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CRANIOFACIAL DEVELOPMENT WITH
VITAMIN D RESISTANT RICKETS

A Thesis, embodying original work, submitted
in partial fulfilment of the requirements for
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INTRODUCTION

In this thesis the effect of the metabolic disease, Vitamin D resistant rickets (Vit D. R.R.) on craniofacial growth is examined.

The significance of vitamin D to the formation and continued viability of the animal body is well recognised. For this thesis it has been necessary to trace this significance in some detail by reviewing studies on growth and metabolism of bone tissue and its frequent precursor, cartilage. This has been necessary in that it must form the basis for the clinical study of the metabolic disease, Vit.D. R.R.

The present work sought to confirm that individuals affected by the disease did in fact evidence characteristic deformities of the jaw and skull, just as they did in the long bones of their lower extremities. At the same time, working from a knowledge of the basic disease process, and employing present day theory of jaw and skull growth, predicted abnormality could be compared with the observed abnormality.

Whilst not necessarily expecting to prove or disprove a theory, the clinical condition of Vit.D R.R. and the numbers of patients available, provided a rare opportunity to test theories and deductions relating to dento-facial growth.

VITAMIN D DEFICIENCY RICKETS (VIT.D D.R.)

Harris L.J. 1956 (34) presents an excellent chronological survey of the recognition and development of treatment for rickets; the following historical survey is taken from his work.

The first detailed description of rickets appeared in 1650 in the book "De Rachitide" by F. Glisson of Cambridge. Because of investigation of rickets by English workers or because of the special prevalence of rickets in England it became known in Central Europe as the English disease "die englische Krankheit".

The use of cod-liver oil as a treatment for rickets dates back to 1782.

Jules Guerin in 1838 was able to produce rickets in experimental animals, puppies. He substantiated the theory that rickets arose from a faulty diet.

The suggestion of a vitamin deficiency causing rickets was made by F.G. Hopkins; he said: "In diseases such as rickets, and particularly in scurvy, we have had for long years knowledge of a dietary factor; but though we know how to benefit these conditions empirically, the real errors of the diet

are to this day quite obscure. They are, however, certainly of the kind which comprises these minimal qualitative factors that I am considering."

Funk also in 1912 propounded his "Vitamine Hypothesis". He postulated the existence of separate anti-beriberi, anti-scurvy, anti-rickets and anti-pellagra "vitamines".

The recognition of the vitamins occurred in this period. Osborne and Mendel in 1913 and McCollum and Davies in 1913 identified vitamin A as being present in cod-liver oil and curing xerophthalmia and restoring normal growth in rats. Eijkman, in 1890, identified vitamin B in rice, bran and wholemeal cereals and found it cured beriberi. Holst and Frolich in 1907, 1917 found vitamin C, from fresh fruits, cured scurvy.

In 1918 E. Mellanby found that rickets could be prevented by such fats as cod-liver oil - as was already known - but not by various vegetable oils, such as linseed or olive oil.

American workers in 1921 found experimental rickets could be produced by an imbalance of the mineral elements in the diet. In 1922 McCollum et. al. separated the anti-rachitic factor, renamed

vitamin D₁ from vitamin A proper. The main points of distinction between the vitamins A and D were differences in distribution and differences in stability to heat. This form of vitamin D is now known as vitamin D₂.

In 1890 Palm had pointed out that rickets was most prevalent wherever sunlight was deficient. Huldshinsky (1919) found that rickets could be cured by artificial light therapy; then in 1924 it was found that irradiation of the rachitic animal's food was also effective. It was correctly deduced at this time that the irradiation activated a vitamin precursor in the skin or food.

The pure vitamin formed by the activation of the provitamin was isolated and officially named ergocalciferol. Askew et. al. 1931 and Windans 1931 were responsible for its isolation.

By 1933 it was realised the vitamin found in the greatest amount in cod-liver oil was not identical with that formed by irradiating ergosterol. This form of the vitamin, named D₃, can be obtained artificially by irradiating 7-dehydrocholesterol. Its new name is cholecalciferol. This is the vitamin produced in the animal body by the action of ultra-violet rays.

Public Health measures have been taken by government authorities in many countries to guard against risks of widespread deficiency of vitamin D in infants and nursing mothers.

The result is that severe rickets, so prevalent in certain areas at the start of this century, has been almost completely eliminated. Mild rickets may still remain, however.

Vitamins can be defined as substances that are present in food in relatively minute proportions and are distinct from the main components of the food. They are necessary for the normal nutrition of the animal organism, and their absence results in a specific deficiency disease.

Rickets is the specific deficiency disease resulting from the absence of vitamin D. It is seen principally in early childhood, and is characterised by inadequate calcification of the bony structures, especially the newly forming bone. This results in a liability to bony abnormalities and deformities such as enlarged epiphyses; knock knees or bowed legs. The characteristic bio-chemical abnormalities are the low levels of blood phosphate and sometimes blood

calcium, and in active rickets the raised blood phosphatase level.

The administration of vitamin D to patients suffering from vitamin D D.R. initiates a rise in the levels of blood calcium. Calcification of bones returns to normal and most deformities are spontaneously corrected.

VITAMIN D RESISTANT RICKETS (VIT.D R.R.)

Tapia et. al. 1964 (74) report that rickets due to hypovitaminosis D is now rare in America even in infants. Intestinal malabsorption being the only common cause of deficiency rickets. Rickets in children is usually caused by metabolic defects, such as those involving the renal tubules.

Roentgenographically, all forms of metabolic rickets resemble infantile vitamin D deficiency rickets. Differential diagnosis depends on the analysis of serum biochemistry.

In the most common form of metabolic rickets, often called "rickets resistant to vitamin D", the chief finding is persistent hypophosphatemia. There is little agreement as to the cause of this disturbance and no assurance that all patients conform to the one disease pattern.

The fault may be sex linked, dominant or recessive and it has also been reported sporadically. Some sporadic cases may be so classed from lack of sufficient information of the family history to confirm an inheritance pattern.

It is usually considered that the metabolic defect lies in the mechanism of reabsorption of

phosphorous from the renal tubules, but not all investigators have found evidence of such a defect. A defect of phosphate reabsorption may be an isolated lesion, or it may occur with other specific functional tubular lesions e.g. renal glycosuria or aminoaciduria.

The concept that vitamin D resistant rickets differed from vitamin D D.R. only in its response to normal doses of vitamin D was put forward by Albright when he discovered the healing effects of massive doses of vitamin D.

Since Albright's publication, evidence has accumulated that, although this form of rickets resembles vitamin D D.R., the bone tissue of these patients is not normal.

The high doses of vitamin D and the persistent hypophosphatemia distinguish this metabolic rickets from vitamin D D.R.

The bio-chemical picture of vitamin D R.R. differs from other forms of possible renal tubular defects with accompanying rickets in that there is no acidosis and no abnormal urinary excretion of other ions, amino acids, sugars or proteins.

Serum alkaline phosphatase is increased.

Absorption of calcium and phosphate from the intestine is very poor. That of calcium is so low that little calcium is excreted in the urine - this also occurs in vitamin D D.R.

As phosphate may be lost excessively in the urine and calcium is largely unabsorbed the amount of mineral available for formation of bone is so low that rickets develops in the growing child.

Treatment is still rather unsatisfactory as reports of recurrence of deformities and occurrence of hypervitimosi are quite common. Growth is often very poor.

Engfeldt et. al. 1956 (20) reported that in the past the histological study of skeletal tissue in vitamin D R.R. has shown similar changes that have been identified with vitamin D D.R.

Studies of metabolism have revealed grossly the same metabolic disturbances in both forms of rickets.

These latter authors have demonstrated by microradiography that compact bone structure was not normalised by massive doses of vitamin D, although almost normal gross mineralisation had resulted. Microradiographically they found enormous variations in calcium content in various areas.

COMPARISONS OF VITAMIN D DEFICIENCY RICKETS AND
VITAMIN D RESISTANT RICKETS - WHERE ACTIVE RICKETS
IS PRESENT IN HYPOPHOSPHATEMIC TYPE

	<u>DIAGNOSIS</u>	<u>Vitamin D Deficiency Rickets</u>	<u>Familial Hypo- phosphatemic Vitamin D Resistant Rickets</u>
<u>CLINICAL</u>			
	restless	+	?
	pale	+	?
	flabby	+	?
	DEFORMITIES		
	- enlarged epiphyses	+	+
	- curvature of long bones	+	+
	- pigeon chest	+	+
	- protruding forehead	+	+
	- large head	+	+
	- spinal	+	+
	decreased growth	+	+
	Family History	NIL	+
<u>LABORATORY</u>			
	Serum calcium	N - low	Normal
	Serum phosphate	low	low
	Serum Alk.Phos.	raised	raised

(11)

<u>DIAGNOSIS</u>	<u>Vitamin D Deficiency Rickets</u>	<u>Familial Hypo- phosphatemic Vitamin D Resistant Rickets</u>
Urinary calcium	low	low
Urinary phosphate	low	high
Other ions in urine	no	no

RADIOGRAPHIC

increased width of epiphyses	+	+
"cupping" of epiphyses	+	+
trabecula pattern	N	Coarse, patchy mosaic
cranial sutures	widened	widened
size of cranium	large	increased antero- posterior length
bossing	+	+
craniostenosis	+	+
	(on healing)	(on healing)
developmental age	N	N $\rightarrow$ retarded
craniotales	+	+

HISTOLOGY

proliferation of epiphyseal cartilage	+	+
calcification of epiphyseal cartilage	no	no
osteoid tissue	wide, un- mineralised	wide, un- mineralised

(12)

<u>DIAGNOSIS</u>	<u>Vitamin D Deficiency Rickets</u>	<u>Familial Hypo- phosphatemic Vitamin D Resistant Rickets</u>
<u>TREATMENT</u>		
vitamin D	increase to N (approx. 400 I.U/day)	massive doses
calcium	N	N - high
phosphate	N	N - high
surgery	seldom	often
<u>PROGNOSIS</u>		
mineralisation	returns to N	improved
deformities	usually spontan- eous correction	very variable
growth	returned to N	remains depressed
hyperviti- mosis	No	constant danger

DIFFERENTIAL DIAGNOSIS OF VITAMIN D RESISTANT RICKETS

Williams et. al. 1966 (85) list the diagnostic criteria for hereditary hypophosphatemic Vit.D R.R. as:

- 1) A familial x-linked dominant inheritance pattern.
- 2) Usually rickets is present but the rickets is not responsive to normal doses of vit. D.
- 3) Hypophosphatemia is present and is used as a diagnostic point of importance. The hypophosphatemia is associated with decreased renal reabsorption of inorganic phosphate ions without other renal abnormalities.
- 4) Diminished gastrointestinal absorption of calcium.

INHERITANCE PATTERN

Winters et. al. 1958 (86) in 1958 reported a genetic study of a large kindred affected by vit.D R.R. They also examined the cases of vit. D R.R. previously reported in the literature to ascertain the method of inheritance. The presence of hypophosphatemia was the essential point in transmission of the disease and not rachitic deformities.

They found an x-linked dominant inheritance pattern in the kindred studied and also in cases reported in the literature.

Winters etc. al. 1958 (86) observed a significant deviation from a 1:1 affected male to female ratio, which supported their proposed pattern of inheritance.

More females should be affected than males since an x-linked trait cannot pass from father to son.

The authors found throughout the kindred examined the affected females suffered less severe deformities than affected males (Fig.1).

Stern 1964 (72) claims the gene responsible for the disease has incomplete penetrance as far as bony rachitic lesions and deformities are concerned, due to some secondary bone formation process, but full

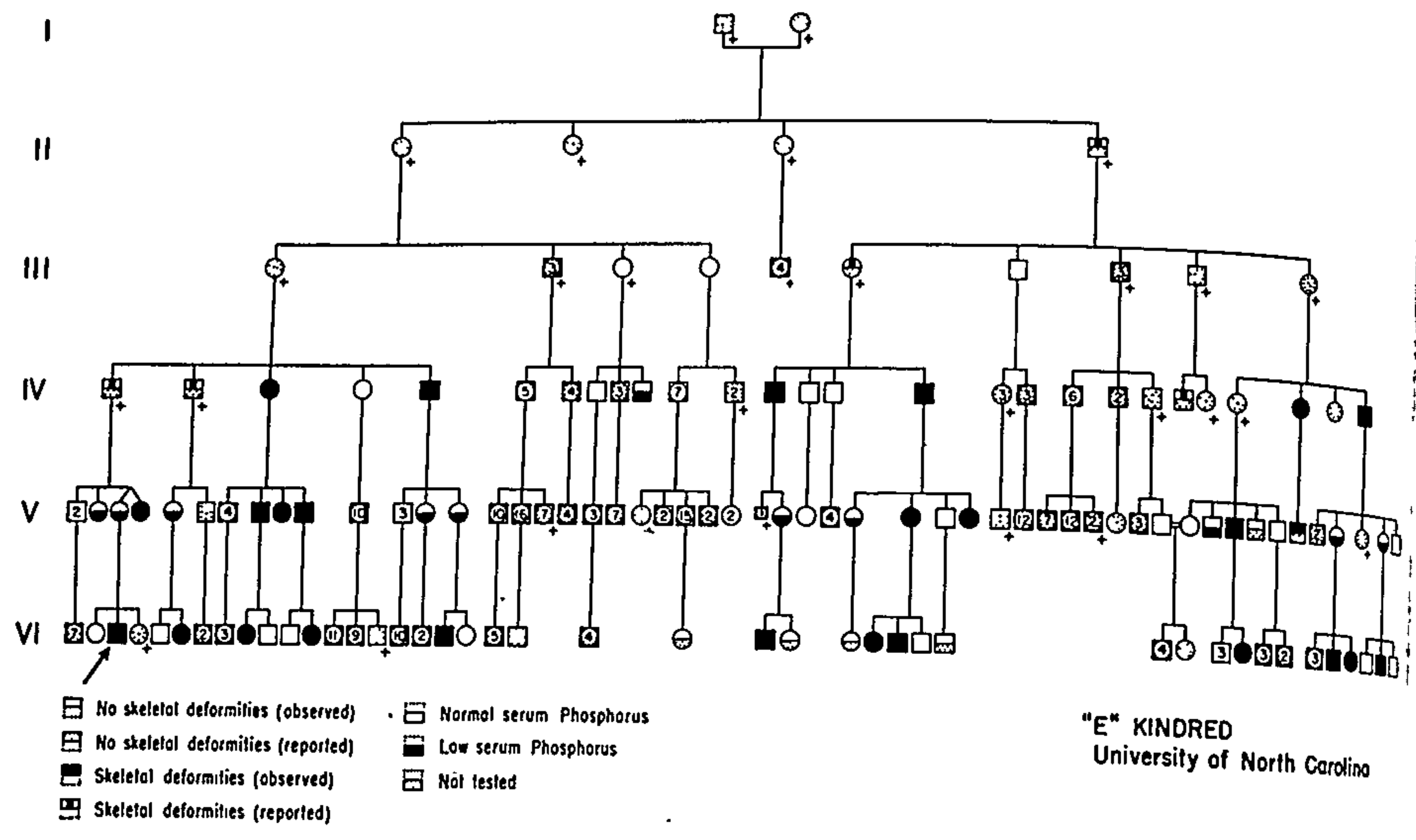


Fig. 1.

FIG. 5. The "E" kindred segregating for vitamin D resistant rickets. The proband is indicated by the arrow.

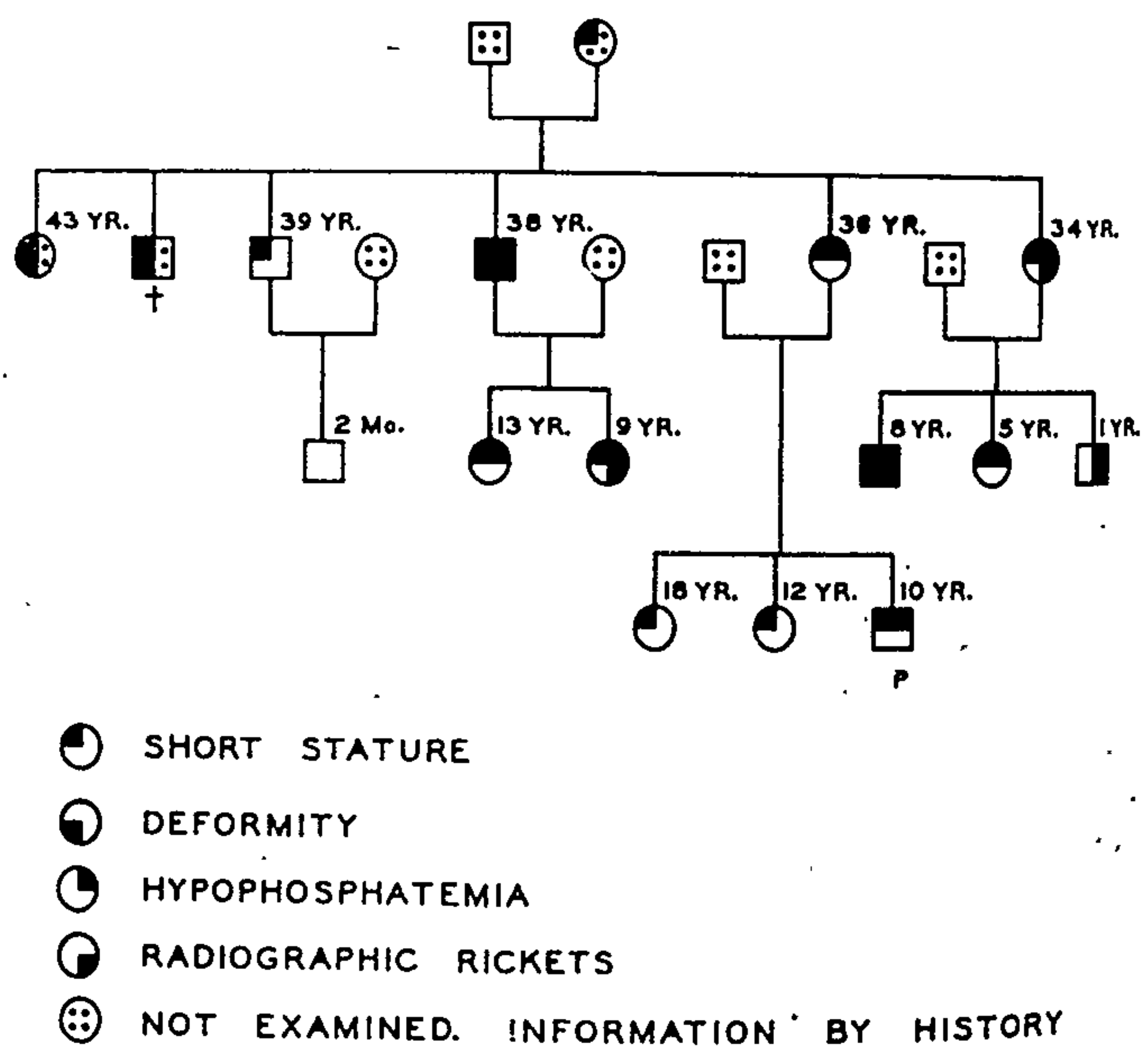


Fig. 2.

Fig 8.—Kindred showing short stature, hypophosphatemia, and rickets in various degrees. The prop-
ositus, K. M. is indicated by P.

penetrance as shown by low serum phosphate levels.

The degree of penetrance is the measure of the reliability with which a genetic trait can be expected to pass to succeeding generations.

Harrison et. al. 1966 (36) state that whilst different patterns of inheritance occur, the phenotypic manifestations are always similar. A patient included as hereditary hypophos. Vit. D R.R. in their group showed male to male transmission through a normal female.

Another patient examined showed the classical x-linked dominant mode of inheritance through three generations (Fig. 2).

HYPOPHOSPHATEMIA

Winters et. al. 1958 (86) and Harrison et.al. 1966 (36) state that hypophosphatemia in hereditary hypophosphatemic Vit. D R.R. is not changed by normal doses of Vit. D. Massive doses of Vit. D, sufficient to produce radiographic healing of the bony lesions, seldom result in an increase in the serum phosphate levels.

Where rachitic lesions are not present in hereditary hypophosphatemia decreased growth still occurs and Harrison et. al. 1966 (36) use this as a diagnostic pointer.

BONE FORMATION

Engfeldt et. al. 1956 (20) as reported above found that mineralised tissue from vit. D R.R. patients could be distinguished from normal mineralised tissue micro-radiographically.

The coarsened trabecula pattern has been attributed to the persistence of a mild mineralisation defect.

TREATMENT OF HEREDITARY HYPOPHOSPHATEMIC
VITAMIN D RESISTANT RICKETS.

Albright et. al. 1937 (2) showed that massive doses of vit. D could control the active rachitic lesions since then this has been the basis of treatment.

Tapia et. al. 1964 (74) give their method of arriving at a vit. D dosage for each patient after diagnosis has been established.

Firstly a twenty-four hour urine specimen is collected and calcium excretion in relation to body weight and calcium intake is plotted on a chart showing the normal range.

Vitamin D is then given in doses from 50,000 i.u. for young children to 100,000 i.u. for children above 6 years of age. The effect of the dose on urinary calcium excretion is determined every three to five days. If a rise in the urinary calcium does not occur promptly, the dosage is consecutively doubled until a rise is noted. The urinary calcium should rise steadily towards the normal mean at a rate which will bring the urinary calcium to the mean in about four weeks.

As the urine calcium level nears the mean normal

value, the vitamin D dosage is adjusted downwards usually by 25,000 units at a time, so that the 24 hour urine calcium remains approximately at the normal mean value for the child's weight and calcium intake.

Urine calcium values 3 standard deviations or more above the mean, are evidence of hypervitaminosis D, whether the serum calcium is elevated or not and the dosage of vit. D must be reduced immediately.

