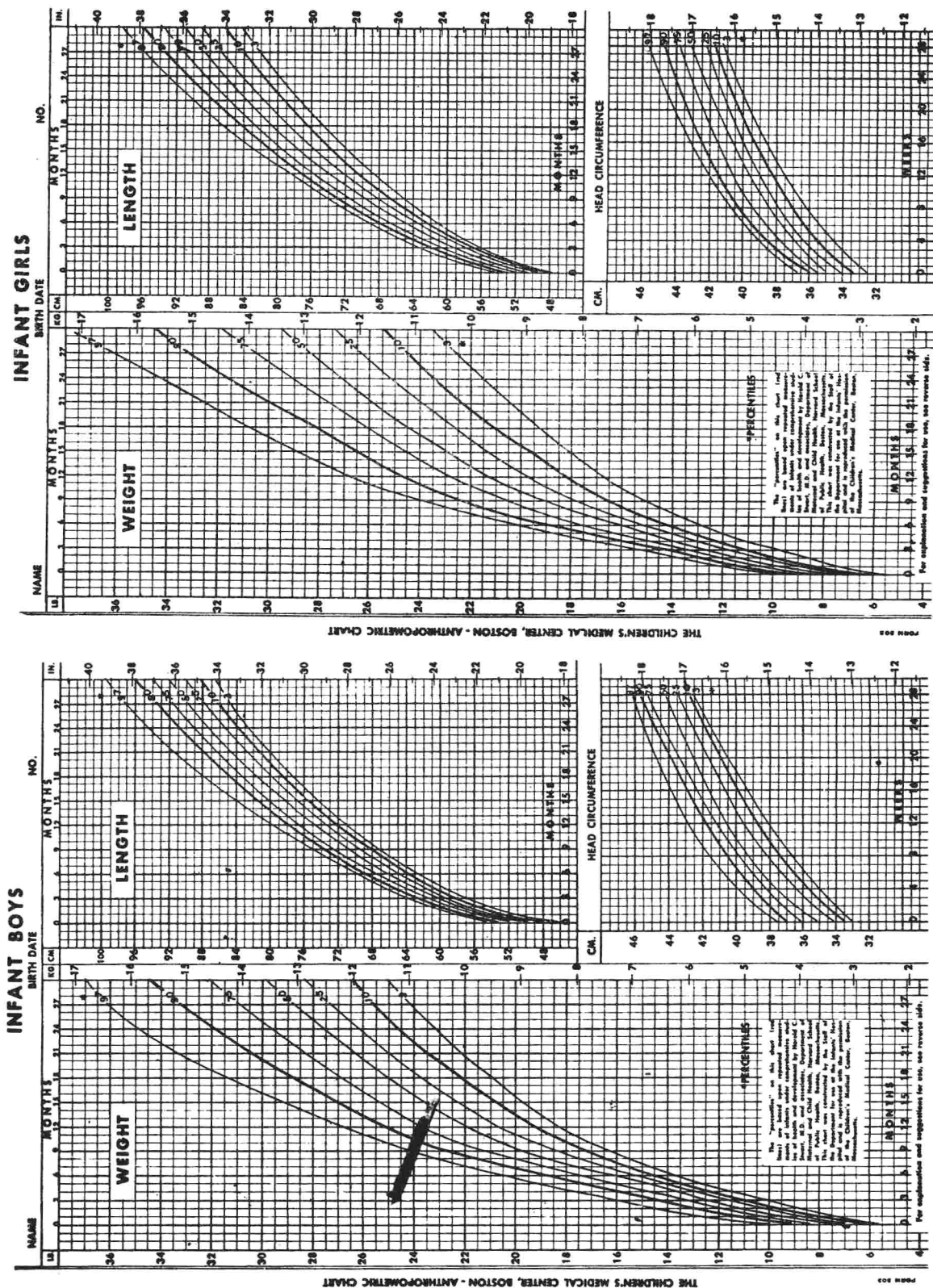
the genitalia, when the child ages, are diminutive counterparts of the adult organs. The body proportions remain essentially those of a child and the secondary sexual characteristics are not marked. Osseous development is essentially normal, except that the epiphyses remain open even until advanced age and the bone age is consequently retarded. By x-ray it can be seen that the nasal sinuses also retain their juvenile appearance. The bones of the pituitary dwarf appear to be weaker than normal bones, however, and abnormalities of form and of the epiphyses are found in the weight-bearing bones. The head of the femur may be flattened and resemble Legg-Perthe's disease.

Despite genital infantilism and inapparent secondary sexual development, several matings productive of offspring have been recorded. Some of these offspring have been of normal size and developed normally, but there is at present insufficient data to determine the incidence of dwarfism in the children of dwarfs.