Radiographic changes do not appear early in treatment and often after a month of adequate treatment no evidence of healing of bone lesions can be observed.

The initially established dosage must be constantly reviewed as the requirements of vit. D vary during the child's life. The preadolescent growth spurt normally requires an increase in dosage of vit. D.

Tapia et. al. 1964 (74) prescribe "a good diet, containing a quart of milk products", to ensure an adequate calcium intake.

Stearns found the estimation of urinary calcium as a test for the adequacy of the vit. D therapy as described above, is the most sensitive indicator

available. As the range between the necessary dosage and overdosage is always narrow, urinary calcium estimations should be performed regularly throughout treatment.

The abnormal rise in urinary calcium from over-treatment precedes a rise in serum calcium by days or weeks. Acute hypervitaminosis D occurs after operative procedures involving immobilisation of the patient unless the vit. D is discontinued for a time before operation.

The improved accuracy of treatment from urinary calcium estimations against serum calcium variations is demonstrated in Fig 3 from Tapia et. al. 1964 (74) of the biochemical data during the course of therapy of one of their patients.

Tapia et. al. 1964 (74) state that after completion of growth, patients in whom the disease is mild, may maintain normal urinary calcium excretion without continued treatment with vit. D. Others, whose vit. D requirements during growth is very high, may always need additional vit. D, although less than they needed during growth. During pregnancy and menopause the danger of osteomalacia may be very real.

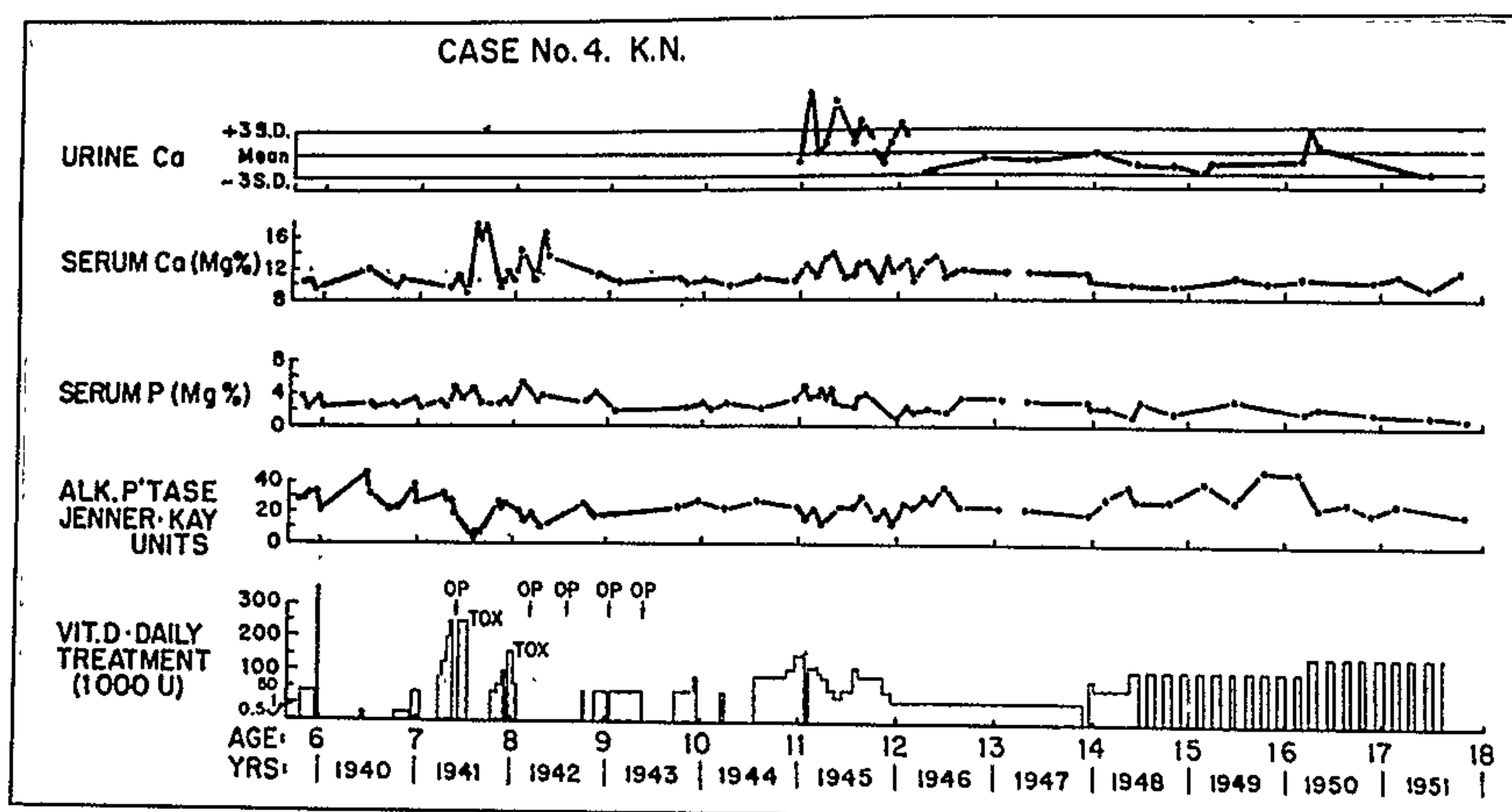


Fig. 3

FIG. 3
Chemical data during the entire course of therapy (Case 4, K. N.) from 1939 to 1951, showing treatment with vitamin D when guided by serum calcium values and when determined by urinary calcium levels. Interrupted vitamin-D therapy blocks indicate irregular therapy at home.

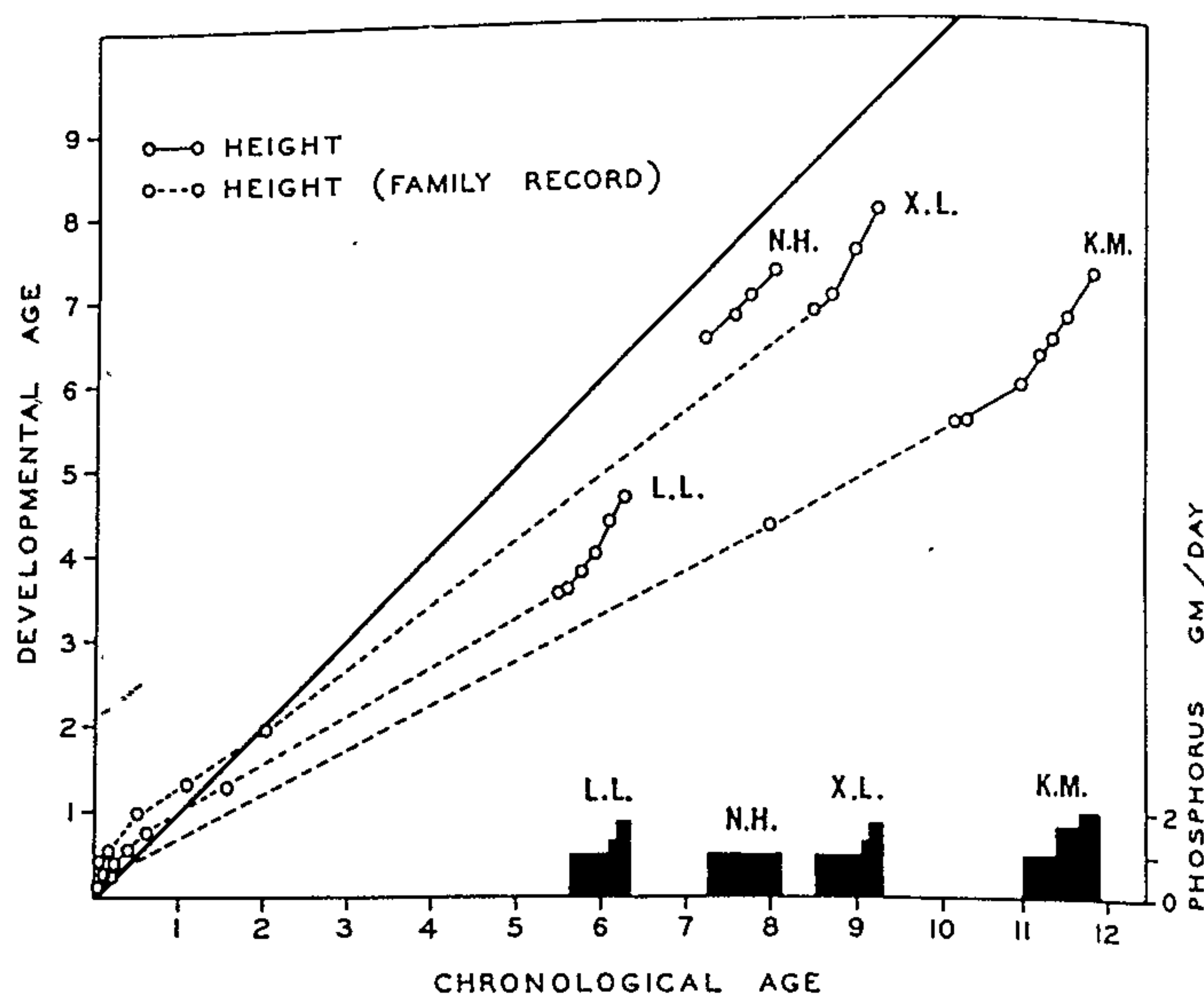


Fig. 4

Fig 9.—Growth graphs of K. M. and three cousins before and during period of oral phosphate treatment. The height is expressed as height-age in relation to the normal development age. The period of phosphate treatment is shown by the *solid black blocks* along the abscissa. The heights recorded for the period before the first visit to the clinic were obtained from records kept by the families. These are shown by *dashed lines*.

Treatment is thus a long term problem and the needs of the individual must be assessed throughout life.

No patient exhibits completely satisfactory growth but results in the younger patients show that deformity and dwarfism are no longer stigmata of the disease.

Harrison et. al. 1966 (36) produced an acceleration in growth rate by supplementing the diet with phosphate. The patients involved were suffering with dwarfism and hypophosphatemia but were without rachitic lesions. The changes produced are shown in Fig. 4.

Tapia et. al. 1964 (74) found that the severe leg deformities observed in untreated patients on admission usually improved with adequate vit. D therapy. However, a complete correction was never observed.

In their earlier patients, operative procedures were undertaken before the strict regulation of vit. D dosage was possible. In these cases the deformities usually recurred.

In patients with adequate vit. D therapy, the surgical corrections were permanent, even in patients operated on at seven years of age.

They found tibial corrections more stable than femoral corrections.

(TABLE 1).

TABLE II

RESULTS OF OSTEOTOMY FOR CORRECTION OF BONE DEFORMITIES IN VITAMIN-D RESISTANT RICKETS UNDER INADEQUATE VITAMIN-D THERAPY*

Case	Osteotomy		Result	Postoperative Observation
	Age (Years)	Site		
E.G.	4	R. mid. tibia	Correction	15 years
	4	L. mid. tibia	Correction	15 years
E.T.	6	R. dist. femur	Recurrence	46 years
R.Y.	6	R. mid. tibia	Correction	21 years
	6	L. mid. tibia	Correction	21 years
K.N.	8	R. dist. femur	Recurrence	19 years
	8	L. dist. femur	Recurrence	19 years
	8	R. prox. tibia	Recurrence	9 years
	8	L. prox. tibia	Recurrence	9 years
	8	R. dist. femur	Recurrence	9 years
	8	L. dist. femur	Recurrence	9 years
L.B.	9	R. prox. tibia	Recurrence	10 years
	9	L. prox. tibia	Recurrence	10 years
C.M.	12	R. dist. femur	Correction	7 years
	12	L. dist. femur	Correction	7 years
	12	R. mid. tibia	Correction	7 years
	12	L. mid. tibia	Correction	7 years
E.T.	13	R. prox. tibia	Correction	39 years

* Two patients (E.G. and L.B.) are also in Table III since late osteotomies were necessary.

Table 1

TABLE III

RESULTS OF OSTEOTOMY FOR CORRECTION OF BONE DEFORMITIES IN VITAMIN-D RESISTANT RICKETS UNDER ADEQUATE VITAMIN-D THERAPY*

Case	Osteotomy		Result	Postoperative Observation
	Age (Years)	Site		
A.K.	7	R. mid. tibia	Correction	19 years
V.Y.	7	L. mid. tibia	Correction	19 years
	13	L. dist. femur	No correction**	5 years
R.V.	16	L. prox. tibia	Correction	2 years
	16	R. dist. femur	Correction	6 years
E.G.	17	L. dist. femur	Correction	5 years
	18	L. prox. tibia	Correction	6 years
L.B.	17	R. prox. tibia	Correction	5 years
	17	R. dist. femur	Correction	3 years
	17	L. dist. femur	Correction	3 years
	17	R. prox. tibia	Correction	3 years
R.V.	23	L. prox. tibia	Correction	3 years
	23	R. prox. tibia	Correction	6 months
	23	L. prox. tibia	Correction	6 months

* Two patients (E.G. and L.B.) are also included in Table II since early osteotomies were performed under inadequate vitamin-D therapy.

** Incomplete surgical correction.

GROWTH IN HYPOPHOSPHATEMIC VITAMIN DRESISTANT RICKETS

Retarded linear growth has been constantly reported with this disease. (Winters 1958 (86), Harrison 1966 (36), Tracey and Campbell 1968 (77) Steendijk 1962 (73).) These authors have found reduced stature in patients who have not suffered the bone lesions of rickets and have no deformities. The patients all exhibited hypophosphatemia.

Until recently quantitative measurements of growth in vit. D R.R. were scarce. This is probably due to the small number of patients available for each study. More recently the patients' progress has been recorded on height and weight charts showing their relation to the normal population.

Harrison et. al. 1966 (36) found normal growth in the first six months of life then an obvious retardation in growth. Two characteristic height and weight charts are presented below - Figs. 5 and 6.

Winters et. al. 1958 (86) compiled a summary of the findings in cases reported in the literature previous to their study. (TABLE 2). This table shows height to be reduced more often than weight.

Tracey and Campbell 1968 (77) found standing

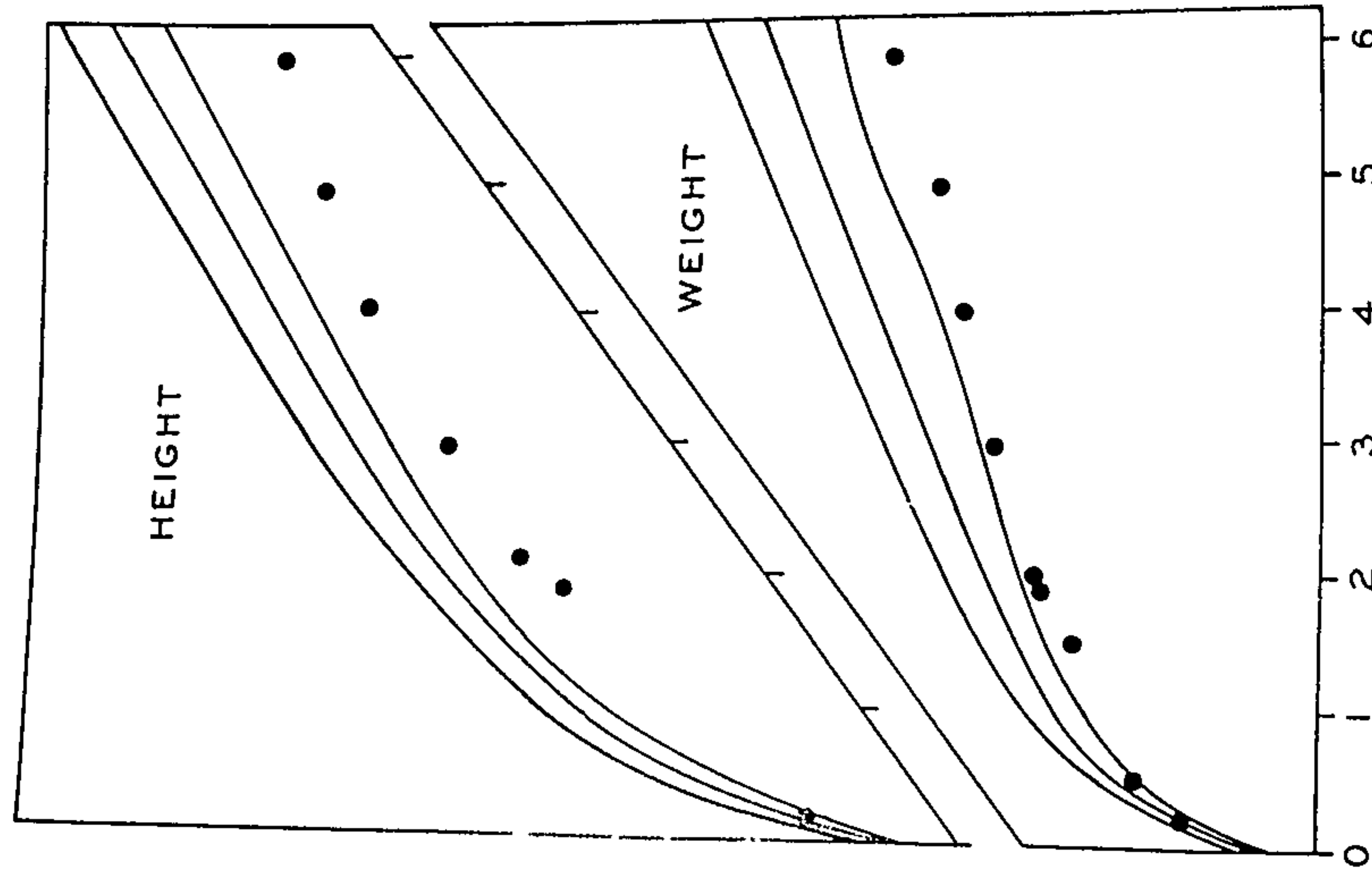


Fig 3.—Growth in height and weight of patients with hereditary hypophosphatemia, H. N. III, birth to 2 years of age.

Fig. 6

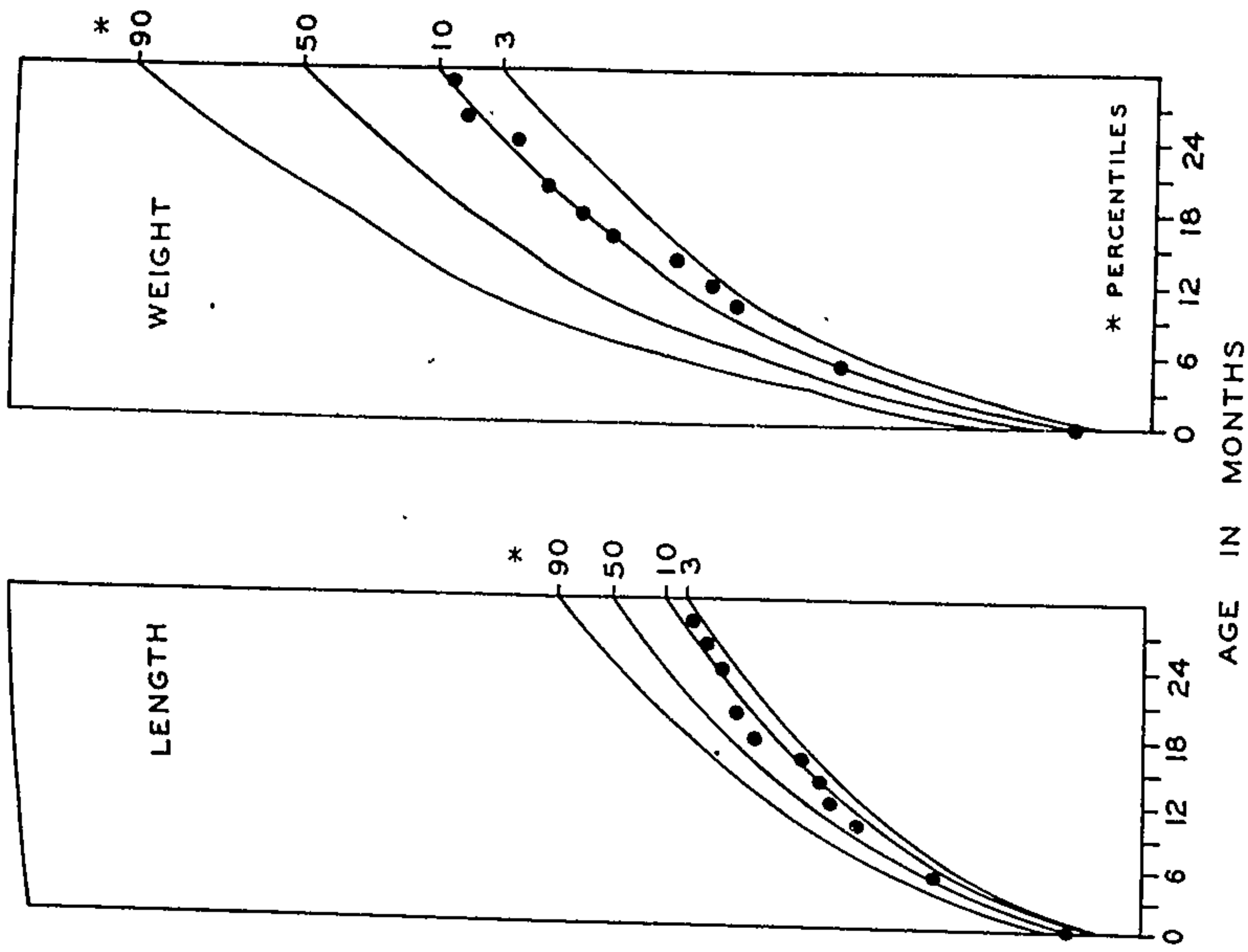


Fig 2.—Growth in height and weight of patient with hereditary hypophosphatemia, O. T., birth to 2 years of age showing slackening of growth beginning during second six months of life.