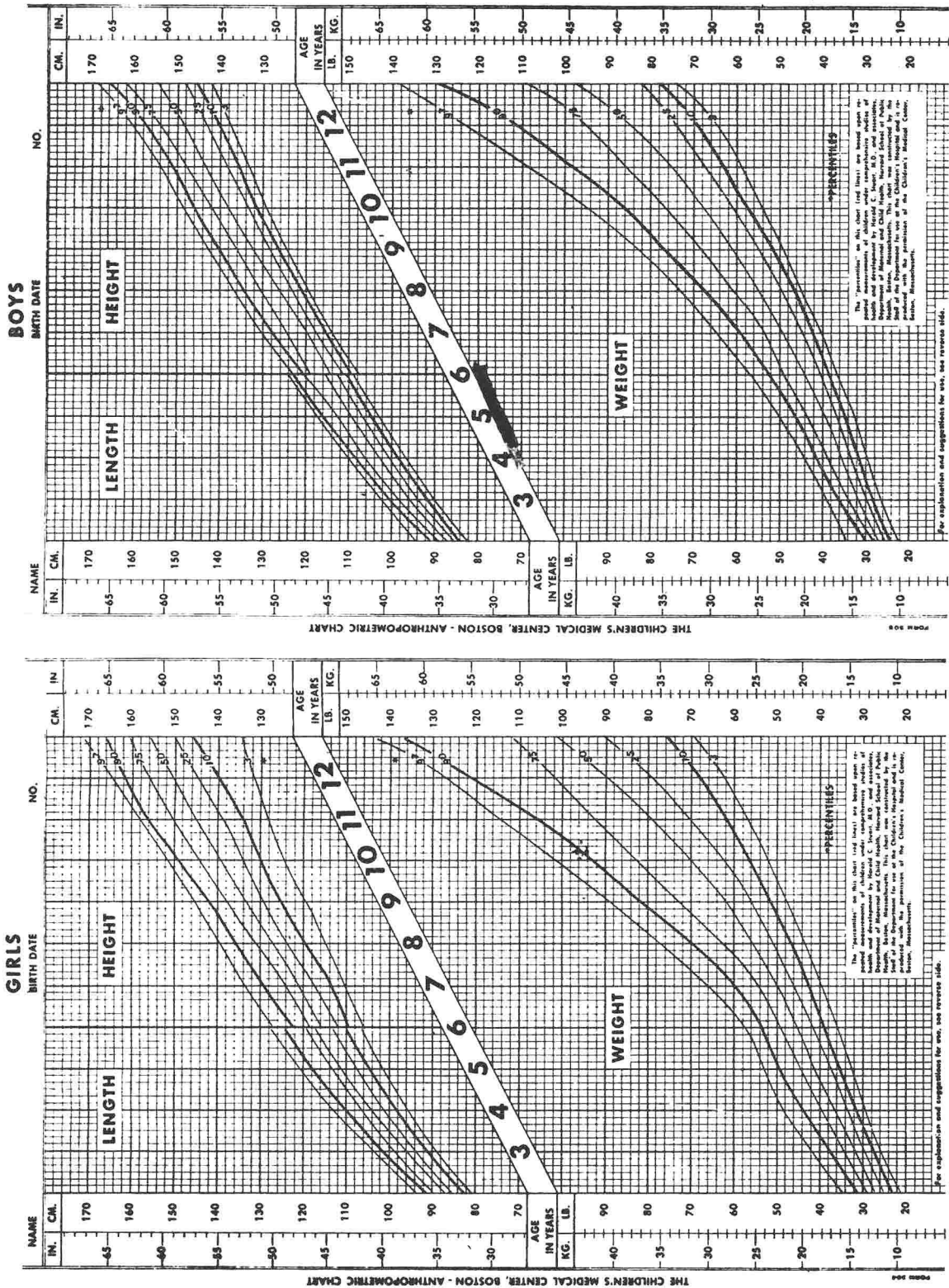
Extremely few anatomic studies have been done on true dwarfs, and the results of those which have been published are confusing. In some dwarfs, cystic degenerative changes of the pituitary have been described, but the question as to whether such individuals were true dwarfs or pituitary dwarfs has never been adequately settled.

We have examined at postmortem only one infant we believed to be a true dwarf. This female child was borne of a normal mother, after a normal gestational period, and weighed 2500 gm. at birth. Very soon it was noted that, although she ate well and her intellectual development appeared to be progressing normally, she simply failed to grow. At 10 months of age she died after a brief illness, the nature of which was never determined. She weighed, at that time, 3350 gm. Innumerable histologic and histochemical studies were done on all organs, but no abnormalities were discovered. The organ weights were those of a normal 3300-gm. infant, but all the organs were noted to be histologically mature.

**Gigantism.** Unlike dwarfism, gigantism has no defined limit and, therefore, a condition of "primary gigantism" cannot exist. Furthermore, the true growth potentialities of the human race are



Figs. 1 and 2. Somatic characteristics of infant boys and girls, and the range of variation, in relation to age. (Courtesy of Dr. Harold C. Stuart and associates and the Children's Medical Center, Boston.)



Figs. 3 and 4. Somatic characteristics of older boys and girls, and the range variation, in relation to age. (Courtesy of Dr. Harold C. Stuart and associates and Children's Medical Center, Boston.)