Fig. 5

TABLE 1.
Summary of Previously Reported Cases in Children

Author	Ref.	Sex	Age at		Deformities*			Ht. †	Wt. ‡	Family History	Ca (mg %)	P (mg %)	Alkaline Phosphatase§	Associated Findings
			Onset	Report	Stall	Wrist	Heel							
Albright <i>et al.</i>	(2, 3, 5)	M	15 m.	16 y.	+	+	+	—	+	—	7.0-10.5	1.8-3.0	16.2 B.U.	
Hughman and Hamilton	(94)	F	2 y.	5 y.	+	+	+	—	+	—	9.6-11.2	1.8-2.7	16.2 B.U.	
Gill	(71)	M	1 y.	4 y.	+	+	+	—	+	—	10.5	2.1	78.7 U.	
Lele	(118)	M	9 m.	3 y.	+	+	+	—	+	—	8.3	2.2	45 B.U.	Mental retardation
Bakwin <i>et al.</i>	(9)	M	6 y.	17 y.	+	+	+	N	N	+	10.1-11.1	1.9	200-250 V.L.U.	Convulsions, 3 m. to 5 y.
Christensen	(33)	M	2 y.	15 y.	+	+	+	—	+	—	ca. 10	ca. 2.1	175-225 V.L.U.	
Christensen	(33)	F	13 m.	13 y.	+	+	+	—	+	—	ca. 10	ca. 2.5	148.7 U.	
Bowau and Lohr	(18)	M	18 m.	2 y.	+	+	+	—	+	—	7.7	2.4	148.7 U.	
Bowau and Lohr	(18)	M	3 y.	4 y.	+	+	+	—	+	—	10.1	2.9	148.7 U.	
McCune	(133)	F	18 m.	9 y.	+	+	+	—	+	—	ca. 10	1.5	15 B.U.	
McCune	(133)	F	18 m.	9 y.	+	+	+	—	+	—	ca. 10	1.5	15 B.U.	
Gunther <i>et al.</i>	(77)	M	2 y.	17 y.	+	+	+	—	+	—	10-11.2	2.0-2.7	7.8-11.8 U.	
Mackay and May	(125)	F	15 m.	7 y.	+	+	+	—	+	—	7.2	2.9	110 K.A.U.	"Flts", 4 m. to 18 m.
Mackay and May	(126)	F	18 m.	17 y.	+	+	+	—	+	—	"N"	2.5-2.6		
Löwy	(124)	M	1 y.	4 y.	+	+	+	—	+	—	10.1	2.8		
Carlson	(29)	M	15 m.	9 y.	+	+	+	—	+	—	10.1	2.3		
Camerer	(28)	F	15 m.	9 y.	+	+	+	—	+	—	11.0	2.2	465 U.	Mental retardation
Woolley	(206)	M	20 m.	2 y.	+	+	+	—	+	—	<8.0	1.3	20 B.U.	
Lindsay	(119)	F	10 m.	4½ y.	+	+	+	—	+	—	11.8	2.2	27.3 K.A.U.	
Lindsay	(119)	F	10 m.	8 y.	+	+	+	—	+	—	10.0	2.4	31.1 K.A.U.	
Freeman and Dunaky	(68)	F	14 m.	6 y.	+	+	+	—	+	—	11.3	2.5	19 B.U.	
Holt	(97)	M	Infancy	15 m.	+	+	+	—	+	—	9.5	3.8	17 K.A.U.	
Holt	(97)	F	18 m.	5 y.	+	+	+	—	+	—	10.3	2.4	13.9 K.A.U.	
Holt	(97, 122)	F	10 m.	4 y.	+	+	+	—	+	—	10.9	2.5	19.2 K.A.U.	
Holt	(97)	F	14 m.	3 y.	+	+	+	—	+	—	"N"	"L"		
Holt	(97)	M	10 m.	15 y.	+	+	+	—	+	—	8.6-9.7	2.7-2.8		
Powell	(153)	M	2 y.	3½ y.	+	+	+	—	+	—	15.2†	2.2	72 K.A.U.	
Imerslund	(101)	M	1 y.	5 y.	+	+	+	—	+	—	10.9	2.8	14.3 B.U.	
Pedersen and McCarroll	(147)	M	11 m.	4 y.	+	+	+	—	+	—	11.2	2.4	28 B.U.	
Pedersen and McCarroll	(147)	F	16 m.	5 y.	+	+	+	—	+	—	10.8	2.0	18 B.U.	
Pedersen and McCarroll	(147)	F	17 m.	3 y.	+	+	+	—	+	—	10.5	2.1	15 B.U.	
Faneoni and Girardet	(59, 192)	M	1½ y.	6 y.	+	+	+	—	+	—	10.4	2.5	12.6 B.U.	
Faneoni and Fote	(36)	M	2 y.	7 y.	+	+	+	—	+	—	10.2	2.0	31 K.A.U.	Celiac disease in infancy
Coleman and Foot	(145)	M	11 m.	3 y.	+	+	+	—	+	—	8.2	2.8	6.9-19.5 U.	Craniosynostosis
Paul	(145)	M	11 m.	3 y.	+	+	+	—	+	—	11.0	1.8	72 K.A.U.	Intermittent diarrhea in infancy
de Wet	(202)	F	10 y.	15 y.	+	+	+	—	+	—				
de Wet	(202)	F	10 y.	15 y.	+	+	+	—	+	—				
Winberg <i>et al.</i>	(203)	F	8 m.	5 y.	+	+	+	—	—	—	9.3	1.7	106 K.A.U.	Albinism
Winberg <i>et al.</i>	(203)	M	20 m.	6 y.	+	+	+	—	—	—	8.9-9.8	1.0-3.5	131 Bu U.	Albinism
Gregerson	(74)	F	12 m.	8 y.	+	+	+	—	—	—	10.2-11.8	2.1-4.4	131 Bu U.	Albinism
Peterson	(149)	M	Birth	19 m.	+	+	+	—	—	—	10.3	2.2	35 Bu U.	
Peterson	(149)	F	2 y.	3 y.	+	+	+	—	—	—	10.7	3.1	9.2 B.U.	
Swoboda	(187)	M	1½ y.	8½ y.	+	+	+	—	—	—	9.1-11.5	2.8-4.3	2.8 K.A.-7.1 B.U.	
Swoboda	(187)	F	3 y.	12½ y.	+	+	+	—	—	—	10.5	2.8	45 K.A.U.	
Swoboda	(187)	M	1½ y.	11 y.	+	+	+	—	—	—	10.0	2.4	63 K.A.U.	
Swoboda	(187)	F	1½ y.	2 y.	+	+	+	—	—	—	10.4	2.7	63 K.A.U.	
Swoboda	(187)	M	1 y.	2½ y.	+	+	+	—	—	—	11.0	2.8	108 K.A.U.	
Swoboda	(187)	F	15 m.	6 y.	+	+	+	—	—	—	10.0	2.1	108 K.A.U.	
Swoboda	(187)	F	1½ y.	14 y.	+	+	+	—	—	—	11.2	2.7	71 K.A.U.	
Tobler <i>et al.</i>	(192)	F	9 m.	5 y.	+	+	+	—	—	—	11.2	2.5	32 K.A.U.	
Tobler <i>et al.</i>	(192)	F	15 m.	6 y.	+	+	+	—	—	—	10.2	2.9	26.8 B.U.	
Tobler <i>et al.</i>	(192)	F	Early years	8 y.	+	+	+	—	—	—	10.4	2.2	18.1 B.U.	
Tobler <i>et al.</i>	(192)	F	20 m.	5 y.	+	+	+	—	—	—	10.8	3.0	5.7 B.U.	Convulsions in infancy
Tobler <i>et al.</i>	(192)	F	2½ y.	8 y.	+	+	+	—	—	—	11.0	2.3	16.5 B.U.	
Tobler <i>et al.</i>	(192)	F	1 y.	9 y.	+	+	+	—	—	—	10.3	1.8	8.3 B.U.	
Tobler <i>et al.</i>	(192)	F	1½ y.	12 y.	+	+	+	—	—	—	9.3	1.3	24.1 B.U.	
Tobler <i>et al.</i>	(192)	F	2½ y.	11 y.	+	+	+	—	—	—	7.4	2.6	13.9 B.U.	
Mitchell and Mitchell	(134)	F	13 m.	11 y.	+	+	+	—	—	—	9.8	2.4	15.2 B.U.	
Litman <i>et al.</i>	(120)	F	Birth	3½ y.	+	+	+	—	—	—	11.8	1.9	19.2 B.U.	
Litman <i>et al.</i>	(120)	F	2 y.	4 y.	+	+	+	—	—	—	"N"	2.6	"H"	
Litman <i>et al.</i>	(120)	F	21 m.	6 y.	+	+	+	—	—	—	10.6	3.0	35 K.A.U.	
Litman <i>et al.</i>	(120)	F	Age of walking	3½ y.	+	+	+	—	—	—	10.0	1.0	18 B.U.	
Litman <i>et al.</i>	(120)	F	3 y.	4 y.	+	+	+	—	—	—	"N"	"L"	23 K.A.U.	
Litman <i>et al.</i>	(120)	F	3 y.	4 y.	+	+	+	—	—	—	10.1	3.0	13.9 B.U.	
Litman <i>et al.</i>	(120)	M	14 m.	3 y.	+	+	+	—	—	—	9.7	3.3	32.4 K.A.U.	
Daeschner	(41)	F	8 m.	9 y.	+	+	+	—	—	—	10.4	3.7	26 K.A.U.	
Daeschner	(41)	F	8 m.	9 y.	+	+	+	—	—	—	8.6	3.2	25 B.U.	Convulsions in infancy

Criteria for inclusion in this table: (1) development of active rickets despite either prophylactic vitamin D or therapy for deficiency rickets; (2) hypophosphatemia; (3) evidence excluding steatorrhea, glomerular disease, acidosis, and the Fanconi syndrome with reasonable certainty.

* See text for discussion of deformities. A blank space indicates no information or a negative finding.

† Reduction of height below normal indicated by —; normal height for age indicated by +.

‡ Reduction of weight comparable to or greater than reduction of height indicated by —; normal weight or weight reduced to a lesser degree than height indicated by +.

§ B.U. indicates Bodansky units (normal values for children, 3-13 units (187)); K.A.U. indicates King-Armstrong units (normal values for children, 15-20 units (187)); V.L.U. indicates Vermlaren Lundsteen units (normal values for children, 43-147 (187)); Bu U. indicates Buch units.

¶ Prior to 1933, the normal range for B.U. was 5-9 (3).

|| Units not specified, but normal values stated to be 10-12.

** Units not specified, but normal values stated to be 90-310.

†† Receiving vitamin D therapy at time of determination.

Table 2

height to be severely retarded in their patients. (Severe retardation being below the third percentile.) They also noted that sitting height was moderately retarded. (Moderate retardation was scored between the third and fifth percentiles.)

Steendijk 1962 (73) found decreased span values in patients with no clinical deformities of the arms. Radiographic examination revealed slight bowing of the bones of the arms in these patients.

Harrison et. al. 1966 (36) found that the growth retardation which occurred after about 6 months of life was accompanied by lowering of the serum phosphate levels.

In their series of patients only one achieved normal growth. In this case hypervitaminosis D had caused hypercalcemia and nephrocalcinosis resulting in a diminished glomerular filtration rate. This reduced filtration rate allowed the patient to maintain normal serum phosphate levels within the a "normal" range.

Harrison et. al. 1966 (36) mention the possibility that growth retardation is a separate manifestation of the underlying metabolic error. However they feel the close relationship between the

development of hypophosphatemia and growth retardation after about 6 months of normal growth indicates that the phosphate deficiency results in growth retardation. This conclusion is supported by the normal growth in the patient who suffered renal damage which resulted in "normal" serum phosphate levels.

DEVELOPMENT OF DEFORMITIES IN RICKETS

In 1932 Park (59) described the way in which deformities developed in children with rickets. These ideas have not changed or been enlarged upon since that time.

Park states that the degree of involvement of the ends of the long bones is in direct proportion to the rapidity of growth of the epiphyseal cartilage; this also applies to the shaft where the involvement depends on the rate of osteoblastic growth.

This is supported by the clinically observed points of severest deformities.

He described "sitting" deformities which appear in rachitic children before they learn to walk. He states that a rachitic child sits for long periods with his legs crossed and supporting his body weight with his arms. This posture leads to an exaggerated frontal curvature of the radius and ulna and deformities of the leg bones to correspond with the way in which they are crossed while sitting.

Where deformities occur after the child stands, the bends are always sideways - these are "standing" deformities, Fig. 7. If bends are present in the anteroposterior direction then rickets has occurred



Fig. 7

during the sitting stage.

The action of muscles on the development of the deformities is shown in the "sabre shin" deformity.

The achilles tendon pulls the foot backwards and with the softening produced by rickets between the epiphysis and diaphysis the head of the epiphysis is displaced backwards. With growth in length this bend moves higher above the ankle and in the adult it is found near the middle of the shin. This bend can never be above the middle as it originates in the lower end.

The curvature of the humerus occurs slightly above the insertion of the deltoid muscle. Growth at the upper end occurs twice as rapidly as growth at the lower end, so the curvature gradually descends but always remains slightly above the insertion of the deltoid.

Park believed the deformities of the skull resulted from active rickets in the first 6 months of extrauterine life as this is the period of most rapid growth in the bones of the skull.

By dating the time of occurrence of rickets by the deformities produced Winters et. al. 1958 (86)

concluded that most of the previously reported cases had a definite disorder at or shortly after birth.

The most common clinical results of the bony deformities are genu varum - bowlegs - and genu valgum - knockknees.

Coxa vara, - a decrease in the angle between the neck and the shaft of the femur, - and coxa valga - an increase in the angle between the neck and shaft of the femur, - are also quite common.

Steendijk's 1962 (73) measurements of the upper body segment were within a normal range. He states this indicates the growth and shape of the spine was normal.

CRANIOFACIAL AND DENTAL DEVELOPMENT IN
VITAMIN D RESISTANT RICKETS AND VITAMIN D
DEFICIENCY RICKETS.

Tracey and Campbell (77) stated in 1968 that growth studies in children with vit. D R.R. are lacking in quantitative appraisal of dentofacial development. Their study was the first to produce any quantitative results in this field. Their method involved measuring dimensions in the maxilla and mandible only. They did not attempt to extend their measurements to the developing cranial base so there have been no quantitative appraisals made of this important area.

Some of the findings from their 9 cases are presented below.

Children below the 25th percentile in facial and body measurements are shown in Table 3.

Growth retardation in individual children is shown in Table 4.

The landmarks used by Tracey and Campbell are shown in Figs 8 and 9.

Their measurements reveal that growth in the mandible was normal in almost all dimensions.

Maxillary growth was retarded in height and

Table 2 ■ Children below the 25th percentile in facial and body measurements.

Mandible					Maxilla					Body		
Height	Length		Width		Height	Length		Width		Stature	Sitting height	Sample size
Con-Go	Go-Pog	Con-Pog	L-R Go	L-R Con	NMS-ANS	DAM-IOM	ANS-PTM	L-R ZMS	L-R PTM			
4	1	2	2	3	6	4	5	2	2	9	7	9

Table 3

Table 3 ■ Growth retardation in individual children.*

Patient	Chronologic age Yr-Mo	Mandible					Maxilla					Physical growth	
		Height	Length		Width		Height	Length		Width		Stature	Sitting Ht
		Con-Go	Go-Pog	Con-Pog	L-R Go	L-R Con	NMS-ANS	DAM-IOM	ANS-PTM	L-R ZMS	L-R PTM		
1	4.4	moderate			..	..					..	severe	moderate
2	3.9	moderate		moderate					slight		..	severe	severe
3	12.0			moderate		..				moderate	..	severe	moderate
4	4.6					..					..	severe	severe
5	7.5					..	moderate				..	moderate	..
6	9.4		severe				slight	moderate			..	severe	severe
7	8.0				slight						..	severe	
8	11.0						moderate		severe		slight	severe	moderate
9	2.9										..	severe	moderate

*Growth was normal unless otherwise noted.

Table 4

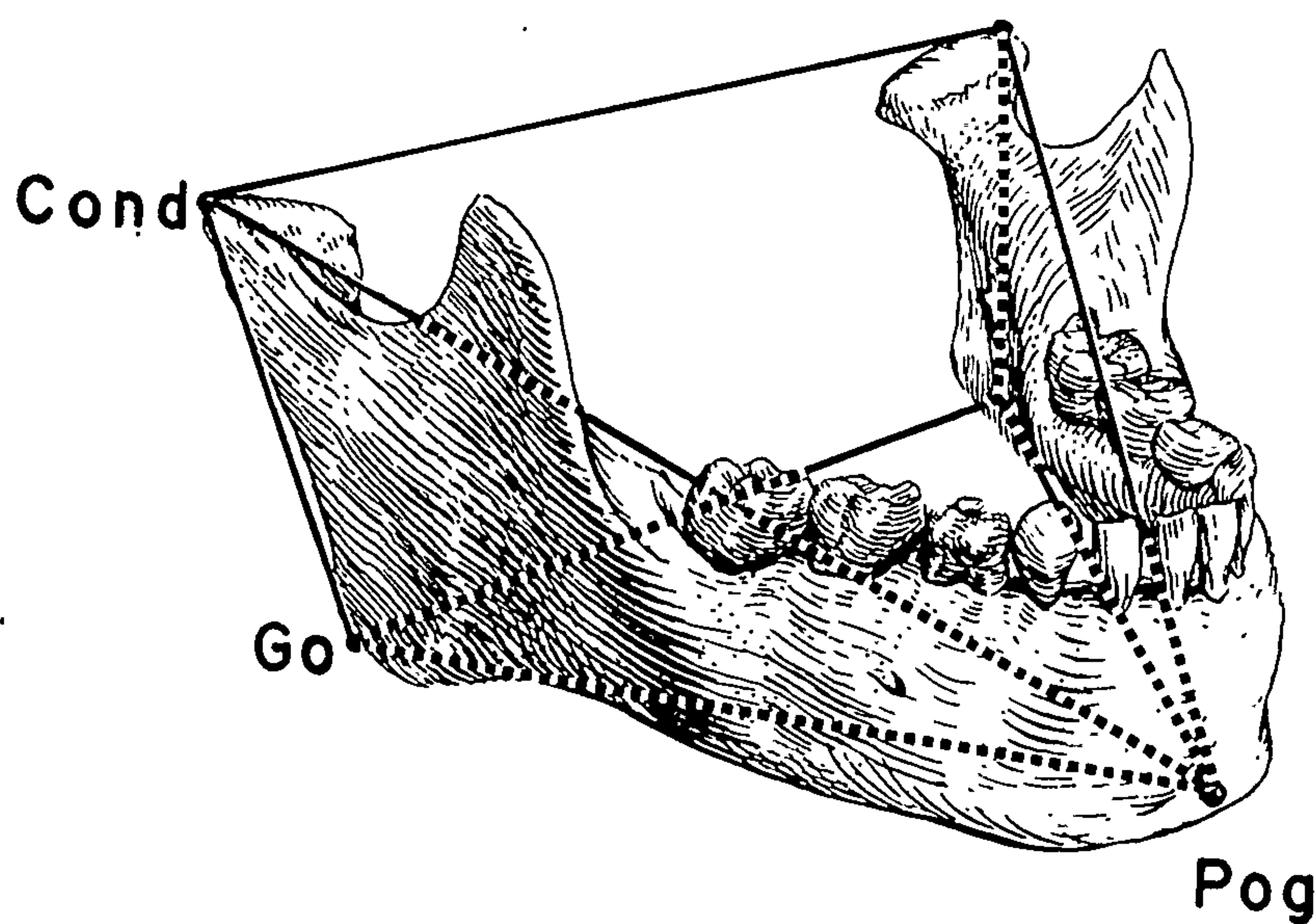


Fig. 8

Ermer 64

Fig 5 ■ Mandibular landmarks and dimensions measured.

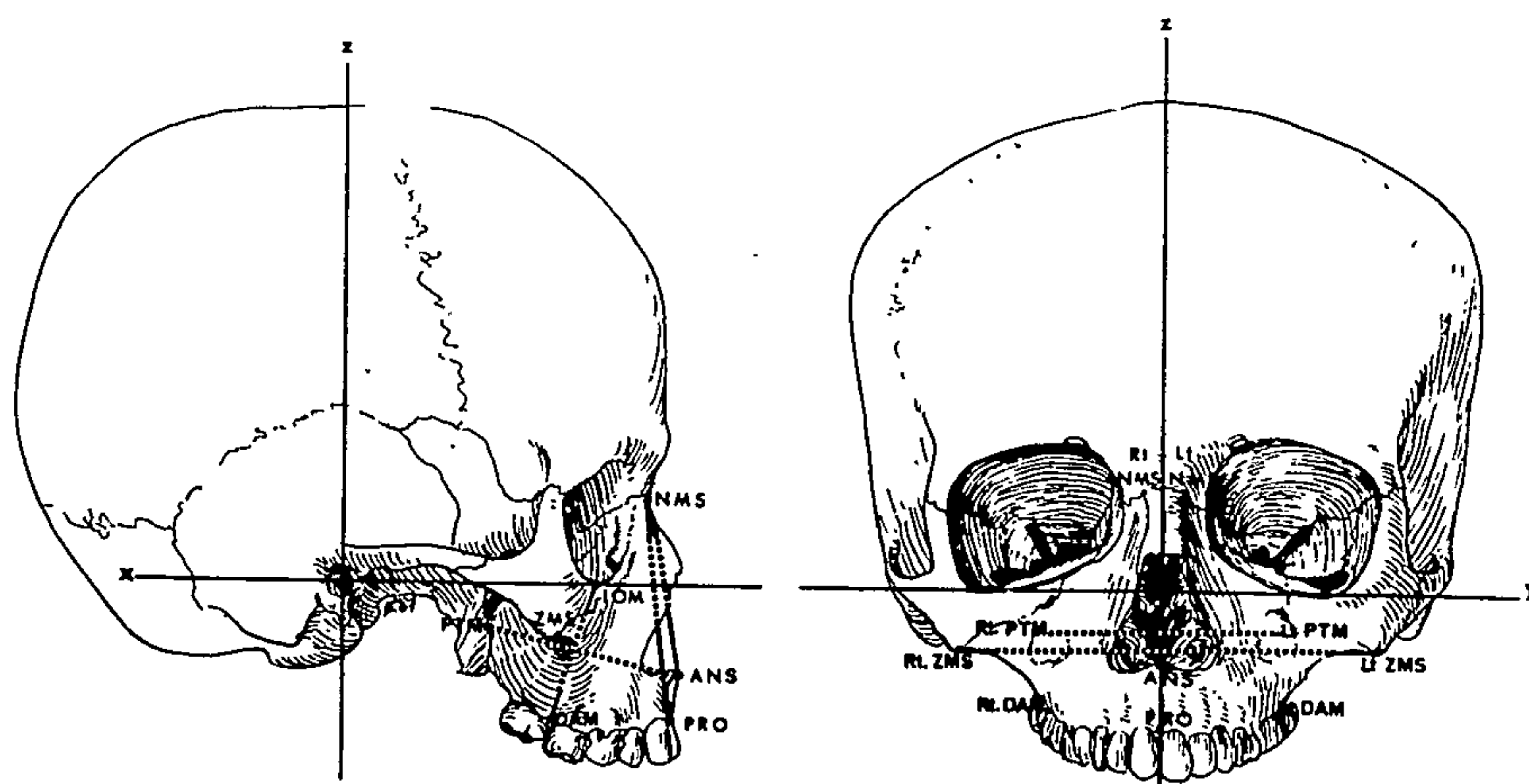


Fig. 9

length. The authors measured maxillary height from the naso-maxillary suture (N.M.S.) to anterior nasal spine (A.N.S.) and this measurement was below the 25th percentile in six of their nine patients. Maxillary length was measured from A.N.S. to pterygomaxillary fissure (P.T.M.) and this measurement was below the 25th percentile in five patients.

The authors found severely retarded statural growth (below the 3rd percentile) in 8 out of their 9 patients. The remaining patient showed moderate retardation (below the 5th percentile) in statural growth.

Tracey and Campbell 1968 (77) did not examine occlusal relationships of the jaws in their cephalometric x-rays or in their dental study casts. Study casts were used to determine dental age by tooth eruption.

Skeletal and dental maturation were examined against chronological age. Dental age was assessed on tooth calcification patterns and eruption times. Their results are shown in Fig. 10 and Table 5.

Retardation in bone age was found in the case of the eldest two children only. Their bone age fell more than 2 standard deviations below the normal.

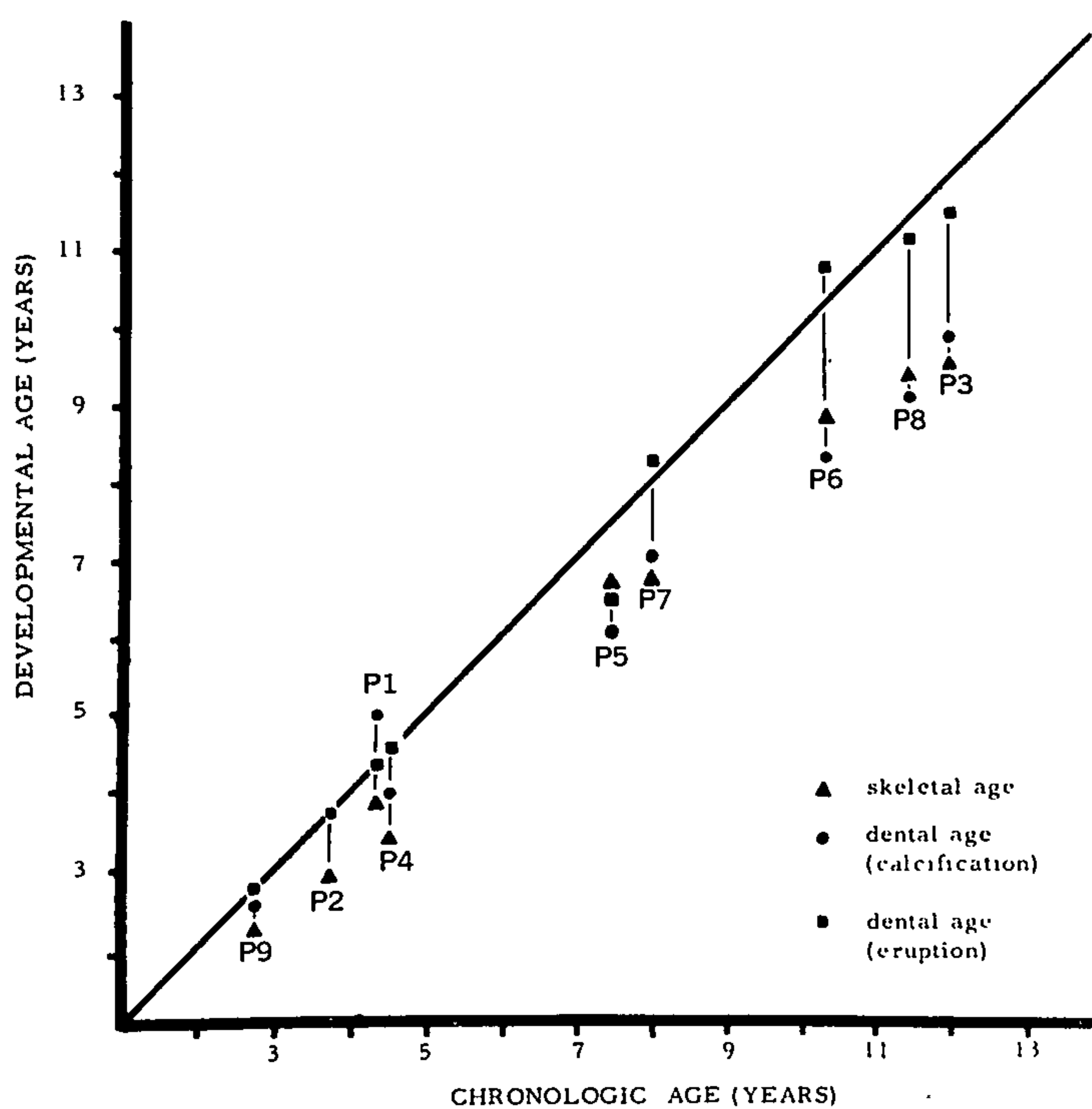


Fig. 10

Fig 7 ■ Skeletal, dental (eruption), and calcification ages of patients (P).

Table 4 ■ Chronologic, bone, and dental age in years.*

Patient	Chronologic age	Bone age	Dental age calcification	Dental age eruption
1	4.3	3.8	5.0	4.3
2	3.8	3.0	4.1	3.8
3	12.0	10.1*	10.1	11.3
4	4.5	3.6	4.0	4.4
5	7.4	6.9	5.9	6.7
6	10.3	8.9	8.6	10.7
7	8.0	6.8	7.3	8.2
8	11.4	9.4*	9.4	11.2
9	2.8	2.3	2.2	2.5

*Retarded.

Table 5

Harrison et. al. 1966 (36), and Steendijk 1962 (73), noted slight skeletal age retardation. Steendijk followed his patients through adolescence and related the retardation to late maturation. All of these writers conclude that skeletal retardation is not a feature of the disease.

Brash 1956 (12) looks at the effects of rickets in the jaws. He says Fleischmann in 1877 originally described a narrowing of the jaws and a special shape of the mandible in rickets. Many other authors have described similar abnormalities and associated them with rickets, but Brash says there is a lack of any satisfying demonstration of the relationship between jaw form, tooth position and rickets.

Kaukhaus 1957 (43) states that anterior open-bite was the most serious malocclusion associated with rickets. Other abnormalities reported by him were narrowness of the upper jaw, short anterior cranial base, short mandibular ramus and a flat gonial angle of the mandible.

He does not report his material and no quantitative values are supplied.

Hatfield 1919 (38) examined 15 children with rickets and although he observed some abnormalities

he stated the deformities were not prominent.

Anderson and Hurne 1940 (3) examined 33 children who had been treated for rickets. They found an open bite in five cases and suggested that this could be associated with rickets. However, the material as a whole showed good dental development with possibly less malocclusion than would be expected in a random sample of the population.

Friel 1922 (25) examined 520 children in post-war Vienna. Their war time diet had been very poor and rickets was very common even pre-war.

Height and weight measurements showed the children were underdeveloped. Caries and early loss of deciduous teeth were extremely common.

Friel found that eruption time was significantly delayed in severely affected children.

He felt the amount of malocclusion observed was within a "normal" or expected range; this did not include malocclusions due to the local cause of premature loss of deciduous teeth. He observed a few cases with slight anterior open bite.

The observation of Garn et. al. 1965 (27) that dental calcification in children with developmental disorders was delayed or advanced in the same direction as skeletal maturity, but to a lesser

extent, could be applicable to Friel's observations on eruption times. The reported delayed eruption of the teeth may be directly associated with the children's general underdevelopment, and not specifically with rickets.

Marks et. al. 1965 (50) made a study of dental and cephalometric abnormalities in children with vit. D R.R. Unfortunately they did not report any quantitative results from their study.

Previously reported abnormalities confirmed by their observations were:

- 1) Increased anteroposterior diameter of the skull - this was their most consistently observed abnormality but they did not give any quantitative assessment of the increase.
They did not give other observations from their cephalometric x-rays,
- 2) Enlargement of the pulp chambers of the teeth,
- 3) presence of interglobular dentine,
- 4) absent or poorly defined lamina dura surrounding the teeth,
- 5) fistulae from periapical abscesses,
- 6) delayed eruption of teeth. (This was only found in one of their nine cases.)

Their observations did not support presence of enamel hypoplasia due to vit. D R.R. - They found enamel hypoplasia in one case only and this patient also suffered from hypoparathyroidism.

Tracey and Campbell 1968 (77) found enlarged pulp chambers in the three boys in their sample. Two of these had a history of spontaneous dental abscesses.

Winters et. al. 1958 (86) found abnormal craniofacial growth, - skull deformities, - reported throughout the earlier literature on vit. D R.R.

The summary of their findings is presented in Table 2, on page 28.

The author's chief interest in skull deformities was to date the age of onset of the disease according to the ideas of Park 1932 (59).

(reported on page 30). Thus they gave no details of the deformities reported, simply recording any deformity as a positive finding.

The cranial deformities reported by Marks appear to be the most common; the increased antero-posterior dimension of the skull is associated with frontal and occipital bossing and increased thickness of the frontal, parietal and occipital bones.

Koeff 1959 (45) examined 203 children with a history of rickets. He found that 49% of these children had orthodontic anomalies. The author found identical types of anomalies in children who had not suffered from rickets.

Koeff concludes there is no type of anomaly which is characteristic of rickets. "Rachitic" contraction of the upper jaw is the same as a contracted upper jaw in any section of the population. He states that the role of rickets as an aetiological factor in the development of dental anomalies has been overemphasised in the past.

DENTAL ABNORMALITIES

Although enamel hypoplasia has not been associated with vit. D R.R. spontaneous dental abscesses have been observed by Tracey and Campbell 1968 (77) and Marks 1965 (50).

Harris and Sullivan 1960 (35) examined a case of familial hypophosphatemic vit. D R.R. showing numerous periapical abscesses drained by fistulae. The involved teeth did not display clinical caries.

Microscopic examination of the infected teeth revealed decreased enamel thickness and defective formation and union of the dentine. This defective dentine is known as interglobular dentine.

When the thin enamel covering wore away the exposed defective dentine permitted ingress of infection, without the normal process of decalcification, causing necrosis of the pulpal tissue which results in periapical abscess formation.

Shafer et. al. 1960 (70) state that the response of developing dentine is very sensitive to vit. D deficiency. This sensitivity can be used as a biological indicator of the presence of adequate amounts of vit. D in the diet.

Dentine normally calcifies by coalescence of

small calcospherites starting at the predentine - dentine border; where vit. D is deficient this coalescence is incomplete, and when adequate amounts of vit. D are again present in the diet coalescence begins again at the predentine - dentine border leaving a marker zone of interglobular dentine.

CRANIOSTENOSIS IN VITAMIN D RESISTANT RICKETS

Reilly et. al. 1964 (61) found the incidence of craniostenosis in the general population was 0.022%. In their sample of 59 rachitic children 19 exhibited craniostenosis by 9 years of age.

They felt that stenosis occurred following treatment of active rickets, when the wide, uncalcified sutures of active rickets returned to normal; in some cases this healing progressed too far, resulting in accelerated maturation, and producing complete obliteration of the sutures.

Incidence and severity of craniostenosis appeared related to the age of occurrence, and to severity of the rachitic lesion.

Craniostenosis did not appear to be related to the specific type of rickets, nor to the serum chemistry or vitamin D intake.

The authors noted that craniostenosis occurs in hypophosphatemic type of rickets; they feel that in all cases the closure of the suture is due to an inherent mesenchymal defect in the process of suture growth.

The significance of craniostenosis may be only cosmetic, but in some cases it appears to have

resulted in increased intracranial pressure and neurological damage.

Coleman 1954 (15) presented a case report of a patient with craniostenosis and vitamin D R.R., where fusion of the sagittal suture had occurred by 3 years of age; increased anteroposterior length of the skull was also noted.

Winters et. al. 1958 (86) found three cases of craniostenosis previously reported in the literature, including the one by Coleman, in association with vitamin D R.R. and suggested that there is thus more than a coincidental relationship.

Moss in 1957 (52) hypothesised that malformations in the cranial base produce changes in the organisation of the dura mater which are causally related to synostosis of the cranial sutures.

He showed that basal deformations and synostosis occur in cleft palate patients.

He measured the planum angle* in cleft and non-cleft patients with ridging and without ridging (a bony ridge over the frontal suture was found to form after premature synostosis of the frontal suture) and

* Planum angle is formed by planum sphenoidale and the dorsal surface of the occipital bone from basion to sella.

found a relationship between this angle and the presence or absence of ridging in either the cleft or non-cleft patients.

The mean values found were:

cleft patients with ridging	104.3°
non-cleft patients with ridging	105.9°
cleft patients without ridging	114.9°
non-cleft patients without ridging	119.5°

Marks et. al. 1965 (50) felt that craniostenosis was rare in association with vit. D R.R.

Grumberg 1947 (29) says that fusion of cranial sutures appears to be associated with displaced primary ossification centres in the embryonic rabbit.

The resultant anomalies were compatible with a healthy cage life.

The fusions are present in the rabbit while the basis of the skull is still cartilaginous and quite normal.

Bertelsen 1958 (7) examined the effect of cranial stenosis on the base of the skull. He found an increase in the angle formed by the anterior and posterior sections of the cranial base - lordosis - in oxycephalic patients. In cases of

craniofacial dysostosis there was kyphosis of the cranial base. Both oxycephalic and craniofacial dysostosis had resulted in increased intracranial pressure in the cases examined. Bertelsen says a secondary effect of increased intracranial pressure is lordosis of the cranial base and says the kyphosis found in craniofacial dysostosis is due to a counter-pressure from the hypoplastic maxilla and vomer. Bertelsen states that changes in the cranial base have very little primary effect on the development of cranial stenosis.

There is general disagreement on the mechanisms of craniostenosis and particularly the role of the cranial base in the production of craniostenosis.

As the cranial base and facial structures are the most important regions under consideration in this thesis the statement by Moss and Young 1960 (53) is of great interest. They cite some unpublished work by Young indicating that components of the facial skeleton, such as the nasal bones are not affected by alterations in the size and shape of the cerebral capsule.

VITAMIN D METABOLISM

ABSORPTION

De Luca 1967 (18) presented a very comprehensive study of the metabolism and actions of vit. D. He found that vit. D is absorbed from the jejunum and perhaps the ilium; the actions of the bile salts aids absorption.

It enters the lymphatic system with 80% of the vit. D appearing in the chylomicron fraction. It is believed that little chemical change takes place at this stage although esterification may help absorption.

CONJUGATION WITH CARRIER SYSTEM

Vit. D is taken up by the liver and attached to a protein carrier system for transport to the cells. The general carrier is the α_2 globulin fraction of the blood; as yet no single protein has been demonstrated as the carrier specifically of vit. D. The α_2 globulin proteins have an important role in the transfer and metabolism of vit. D by the tissues of the body.

Avoili et. al. 1967 (4) suggest that to this stage the process of vit. D uptake, and conjugation with a protein carrier system, is normal in vit. D R.R. and familial hypophosphatemia.

STORAGE

The method and place of storage of vit. D is not known.

High levels of vit. D have been found in bone, liver, blood and kidneys suggesting that any or all of these areas could be the sites of storage. Most support has been given to the theory of the liver being the site of storage, but the liver stage may be only associated with the combination of vit. D and the carrier protein system.

It has been demonstrated that bone and intestinal mucosa acquire the highest levels, per cell, of vit. D.

METABOLITES OF VIT. D

Some metabolites of vit. D have been identified and their therapeutic value estimated. The phosphate and acetate esters have been shown to have full biological activity by De Luca.

The sulphate ester has been produced with large doses of vit. D but its importance in physiological dosage is not known.

Other metabolites have been demonstrated but not identified. One of these, known as the peak IV metabolite, from paper chromatography, appears to

be the active metabolite.

The peak IV metabolite is faster acting than vit. D. It is found in the blood of normal patients and vit. D R.R. patients.

Avoili et. al. 1967 (4) have demonstrated a decreased rate of turnover of vit. D in patients resistant to vit. D therapy, particularly the familial hypophosphatemic type. This results in a decrease in the levels of the peak IV metabolite found in the blood and bone of these patients.

These workers also demonstrated an abnormal production of water soluble vit. D metabolites, which were eliminated in the urine, suggesting an association with the hyperphosphatemia.

In the normal case most of the vit. D is excreted into the small intestine via the bile; the actual products which appear in the faeces have not been identified.

LOCATION WITHIN THE TISSUES

Kodicek, E and Thompson, G.A. 1965 (44) found that vit. D becomes located in tissues which are significant in the translocation of calcium and other divalent ions and which have a high phosphate turnover. The most important of these tissues are

- a) the absorbing mucosa of the small intestine;
- b) the proximal convoluted tubules of the kidney;
- c) membranes of cardiac and striated muscle; and
- d) rachitic bone - far more than normal bone.

They found about half the vit. D in the body located in the liver.

Kodecik and Thompson 1965 (44) examined the location of vit. D (or a metabolite) in bone. They found the greatest accumulation in the cytoplasm of the young flattened chondrocytes. Very little was located in the cytoplasm of the hypertrophied chondrocytes, or in the small epiphyseal chondrocytes or in periosteal fibroblasts; and none was located in osteocytes.

The inference derived by the authors is that vit. D is associated with the production of a calcifiable organic matrix; and that vit. D is of greater importance in endochondral ossification than in appositional bone growth.

De Luca 1967 (18) found that labelled orotic acid was incorporated into nuclear R.N.A. following the administration of 10 i.u. of labelled vit. D. Labelling did not occur in ribosomal or mitochondrial R.N.A.; he suggested that the labelled R.N.A.

fraction was messenger R.N.A.

In further studies of sub cellular location he found the biologically active peak IV metabolite to accumulate at specific receptor sites in the outer nuclear membrane of the cells studied.

ACTIONS AND EFFECTS OF VITAMIN DA. ON CALCIUM AND PHOSPHATE

Vit. D increases the absorption of calcium from the gastrointestinal tract. In vit. D D.R. administration of vit. D results in increased serum calcium levels.

From his study on cellular location of labelled vit. D De Luca 1967 (18) suggested that the expression of vit. D action on intestinal calcium transport and bone mineral mobilisation involves the transcription of D.N.A. into messenger R.N.A. and the translation into a functional protein.

Neuman and Neuman 1957 (56) as reported on p.83 state that an active cellular mechanism must be present for absorption of calcium from the intestine against an ion gradient.

De Luca 1967 (18) suggests that vit. D could be important in the formation of a carrier protein for calcium which would enable calcium to be absorbed against an ion gradient.

De Luca 1967 (18) found that the mitochondria of a kidney cell, which actively takes up calcium, is stimulated to release this calcium by the action of vit. D. He attributed this to an effect on the

permeability of subcellular membranes.

McLean and Bundy 1963 (51) support the idea that vit. D enables calcium to be recycled, so that calcium is transferred within the skeleton to meet local needs. They felt that this recycling is carried out by factors influencing reabsorption rather than accretion. The stimulus should originate in the parts in need of additional material.

The Lancet 1968 (49) states that calcium deficiency alone leads to diminished amounts of bone not failure of calcification.

Follis 1958 (23) stresses the importance of a normal calcium and phosphate product for calcification. L.J. Harris 1956 (34) also supports this idea.

Winters et. al. 1958 (86) show that the calcium phosphate product seldom reaches normal levels in familial hypophosphatemic vit. D R.R. cases even when treatment has been successful in producing calcification of rachitic bone.

Williams et. al. 1966 (85) feel that increased absorption of phosphate from the intestine is probably secondary to calcium absorption.

Bayer et. al. 1956 (5) found the phosphate in bone salts following the administration of vit.D was skeletal and dietary, and support the idea of mobilisation of minerals from the bone following administration of vit. D.

B. INTERACTIONS WITH PARATHYROID HORMONES

Albright et. al. 1937 (2) originally postulated that secondary hyperparathyroid secretion occurred to maintain blood calcium levels and this resulted in increased loss of phosphate in the urine.

They found hyperplasia of the parathyroid glands and decreased reaction to injected parathyroid extract.

Following removal of one of the glands serum calcium levels decreased, serum phosphate levels increased, and serum alkaline phosphatase levels decreased.

Copp 1964 (16) has shown more recently that two hormones are secreted by the parathyroid gland.

1. Parathormone - raises the serum calcium level,
 - enhances calcium absorption from the intestine,
 - enhances renal tubular reabsorption.

Its principal effect is to increase bone resorption, and its action is mediated by the cells.

2. Calcitonin - lowers serum calcium levels;
it is very fast acting.

The bulk of the hormone calcitonin is produced in the thyroid gland (Lancet 1966 (48).); this hormone is now called thyrocalcitonin.

Zetterstrom and Winberg 1955 (87) state there is evidence to support the idea of a direct action of massive doses of vit. D on bone causing mineralisation, or inhibiting parathyroid secretion, and that this action is not secondary to changes in serum calcium and phosphate levels.

The Lancet 1968 (49) states that in osteomalacia the osteoclasts are resistant to the increased secretion of parathyroid hormone before the administration of vit. D.

De Luca 1967 (18) states that bone mineral mobilisation induced by parathyroid hormone is dependent on the presence of vit. D.

C. ON BONE FORMATION

Follis 1958 (23) found that in the healing of rickets following administration of vit. D the inorganic salts deposit in the matrix about the cells which have most recently hypertrophied.

L.C. Johnson 1964 (42) states that mineralisation fails in rickets due to abnormal matrix production. For the first mineral crystal to be formed in the space between the doublet period in the collagen there must be exact orientation of the collagen fibres.

In rickets there is abnormal orientation of the collagen fibres which prevents mineralisation.

Engfeldt et. al, 1956 (20) found an extremely irregular collagen pattern in a biopsy specimen from a patient with vit. D R.R. The collagen consisted of short bundles running in different directions. The abnormal collagen pattern remained unchanged after large doses of vit. D.

They found the unit crystal of apatite had the same dimensions in normal bone, and poorly and highly mineralised rachitic bone. No orientation of the crystallites could be demonstrated.

Avioli et. al. 1967 (4) believe that vit. D may have a direct effect on bone metabolism not related to amounts of calcium and phosphate absorbed. Abnormal vit. D metabolism found by them in vit. D R.R. could result in abnormalities of osteoblastic development.

Villanueva et. al. 1966 (79) found that the rate of bone formation at the osteon in familial hypophosphatemic vit. D R.R. was only 2.2% of the normal rate. They attributed this to a major defect in the osteoblast.

Formation of bone at the cortex was 27% of the normal. They found 12 times the normal number of actively forming osteons present.

. They suggest that a decreased rate of mesenchymal cell proliferation could be the cause of the decreased rate of bone formation.

The Lancet 1968 (49) reports a reduction in the rate of bone remodelling.

Frost 1964 (26) states that a low rate of remodelling is characteristic of osteomalacia where a mineralisation defect is present. Pseudo-fractures or Looser's lines are found in these cases.

Pseudofractures occur where the remodelling rate is not sufficient to adjust the bone to changes in shape. This was observed in severe bowing deformities in the femur. Winters observed pseudofractures in some cases, examined radiographically.

Engfeldt et. al. 1956 (20) suggest there is lively remodelling in both treated and untreated patients.

Bayer et. al. 1956 (5) found the accretion rate of bone salts in vit. D deficiency was originally lower than normal and was raised to normal with vit. D therapy.

In children with vit. D R.R. the accretion rate of bone salts was originally about normal and following massive doses of vit. D it was higher than normal.

Becker et. al. 1964 (6) suggest that vit. D may act as an impurity in the apatite-collagen structure and enhance the bioelectrical effects of mechanical stress reported on page 85.

D. ON RENAL TUBULES

Winters et. al. 1958 (86) states that there is a maximal rate of tubular reabsorption of phosphate, but it is quite variable and influenced by many factors. A maximal rate of tubular reabsorption (T_m) means that when the filtered load (tubular filtration rate X plasma level) is less than the T_m , only very small amounts of phosphorous will be excreted. In resistant rickets the T_m appears to be set at a lower level than normal. They suggest that the T_m is raised, sometimes to normal, by administration of large doses of vit. D.

Hypophosphatemia may persist with a raised T_m only if there is extra-renal removal of phosphate (e.g. into bone) in an amount which would reduce the serum level to less than the equilibrium concentration.

Williams et. al. 1966 (85) say the hypophosphatemia is due only to an abnormal renal resorption mechanism.

De Luca 1967 (18) supports the idea that vit. D therapy results in improved renal resorption of phosphate.

E. ON GROWTH

Steendijk 1962 (73) states that growth is deficient even in treated refractory rickets without deformities, but he does not indicate that the vit. D therapy has caused the deficient growth.

Winters et. al. 1958 (86) also found reduced growth, more often in height than weight, and associated it with the constant hypophosphatemia and not the vit. D therapy.

Cramer and Steenbock 1956 (17) found that growth in rats on a low phosphate diet was decreased by addition of vit. D to the diet. They proposed that the calcification induced by the vit. D caused competition between bone and soft tissue for the limited available phosphate, and resulted in some lack of phosphate for soft tissue growth.

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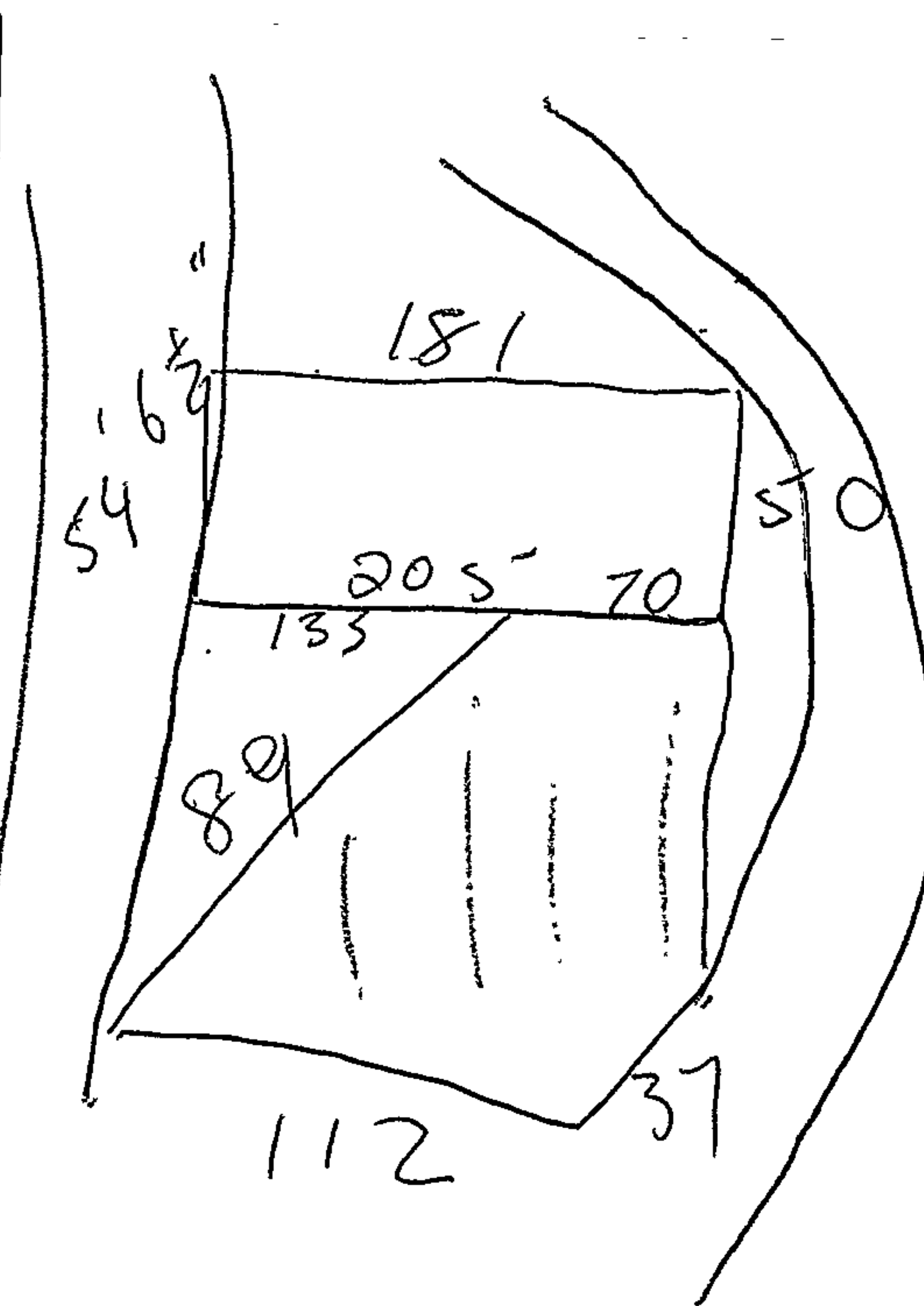
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F. Disintegration of the hypertrophied



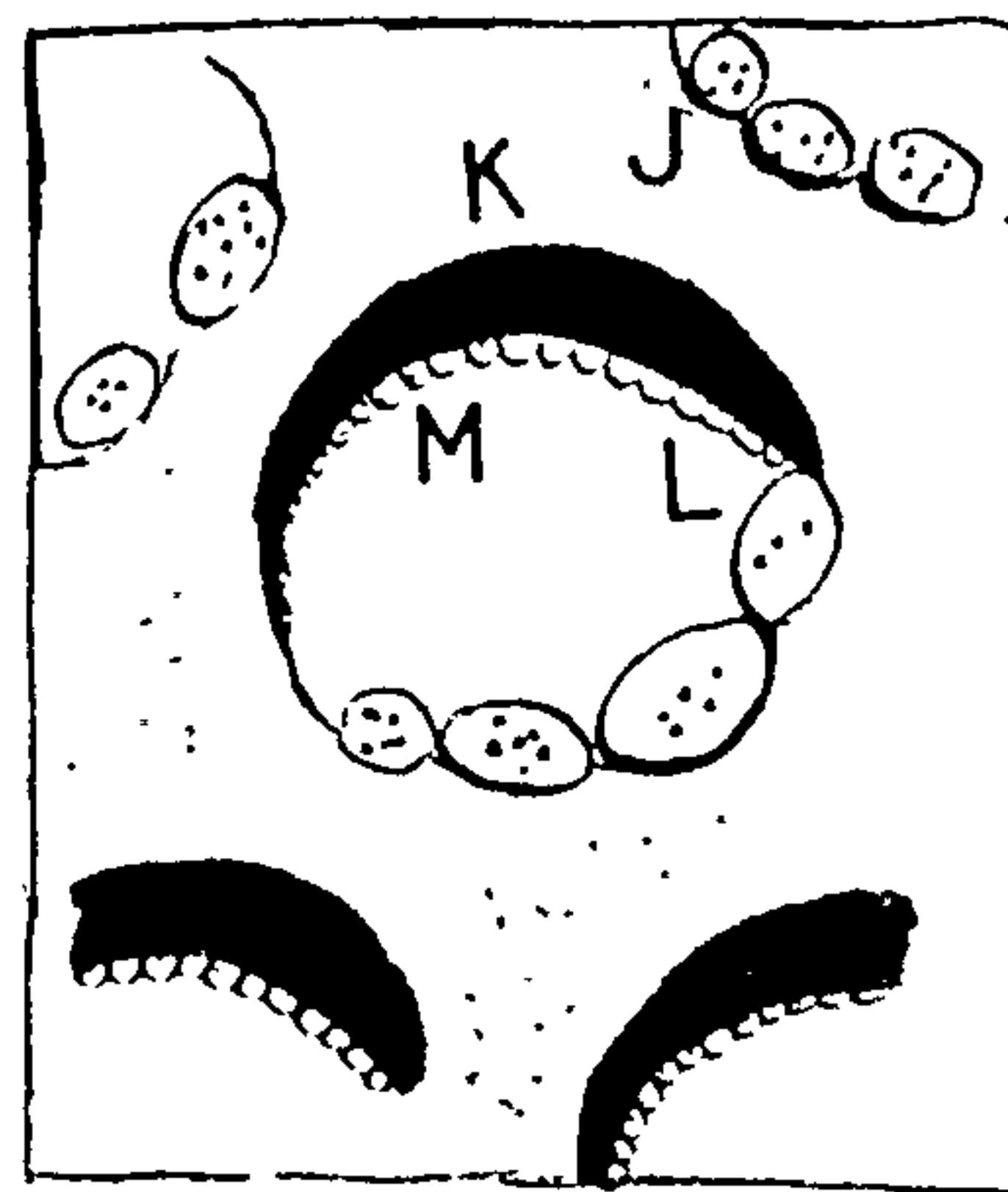
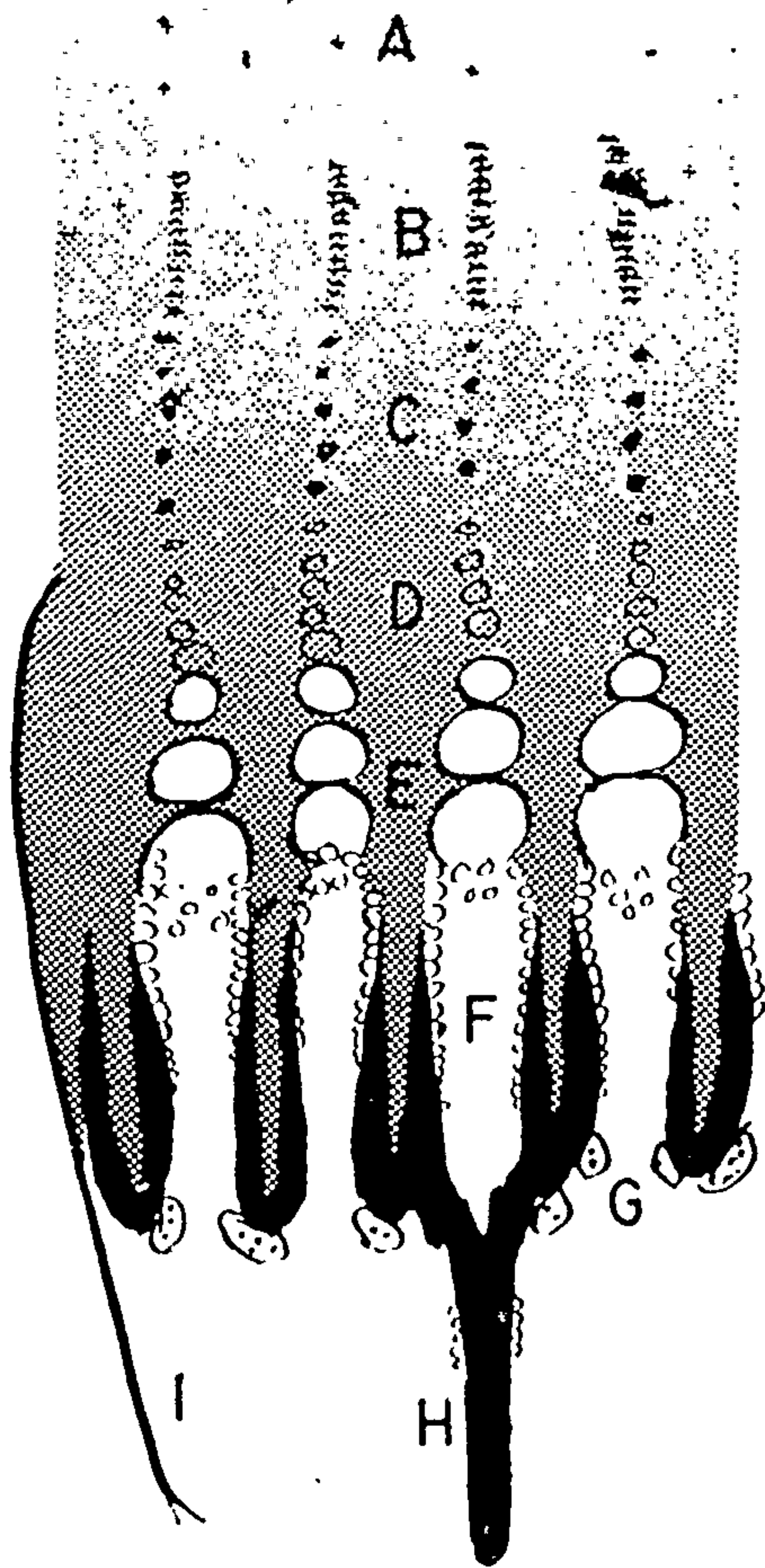


Fig. 11

cartilage cells appears to yield the products which induce the cellular proliferation which results in osteoblastic activity.

G. Following the formation of the primary trabeculae eccentric osteoclastic and osteoblastic activity result in the cutting off or removal of the primary trabeculae and replacement by secondary trabeculae.

L.C. Johnson 1964 (42) has recorded the sequence and timing of the stages of endochondral ossification in the humerus of a young chick.

Cartilage cell proliferation occurs in 6 hours. Matrix secretion and hypertrophy also take 6 hours.

Calcification occurs within 10 hours.

Chondroclastic resorption has occurred in 10 hours.

Mesenchymal cell proliferation takes 8 hours.

Production of a 15 micron layer of osteoid tissue of the primary trabeculae takes 48 hours.

The primary trabeculae is cut off and removed in 8 hours.

This author feels that the well-ordered sequence

of activity suggests that each stage is induced by the preceeding phase of activity.

COLLAGEN MODEL BONE

This occurs in tendon ossification and development of bony prominences, as shown in Fig.12, by L.C. Johnson. 1964 (42) *

- A. Mature tendon with elongated fibrocyte nuclei and bundles of collagen films.
- B. Enlargement of fibrocytes with development of cytoplasm - sulphate staining appears between the collagen bundles.
- C.. Cells develop into typical chondroblasts, poly-saccharides fill the space between the collagen bundles and then begin to infiltrate the bundles.
- D. Collagen fibrils are spread by the infiltrating polysaccharides and the entire area is converted into an homogeneous osteoid.
- E. The collagen birefringence is suppressed, type A autofluorescence appears and staining and reactions characteristic of the phosphate ridge are present.
- F. The osteoid mineralises with the loss of many cells; those cells that remain become typical osteocytes.

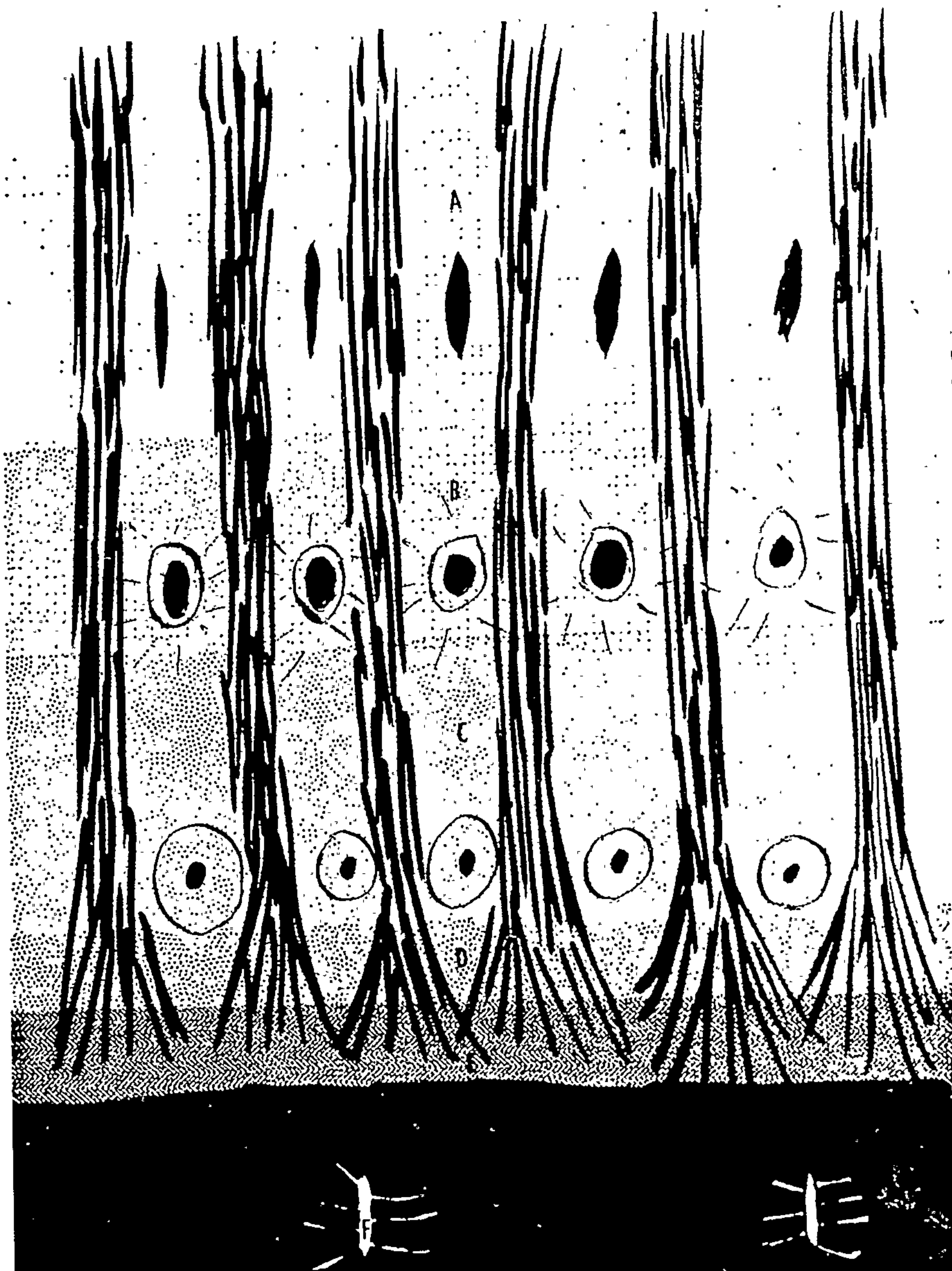


Fig. 12

APPOSITIONAL GROWTH, GROWTH IN DIAMETER

(Fig. 13)

- A. The periostium at its junction with muscle consists of thin collagen bundles and fibroblasts showing occasional mitotic figures.
- B. The mature fibrous periostium with flattened fibrocytes and large collagen bundles.
- C. Region of enlargement of fibrocytes to rounded nuclei with considerable water-clear cytoplasm. This is accompanied by loss of staining and gradual disappearance of collagen in fibro-clasia.
- D. Area of staggered activity. Fibroclasia is most active to produce cavities in the neighbourhood of vessels and lags midway between the vessels to leave the collagen pillars - D -: on these unresorbed remnants of collagen the earliest osteoblasts act to incorporate them in bone.
- E. Layers of osteoblasts subsequently begin to fill the space between the osteophytic pillars and the cortex - (F.)

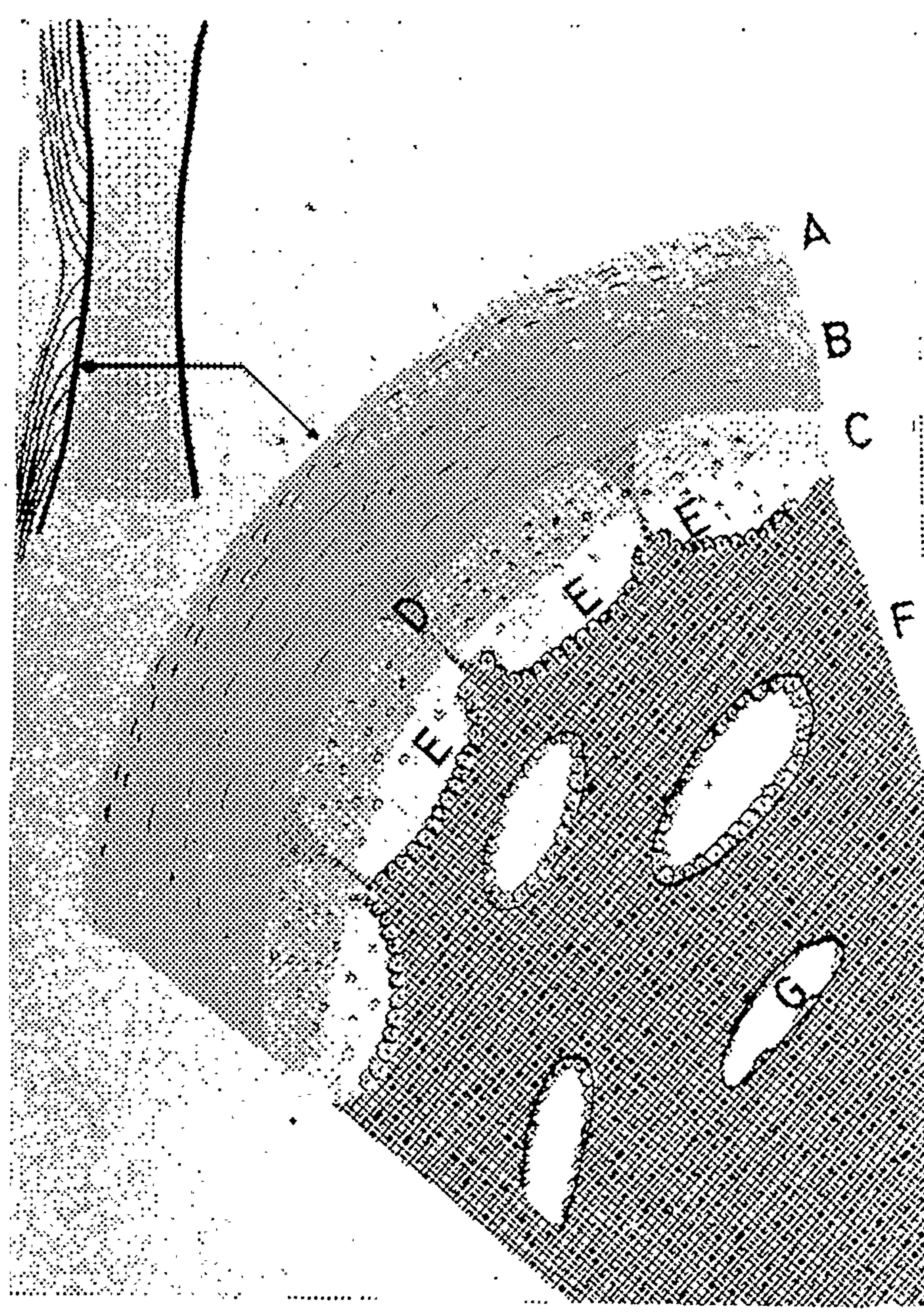


Fig.13

G. Continued osteoblastic activity diminishes the marrow spaces.

L.C. Johnson 1964 (42) states that the sequence in formation of bone from a collagen model, or appositional growth is the same. It is also the same in osteonal bone formation.

OSTEONAL BONE FORMATION. (Fig. 14)

This is a three day cycle which is repeated three times to produce 15 microns of osteoid tissue which is then calcified in one day.

On the first day - represented by "a" - collagen is laid down. This layer is the width of half a bone lamella.

On the second day - represented by "b" collagen is laid down at 90° to the collagen produced on the first day. This change in direction is produced by a mass lateral movement of the osteoblasts.

On the third day - represented by "c" - polysaccharide ground substance is added across the width of one lamella.

This sequence is repeated three times. On the ninth day - represented by "d" - the phosphate ridge* appears and spreads across the entire osteoid seam.

On the tenth day - represented by "e" - the first phase of mineralisation reaches 50 - 70% of the mineralisation capacity of the osteoid tissue.

* see section MINERALISATION, p. 80.

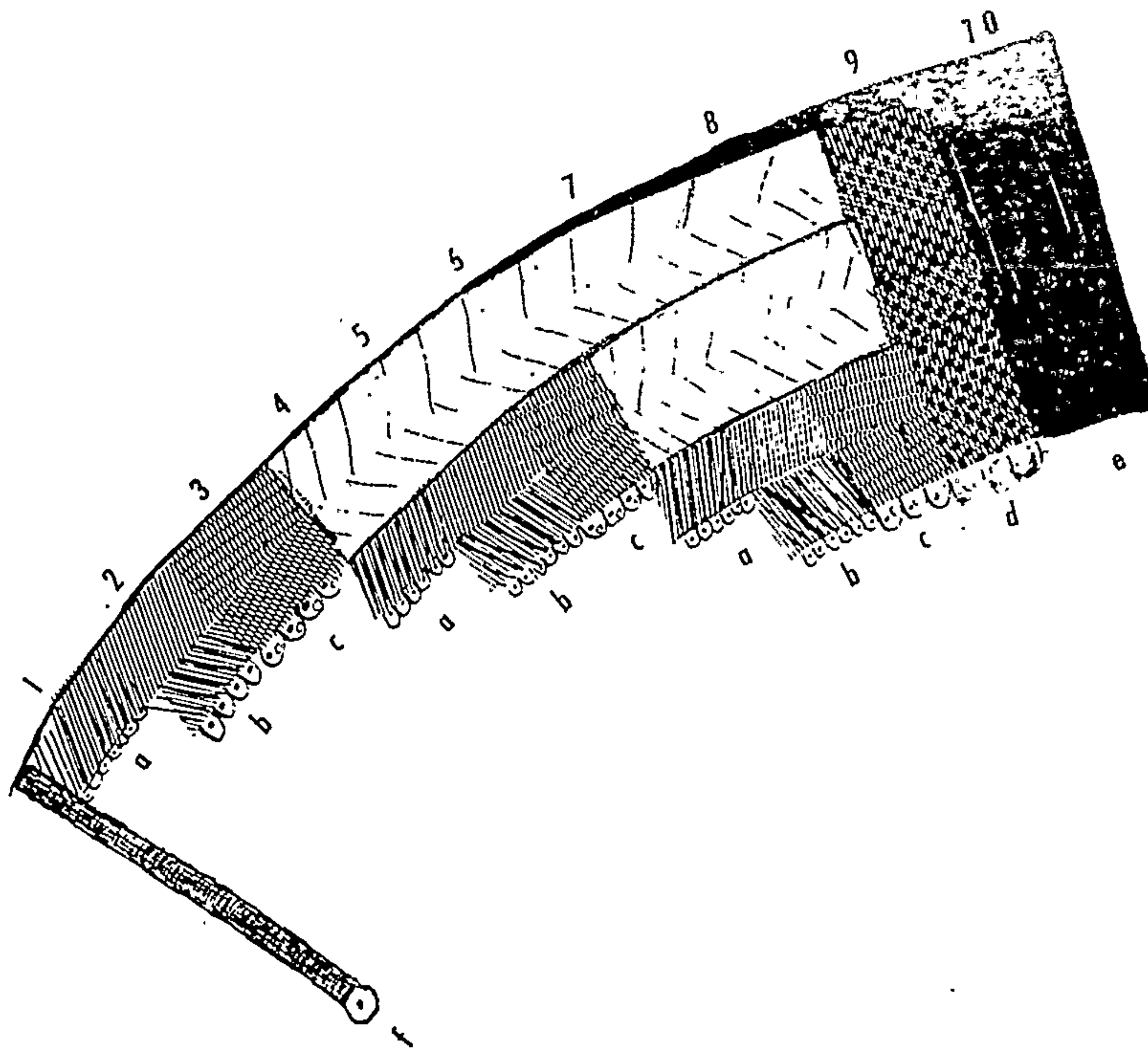


Fig. 14

THE OSTEOLAST (Fig.15)

The osteoblast commences its life cycle as a flattened cell.

In the early stages the secreting cell is packed with haemotoxyn staining ribosomes. Later small vesicles appear, collect together, then fuse to the juxtannuclear demilune which is the site of golgi activity - at the same time the ribosomal content is diminished.

Then the fused vacuoles develop a central spherule.

The demilune undergoes massive enlargement, the nucleus is pushed to the side of the cell and flattened.

Having completed the alternating activities of osteonal bone formation the osteoblast finally disintegrates.

COLLAGEN FORMATION

D.A. Cameron et. al. state that the chief function of the osteoblast is to form collagen. They support the importance of the microsomes in the formation of subunits of collagen - tropocollagen - but say there is scant evidence that the osteoblast produces the ground substance of mucopolysaccharides. L.C. Johnson 1964 (42) suggests that the golgi apparatus is active in the formation of the mucopolysaccharide ground substance.

Nicols 1965 (57) presents a scheme of collagen synthesis by bone cells observed in vitro.

1. Amino acids are synthesised in the bone cell - or actively transported into it - and concentrated in their free (uncombined) state.
2. They are activated and linked to a specific soluble R.N.A. molecule.
3. The soluble R.N.A. is then transported to the polysomes - made up of messenger R.N.A. (m.R.N.A.) and ribosomes - and here the proteins are assembled.
4. The completed proteins are stored in vesicles in the endoplasmic reticulum; these vesicles eventually fuse with the plasma membrane and

release their contents, tropocollagen, into the extracellular space where they polymerise to give collagen fibres.

MINERALISATION

L.C. Johnson 1964 (42) states that matrix formation and mineralisation are always separated in time, and an osteoid seam is present. The junction between the osteoid and mineralised bone is marked by a deep blue haematoxylin staining line, indicating a high concentration of inorganic phosphate. The author refers to this as the "phosphate ridge". (Fig.16).

In mineralisation the osteoid seam becomes speckled with spots of organic phosphates, and the old ridge converts to calcified bone with a sharp reduction in the amount of organic phosphate. At the same time the swollen osteoblast, with its flattened nucleus disintegrates.

The disintegration of the osteoblast and the spotty phosphate activity of the osteoid seam initiate the mineralisation of the matrix.

The loss of type A autofluorescence occurs with calcification at the phosphate ridge. Ordinarily this occurs abruptly but where there is disturbed calcification type A autofluorescence disappears in a patchy manner over a longer distance.

At the phosphate ridge electron microscopic periodicity of collagen is obscured, as simultaneously

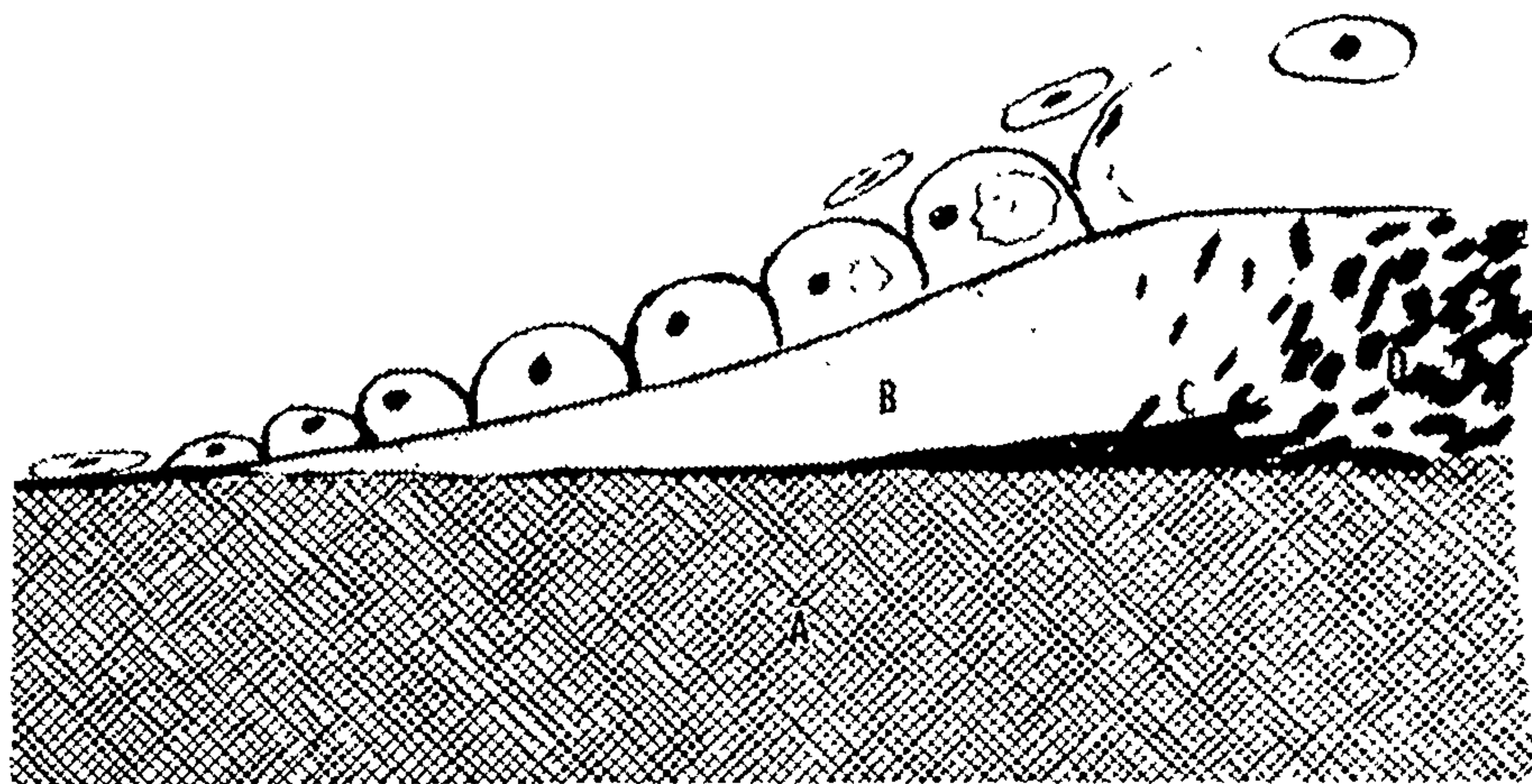


Fig. 16

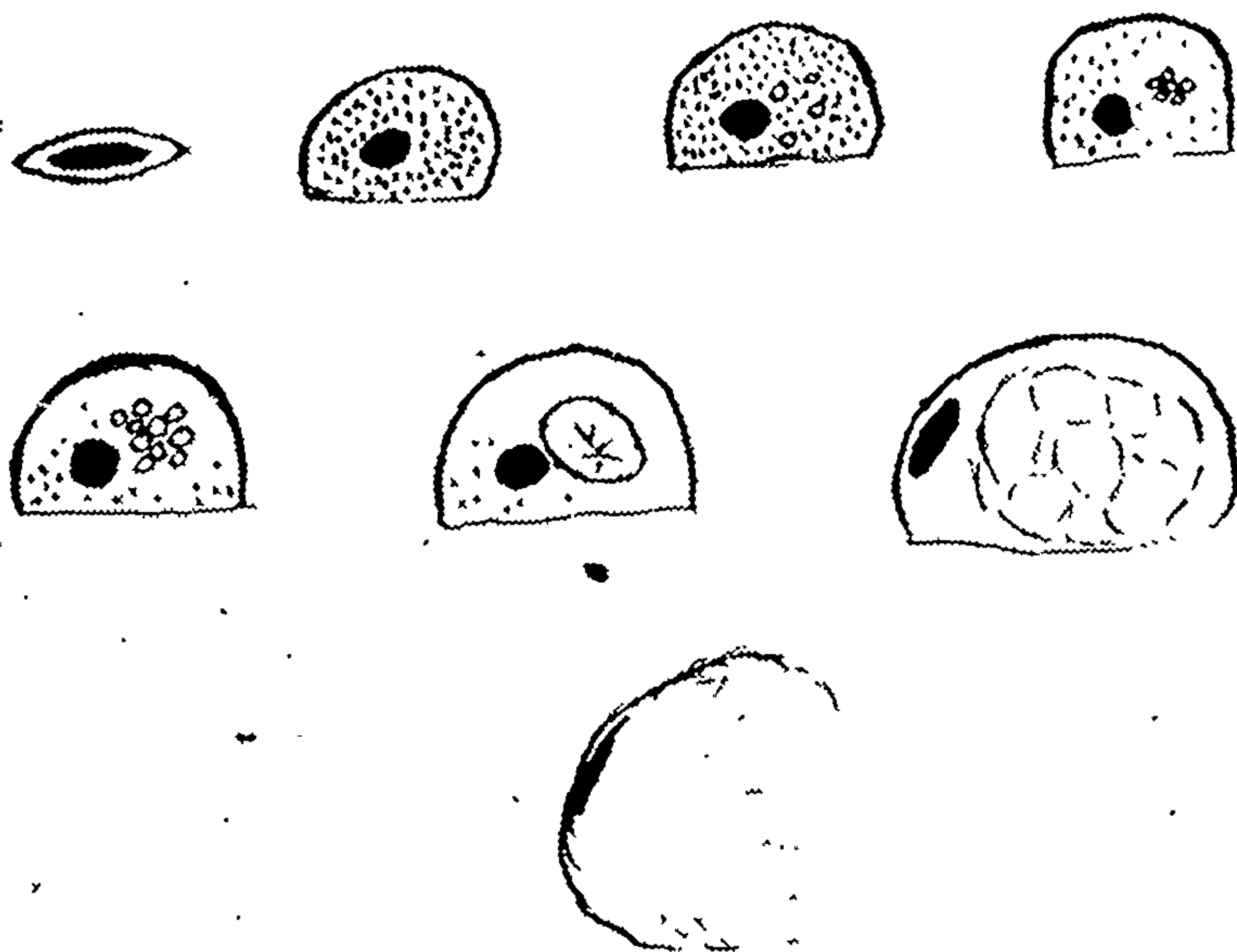


Fig. 15

birefringence is suppressed and the first mineral is added to the collagen in the space between the periodic bands which are observed in electron microscopic examination of collagen.

Nylen et. al. 1960 (58) provide further details of collagen-mineral relations from electron microscopic studies on mineralisation in turkey leg tendon.

They observed a spotty initial mineralisation quickly followed by an abrupt change from nonmineralised to mineralised tendon.

Mineralisation first occurred on the surface of the collagen fibres and then within the fibres.

Mineralisation first took place at the inter-band region, and this area became more dense than the original bands. This gives an inversion of the original collagen striation pattern.

The authors found the hydroxyapatite crystals which formed within the collagen fibrils always had their C axes parallel to the long axes of the collagen fibrils.

RELATIONSHIPS OF BONE AND BODY FLUID

Urist 1964 (78) states that the chemical composition of the fluids of the body is only part of the requirements for calcification of skeletal tissue. The intercellular matrix of cartilage and bone, the chondrocytes and osteocytes, enzymes, nucleation sites, crystal growth phenomena and chemical inhibitors are the other, and equally important, requirement for the development of mineralised tissue in the body.

Alkaline phosphatase is secreted into the blood by growing osteoblasts. It may also have a role in controlling apatite-nucleation inhibitors.

L.C. Johnson 1964 (42) states that alkaline phosphatase appears to be associated with collagen production. It is present in the osteoblasts and osteoid seam. It is also associated with fibroblasts, chondroblasts, and hyper-trophic cartilage cells.

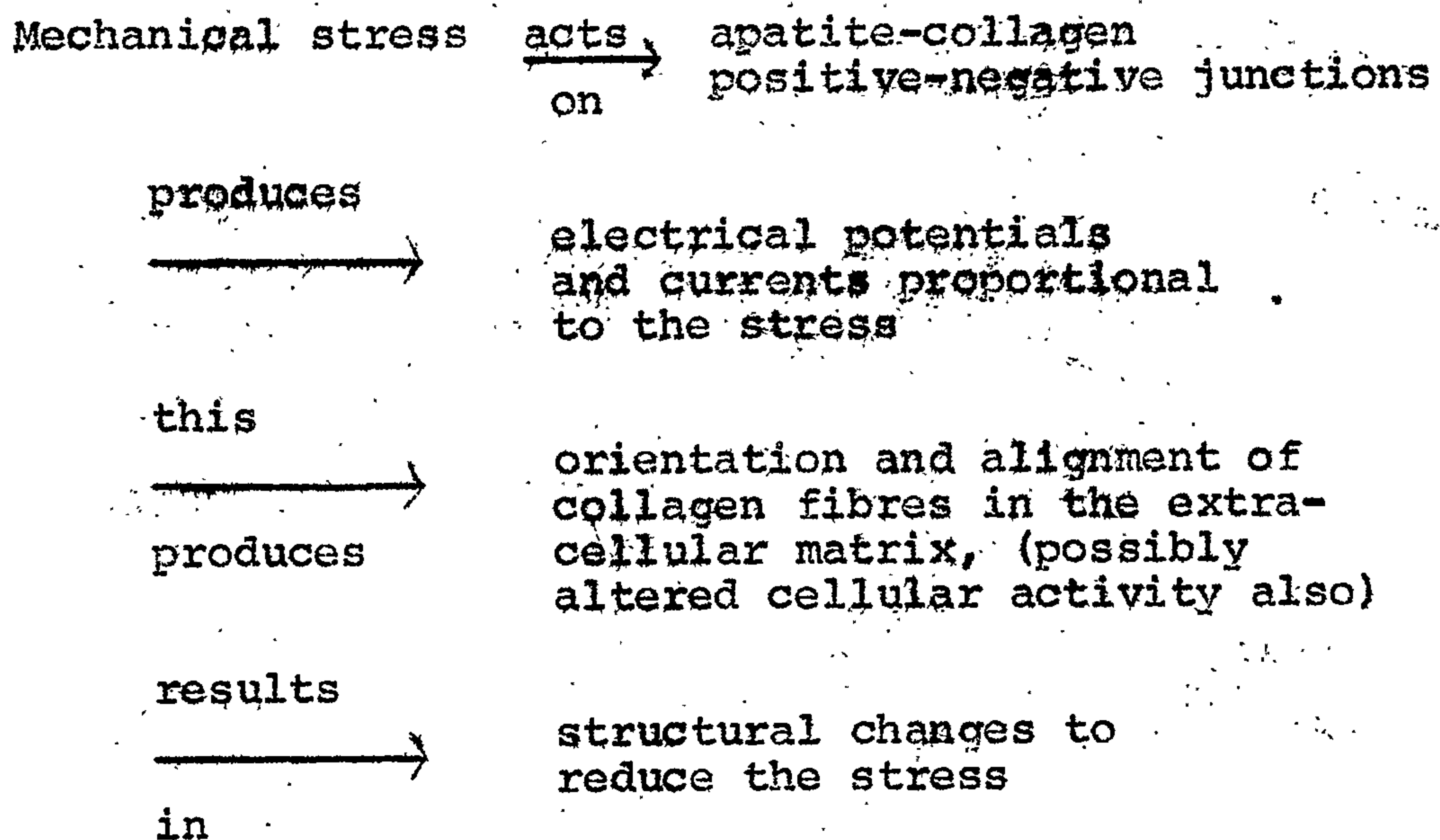
Neuman and Neuman 1957 (56) state that in the absence of solid phase, serum is undersaturated but in the presence of hydroxyapatite crystals it is supersaturated. Thus a cellular mechanism must be present to maintain this supersaturation in vivo,

and to permit absorption of calcium from the intestine against an ion gradient. The driving force for mineralisation is thus present in the serum.

ORIENTATION OF COLLAGEN FIBRES

Shamos 1965 (71) and Becker et. al. 1964 (6) have shown that tropo-collagen and collagen fibres are orientated by weak electrical fields. They have linked this to the electrical potentials generated by mechanical stress.

The diagrammatic scheme by Becker et, al. 1964 (6), of a growth control system is presented below.



FORMATION OF BONESCARTILAGE

Romer 1964 (62) points out the importance of cartilage growth in the formation of an internal skeleton. Cartilage allows growth in length without disruption of areas of articulation which would result if bone could only grow by apposition. He also points out that the columns of fibrous bone formed by endochondrial ossification are replaced during growth by lamellar bone formed by intramembraneous ossification. This replacement commences with the formation of the secondary trabeculae as described on page 68.

James 1962 (40) describes the effect of transplanting a femur of an experimental animal at the late foetal stage into the spleen where no muscle action is present. The secondary characteristics of the bone are developed in detail and persist without stress. He states that the cartilage precursor has the growth potential capable of forming a bone. He then states that when the bone is formed functional stress is necessary for retention of the detailed form.

Moss 1962 (54) says that while intrinsic

(genetic) factors provide potentiality for growth its expression can only occur through extrinsic (functional) factors provided by the matrix.

His concept of a "functional matrix" places the determining role in development not on the individual bone but on the functions with which it is associated. One bone may be associated with different functions - e.g. the palatal process of the maxilla forms the floor of the nasal cavity and the roof of oral cavity and is therefore associated with both respiratory functions and oral function. The functional considerations associated with bone formation include muscles, neural masses, teeth, and spaces - or patency - associated with respiratory and digestive functions.

Scott 1967 (69) subscribes to an idea of a double control of growth. He maintains that endochondrial growth with interstitial cartilage cell proliferation is a primary growth force in length and form. He believes that appositional bone growth in sutures with proliferation of connective tissue is a secondary response to a growth force provided by functional requirements.

The concepts of Scott and Moss outlined above are radical departures from the ideas of Weinman and Sicher 1955 (81). The latter attributed the primary growth force to bone formation in both intra-membraneous and endochondral ossification. Growth of bone allowed the soft tissues to increase and fill the extra space provided for it.

REMODELLING OF BONE

Frost 1964 (26) defines bone modelling as the combined resorption of older bone and the formation of new bone. Both functions are performed by cells and therefore are cell-regulated.

There are two major types:

A. Internal remodelling.

This is the process observed in the interior of the cortex and the large trabeculae. This is responsible for the physical and histological quality of bone.

B. Surface remodelling.

This occurs on periosteal and endosteal surfaces. This is responsible for growth and size of lamellar bone.

The two types are distinguished because the graphs of their activity plotted against age are different, indicating a difference in regulation.

STIMULUS FOR ACTIVITY

Mesenchymal cells are activated at the focus-to-be by a command from some unknown, but probably extracellular, mechanism.

Mesenchymal cells are the pluripotent progenitor cells found in the neighbourhood of the blood vessels in and near bone. All osteoblasts and osteoclasts are produced by the mesenchymal cells.

L.C. Johnson 1964 (42) believes that the stimulus for bone resorption is associated with the breakdown of the phospholipid barrier which protects bone. This interface or barrier is formed on the completion of the osteoblastic cycle in lamellar bone formation.

METHOD OF RESORPTION OF BONE

The mesenchymal cells produce waves of osteoclasts that usually make a resorption space over a period of about 3 months.

In resorbing bone the osteoclasts are flattened out closely over the surface under attack. Frost 1962 (26) and L.C. Johnson 1964 (42) stress the close adaptation of the osteoclast to the bone. This allows the osteoclast to maintain ionic concentrations and pH values which would not be possible if diffusion took place with the extracellular fluids.

L.C. Johnson 1964 (42) describes a microvillous structure of the osteoclast surface adjacent to the bone. This produces a greater area of cell surface for absorption.

Frost 1962 (26) says the bone is removed by the action of low pH and chelating agents.

RATES OF REMODELLING

Remodelling activity occurs in units termed foci by Frost 1962 (26). These may be counted accurately and normal figures derived for different ages. There are resorption and formation foci, and

both are active for a period of about 3 months.

The mean rate of surface destruction and new matrix formation has been found to be about 1 micron each per day. Each focus exhibits only one form of activity at a given time, i.e., resorption or formation activity.

L.C. Johnson 1964 (42) says the rates of remodelling found in his experiments agree with the remodelling rates reported by Frost 1964(26).

CONTROL OF REMODELLING

Frost 1964 (26) suggests that the genetic code present in the mesenchymal cells is of the greatest importance in changing of the foci pattern from resorption to formation.

Control of the rates of remodelling is regulated primarily at the activation state of the mesenchymal cells. Regulation at this level results in changes in the numbers of foci and is responsible for about 80% of the change in remodelling rates. Only about 20% of a change can be attributed to effects of direct regulation on osteoclasts and osteoblasts.

CRANIOFACIAL GROWTHCRANIAL BASE

The bones comprising the cranial base are:

- a) the exoccipital and the basioccipital;
- b) the body, lesser wing and part of the greater wing of the sphenoid, the petrous portion of the temporal bone; and
- c) the cribriform plate of the ethmoid.

These bones are all derived from cartilage by endochondral ossification.

Scott 1959 (65) presents a table of dimensions in different areas of the craniofacial complex, expressed as a percentage of their adult dimensions. Three of these dimensions are presented below:

	Birth	3 years	7 years	10 years
Cranial capacity	24%	82%	90%	95%
Cranial base	56%	76%	85%	90%
Total face height	40%	65%	80%	84%

Growth of the cranial base after birth is shown to be midway between cranial growth and facial growth.

The cranial base can be studied in three sections:

1. Posterior cranial base. This consists of the basioccipital bone and part of the body of

the sphenoid to the pituitary fossa or sella turcia.

2. The anterior cranial base consisting of the cribriform plate of the ethmoid to the foramen caecum and the portion of the body of the sphenoid anterior to the pituitary fossa.
3. The lateral portions of the cranial base.
This consists of the lesser and greater wings of the sphenoid and the petrous portion of the temporal bone.

1. THE POSTERIOR CRANIAL BASE

The sphenoccipital synchondrosis is associated with growth in this area. Scott 1959 (65) believes this growth area persists into adult life - or about 25 years of age.

The period of maximum growth is from late foetal life to 3 years of age.

Brodie 1955 (13) stresses the constant relationships, maintained during growth, of the posterior and anterior sections of the cranial base. This author found that the greatest amount of cranial base growth was completed by 5 years of age in both the anterior and posterior sections. After 5 years of age growth increments were small. Brodie detected a parapubital growth spurt in the cranial base but this was quite small in relation to the growth before 5 years of age.

2. THE ANTERIOR CRANIAL BASE

The sphenoethmoidal suture is the site of growth in this area. Growth no longer occurs here after 7 years of age and Scott 1959 (65) suggests completion by 3 years of age.

Brodie 1955 (13) states that as the upper face is connected to the anterior cranial base growth in the cranial base will influence growth in the upper face. Downward and forward growth can occur in the upper face without affecting the cranial base. Brodie says this growth occurs in the facial sutures.

Bjork 1955 (8) found slight flattening of the cranial base angle between the ages of 12 and 20. He states that individual changes during this period were more important than the mean change. Individual cranial base angles may show either an increase or a decrease.

Bjork 1955 (8) found that N.S.* was a stable reference line during adolescence and it remained in constant relation to the anterior cranial base.

No measurements of cranial base changes in Vit. D R.R. have been found in medical or dental literature. The effect of vit. D deficiency rickets on the cranial base is extremely vague; shortening of the anterior section has been reported by Kankhaus 1957 (43) but the material from which this observation was derived and the method of analysis have not been reported.

* The line from the anterior of the fronto-nasal suture to the mid-point of sella turcia.

3. THE LATERAL PORTIONS OF THE CRANIAL BASE

Scott 1964 (66) states that during foetal life and early infancy cartilaginous growth occurs between the greater wings and the body of the sphenoid.

The greater wings unite with the body of the sphenoid during the first year after birth.

There is no synchondrosis between the lesser wings and the body of the sphenoid.

Tracey and Campbell 1968 (77) measured the width from left to right mandibulae condyle and from the left to the right pterygomaxillary fissure. They found both measurements to be within normal limits. *

Measurements in width of the cranium could be related to growth of the lateral portions of the cranial base in the infant. However, the relationship must become more obscure with age as appositional growth predominates.

The nine children examined by Tracey and Campbell, 1968 (77) ranged in age from 2 years 9 months to 12 years, and their average age was 7 years 4 months.

* Normal growth was recorded where the measurements were above the tenth percentile.

NASAL DEVELOPMENT

Scott 1964 (66) states the nasal capsule (Fig. 17) is formed in cartilage early in foetal life before the appearance of ossification centres.

Posteriorly the capsule is continuous with the cartilage of the cranial base. It extends anteriorly to the fronto-nasal process of the maxilla. The lateral part of the capsule lies in the side walls of the nasal cavities, and on the lower end it turns inward as the cartilaginous skeleton of the developing inferior turbinate process.

The maxillary and premaxillary bones develop on the outer side of the nasal capsule. The palatine bone develops on the inner side of the nasal capsule and the vomer develops in relation with the septal cartilage.

The lateral - or facial - part of the ethmoid replaces the superior lateral section of the nasal capsule, and forms the superior turbinate process.

The perpendicular plate of the ethmoid invades the septal cartilage from above and behind. This is a cranial bone.

The maxillary sinus begins to develop about

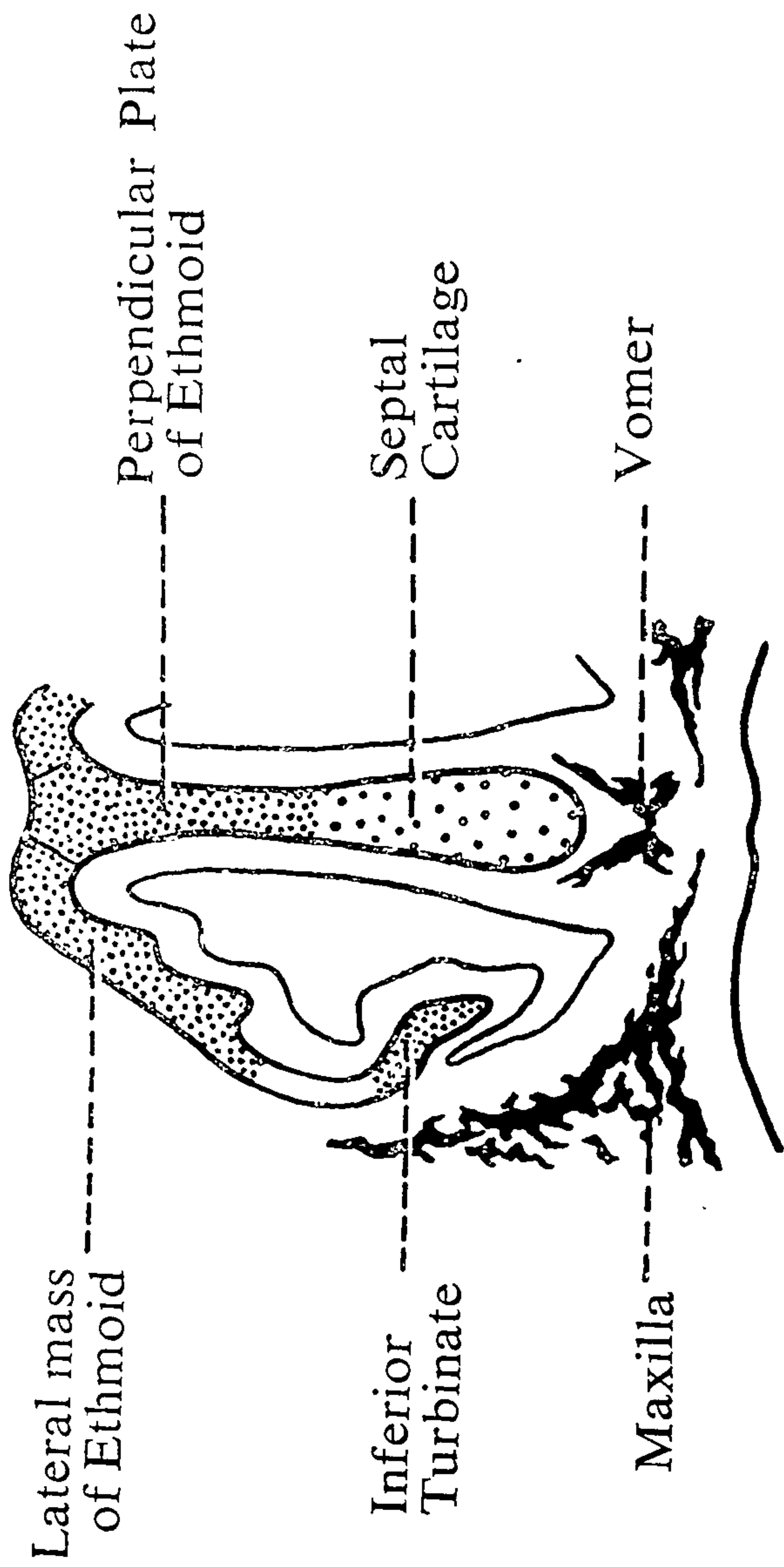


FIG. 40.

Diagram of the nasal capsule and the membrane bones developed in relation to it. Area of the nasal capsule replaced by bone shown in heavy stippling; area of the nasal capsule persisting as cartilage shown in light stippling; area of the nasal capsule which disappears, unshaded.

the middle of foetal life following atrophy of the lateral wall of the nasal capsule between the inferior turbinate and the lateral ethmoid.

Ossification commences shortly after birth in the posterior; superior region of the septal cartilage and extends down as the perpendicular plate of the ethmoid.

Scott 1964 (66) states that bony union does not occur between the lateral ethmoid and the cranial ethmoid until about 3 years of age. At this stage ossification has extended across the cribriform plate and this unites the cranial and facial elements of the ethmoid. Further growth in this area can occur only by apposition.

Bony union between the perpendicular plate of the ethmoid and the vomer occurs in the posterior region of the nasal septum at about 6 years of age. This marks the completion of cartilaginous growth in the posterior of the nasal septum.

The wedge shaped cartilaginous nasal septum is now enclosed by bone on its superior, posterior and inferior surfaces. On its inferior margin the septum rests in the grooved vomer without being attached to it; it has a fibrous attachment to the

maxilla at the anterior end of the vomer.

Scott 1964 (66) regards proliferation of cartilage in the nasal capsule as the most important growth force in the developing face.

EFFECT OF INTERFERENCE WITH THE NASAL STRUCTURES

Wexler and Sarnat 1961 (82) found that surgical trauma in the area of the developing nose resulted in growth changes in the rabbit.

They surgically removed varying amounts of septum, vomer and premaxilla. When only a portion of septal cartilage was removed minimal but definite changes in growth in the young rabbits occurred. The changes noted were shortening and thickening of the premaxilla, and shortening and relative widening of the palate.

When larger amounts of septal cartilage plus vomer and premaxilla were removed the growth was more seriously disturbed. The abnormal growth resulted in short broad snouts, the upper incisors were distal to the lower incisors.

In a later report these authors 1965 (83) found lateral dislocation of the septal cartilage

from the trough of the vomer did not produce any gross differences in the rabbit snout or jaws. The dislocated cartilage tended to return to its normal position and so continuity across the nasal cavity was reestablished. This experiment demonstrated the direct relationship between the degree of trauma to the snout and the resulting deformity.

ABNORMALITIES OF NASAL GROWTH

Moss 1962 (54) states that maxillary growth occurs in response to the need for respiration, and that development of the nasal capsule is the method of growth, with cartilage formation being a filling in process.

Walker 1964 (80) suggests there is an inherent tendency for a bone to develop to a particular form and then a mechanism which maintains this form.

The observations of Ackerman et. al. 1965 (1) on a patient with cebocephalia support Walker's ideas of inherent development of form.

In cebocephalia there is hypoplasia of portions of the rhinencephalon, absence of the nose, and microphthalmia.

The influence of the nasal capsule is extremely limited by the absence of most of the bones in this area. Development of the cranial base is not changed.

The most notable feature found in the period of observation, from 3 years to 8 years old, was the failure of the descent of the maxilla.

They found facial height increased normally in this period and mandibular growth was about normal.

There was no increase in the size of the orbits, without eyeballs, but the orbits were larger than the expected infant orbit.

Grumberg 1947 (31) has studied the effects of abnormal growth of the cranial base and nasal capsule in the mouse.

The first abnormality examined results in congenital hydrocephalus (Fig. 18). The deformity develops in utero on the 13th and 14th day as early cartilage formation occurs. By birth the animal has grown out of the problem, but irreparable damage has been done in the area of the basicranium.

The pre- and post-caudal sections of the basicranium unite at the point where Rathke's

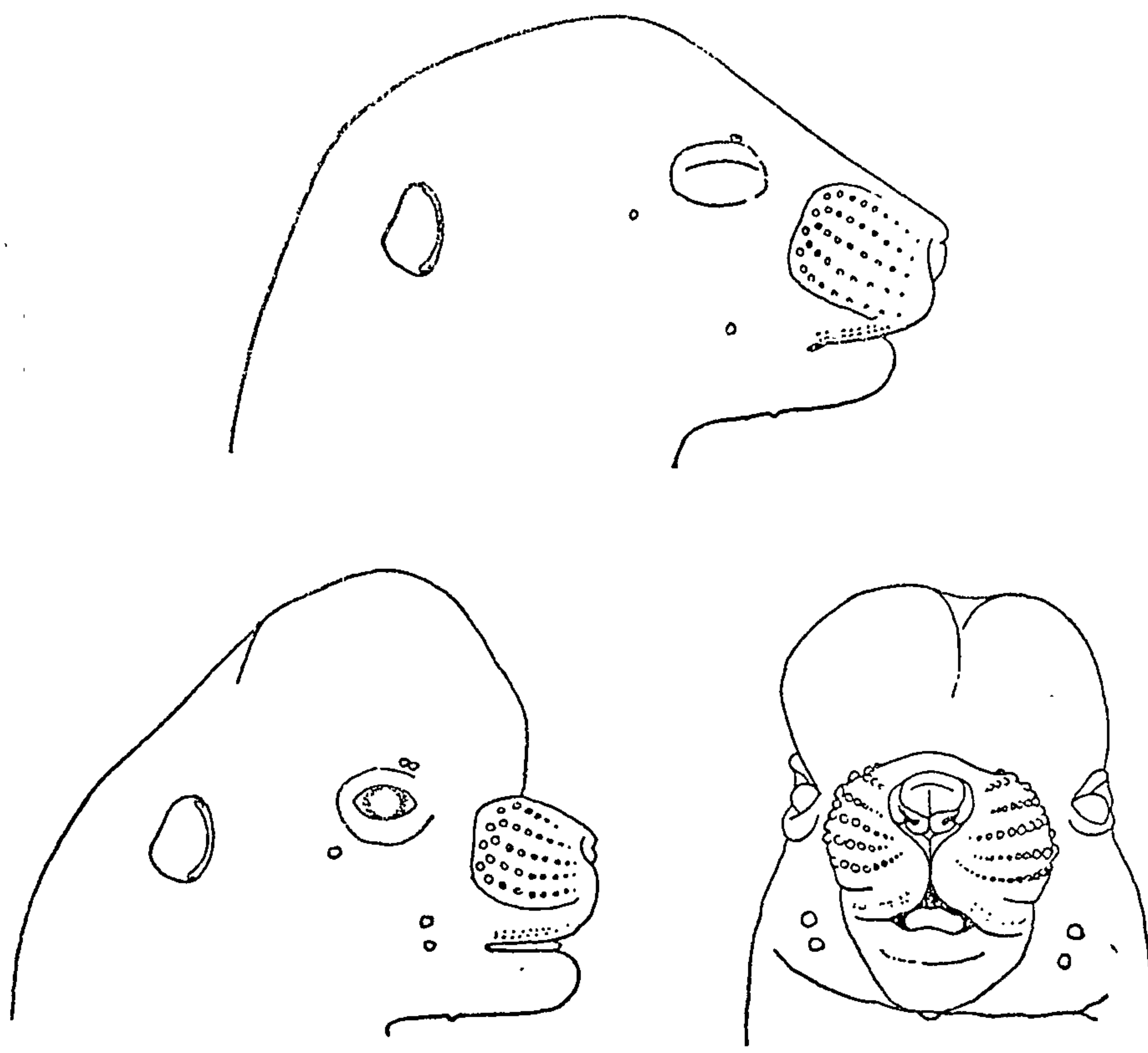


Fig. 18

FIG. 4. Heads of a normal mouse and a congenital hydrocephalus. 18 days old foetuses (litter mates). From GRÜNEBERG, 1943b, by courtesy of the *Journal of Genetics*.

pouch forms the pituitary. Growth retardation occurs in these animals at the time when union should occur in the basicranium. Although union eventually occurs the basicranium and nasal septum are much shortened, and a cranio-pharyngeal canal persists.

The cerebral hemispheres continue to grow and result in dorsal bulging due to the shortened cranial base. Although the calvarium is not formed at this stage the skin exerts pressure on the hemispheres. This results in telescoping of the lower part of the brain and blocks the flow of the cerebrospinal fluid in the fourth ventricle.

Grumberg 1947 (30) describes a genetic abnormality of cartilage formation occurring after birth. Histological examination of the cartilage revealed hypertrophy of the individual cells with deficient matrix production. The abnormality is limited to specific areas, the most severely affected cartilage is in the thorax, trachea and sternum. Cartilage remains normal in the long bones.

A malocclusion appears with the development of the upper jaw falling behind the development of the lower jaw.

Grumberg 1947 (32) also studied the abnormality in the mouse called "Grey-Lethal". In this there is failure of secondary bone absorption, consequently remodelling failure.

This abnormality results in the teeth failing to erupt; non-eruption of the teeth also occurs in human cleidocranial dysostosis and it has been suggested the human disease is a milder, localised version of the grey-lethal condition observed in the mouse.

Low blood phosphate levels - particularly organic phosphate - have been reported in the grey-lethal mouse. The blood calcium levels have been normal. Grey-lethal mice are very resistant to the effects of injected parathyroid hormone, but with a very high dose severe bone destruction occurs.

Bone transplants into normal mice produced resorption; and normal bone transplanted into grey-lethals assumes a structure similar to the hosts. This suggests a substance in the blood is controlling the absorption process of the bone.

Le Roy Johnson 1940 (41) found a patent nasopharyngeal canal in bulldogs. The cranial configuration of the bulldog is quite similar to

that found by Grumberg 1947 (31) in the congenital hydrocephalic mouse.

This suggests that abnormal cartilage growth is important in the development of the characteristically deficient maxilla of the bulldog.

Johnson 1940 (41) also found when he removed the body of the sphenoid, it regenerated without form change.

DEVELOPMENT OF THE MAXILLA

Scott 1964 (66) states that maxillary and premaxillary bones develop on the outer aspect of the nasal capsule. These bones are first formed in membrane and ossification is intramembraneous. The palatine bone, which is also a membrane bone, develops on the inner aspect of the nasal capsule.

In man the maxilla and premaxilla unite early in foetal life and no suture system is visible between them at birth.

The only cartilage associated with the development of the maxilla appears for a period early in the foetal life. This is a secondary cartilage and is associated with the development of the zygomatic process.

During the first few years after birth sutures are present between the maxilla and other facial bones. Growth of the eyeballs and nasal septum result in down and forward displacement of the maxilla and sutural growth can quickly adapt to this changed position. Less growth occurs in these sutures after 3 years and by 10 years they are almost complete.

Termination of sutural growth in this region is associated with union between the perpendicular plate of the ethmoid and the two facial bones - the lateral ethmoid and the vomer.

The chief method of facial growth after the first 10 years is by surface apposition and remodelling. This is associated with continual development of the maxillary sinus.

Bone deposition at the tuberosities is the chief factor producing increase in length of the alveolar process for the eruption of the molar teeth according to Scott.

Enlow and Bang 1965 (22) drew up composite figures of apposition and resorption as they occur in remodelling growth in the maxilla. (Figs 19 & 20).

The overall pattern is of apposition on the distal of the maxilla.

The area between the zygoma and molar teeth - marked T, was the only area where important variation occurred. Resorption or lack of periosteal apposition at T would result in constriction of maxillary arch in the posterior.

The zygoma is affected by growth in width of the nasal cavity and the orbit. The zygoma changes position from A to B by apposition in areas marked + and resorption in areas marked - in Fig. 21.

They found that resorption in the premaxillary region resulted in the anterior nasal spine moving down and slightly posteriorly as shown in Fig. 22

They also found that the floor of the orbit was not affected by pneumatization of the maxillary sinus. As the sinus develops it separates the orbital surface of the maxilla from the dental regions. This expansion must occur in downward direction with the development of the alveolar process.

Bjork 1964 (11) found that the growth pattern of the upper face is not linear and that serial cephalometric X-rays are necessary to find the pattern of the growth curve.

Bjork's growth curve is mainly sagittal

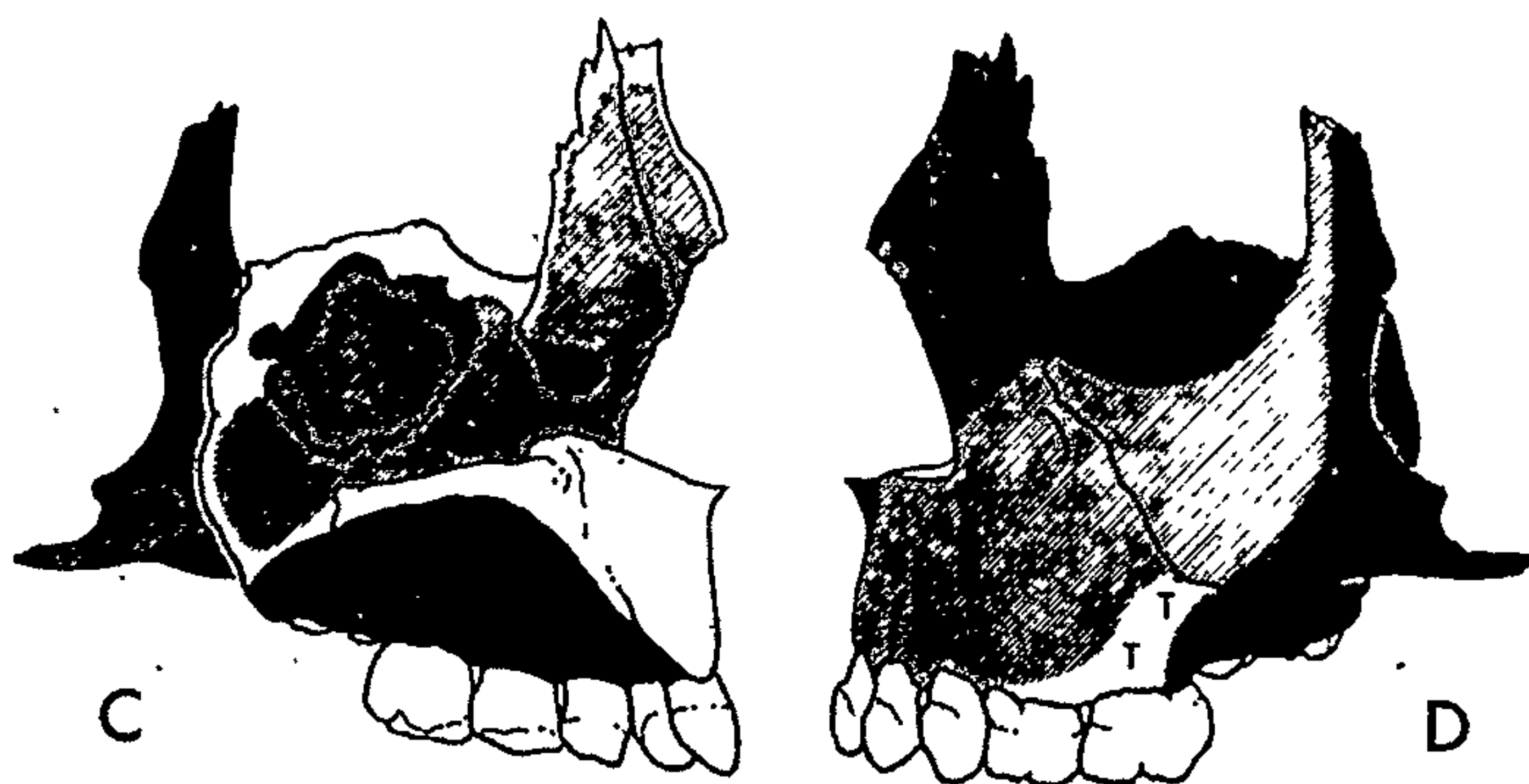


Fig. 1. *A* and *B*, Diagrams indicating distribution of the various *numbered areas* described in the text. *A* shows a medial view of the maxilla, and *B* shows a lateral view. Inset figures show lateral and medial views of the nasal and zygomatic bones. *C* and *D*, Diagrams of medial (*C*) and lateral (*D*) aspects of the maxilla summarizing distribution of various periosteal (dark crosshatch) and *endosteal* (light crosshatch) bone deposits. Note zone of variable endosteal-periosteal transition (*T*) on lateral cortex in molar area. For detailed discussion of each area in all parts of the maxillary bone, see text.

Fig. 19

Fig. 20

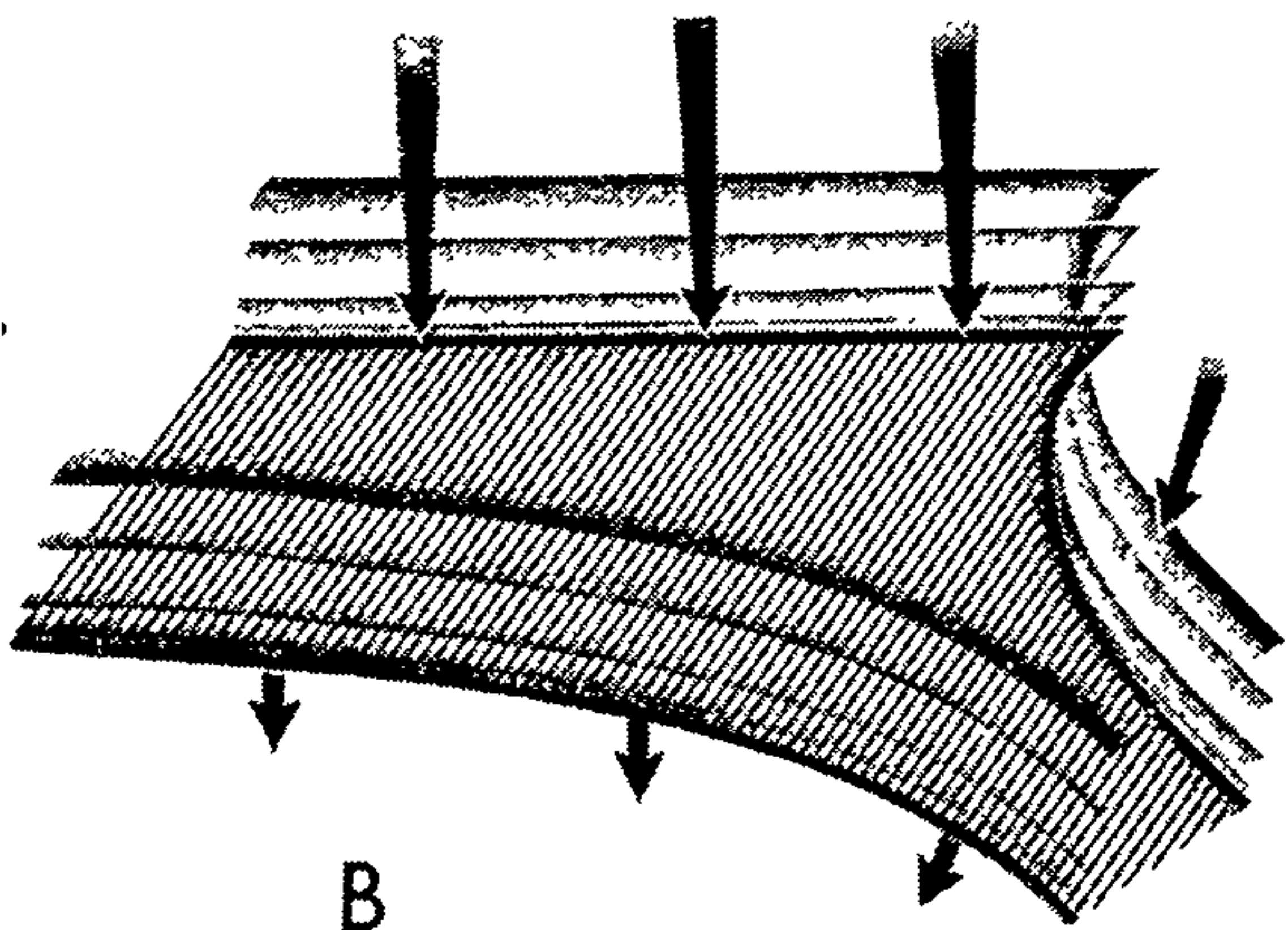


Fig. 21

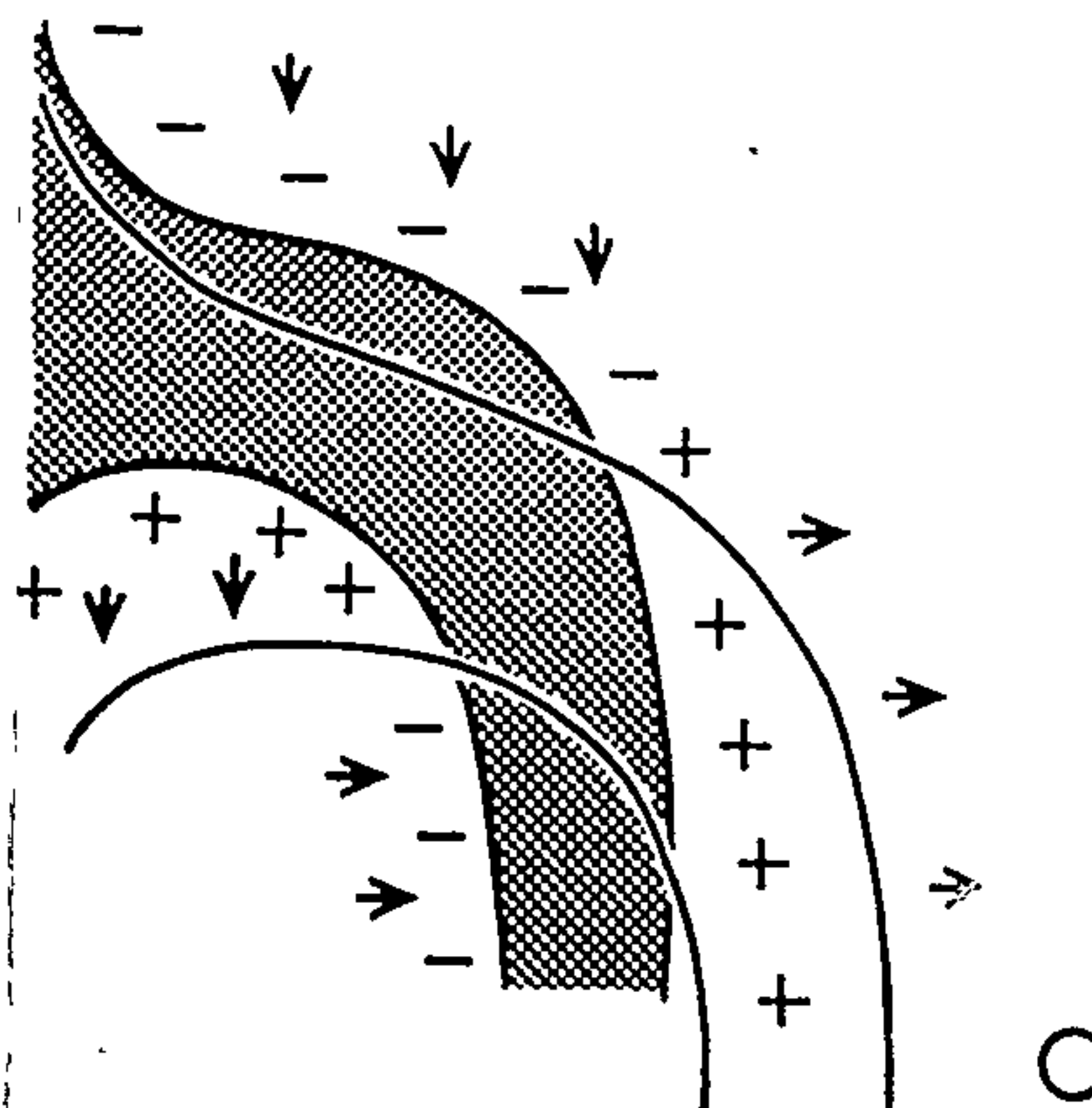


Fig. 22

(horizontal) in a juvenile and becomes vertical during adolescence.

He found the pattern of eruption of the teeth was mostly vertical and an anterior slope was associated with prognathism and posterior inclination with retrognathism.

DEVELOPMENT OF THE MANDIBLE

Meckel's cartilage develops in the mandibular arch during early foetal life. Scott 1964 (68) states that it extends from the developing cranial base in the region of the otic capsule to the midline in the future chin region, where it meets the cartilage of the opposite side.

The mandible develops in membrane on the outer aspect of Meckel's cartilage.

Scott 1964 (68) found part of Meckel's cartilage is incorporated in the body of the growing mandible, and part of it forms the spheno-mandibular and spheno-malleolar ligaments. Its proximal end ossifies to form the malleus of the middle ear.

Scott 1964 (68) refers to the mandible as a

membrane bone. The body and the ramus of the mandible are first produced in membrane and ossification is intramembraneous.

Scott 1964 (68) states there are three main sites of secondary cartilage formation.

1. Condylar cartilage. This appears on the superior and lateral aspects of the bone of the condylar process. This proliferates and results in a cone of cartilage occupying the entire condylar process and extending down the ramus to the level of the mandibular foramen. Endochondral ossification occurs in the older cartilage and extends down the length of the cone, resulting in replacement by bone, of all the cartilage except for the zone in contact with the tissue of the articular surface of the condyle. This zone of cartilage persists into adult life.
2. The coronoid cartilage forms a strip on the anterior and superior aspects of the coronoid process. Ossification has occurred in this cartilage long before birth.
3. The symphyseal cartilages appear at the anterior end of each half of the bony mandible. They

are independent of Meckel's cartilage.

Union occurs in this area soon after birth.

Scott's idea of the role of the condylar cartilage appears to have changed since 1954 when he stated (Scott [69]) that growth of the condylar cartilage maintains contact in the temporomandibular joint as growth down and forward occurs. In 1959 (65) he attributed primary growth to the cartilage of the condyle; he says growth at the condyle thrusts the mandible down and forwards. Appositional growth occurs on the posterior of the ramus.

Enlow and Harris 1964 (21) have studied appositional growth in the human mandible and compiled diagrams of areas of apposition and resorption of bone. These areas are shown in Fig. 23 and Fig. 24.

During growth, the mandible requires extensive remodelling to change from the childhood form to the adult form, as shown by Fig. 25.

This is not a simple process of elongation; it involves a gradual remodelling of the complete mandible.

These authors found most variation in the area of the chin. In some individuals resorption occurred

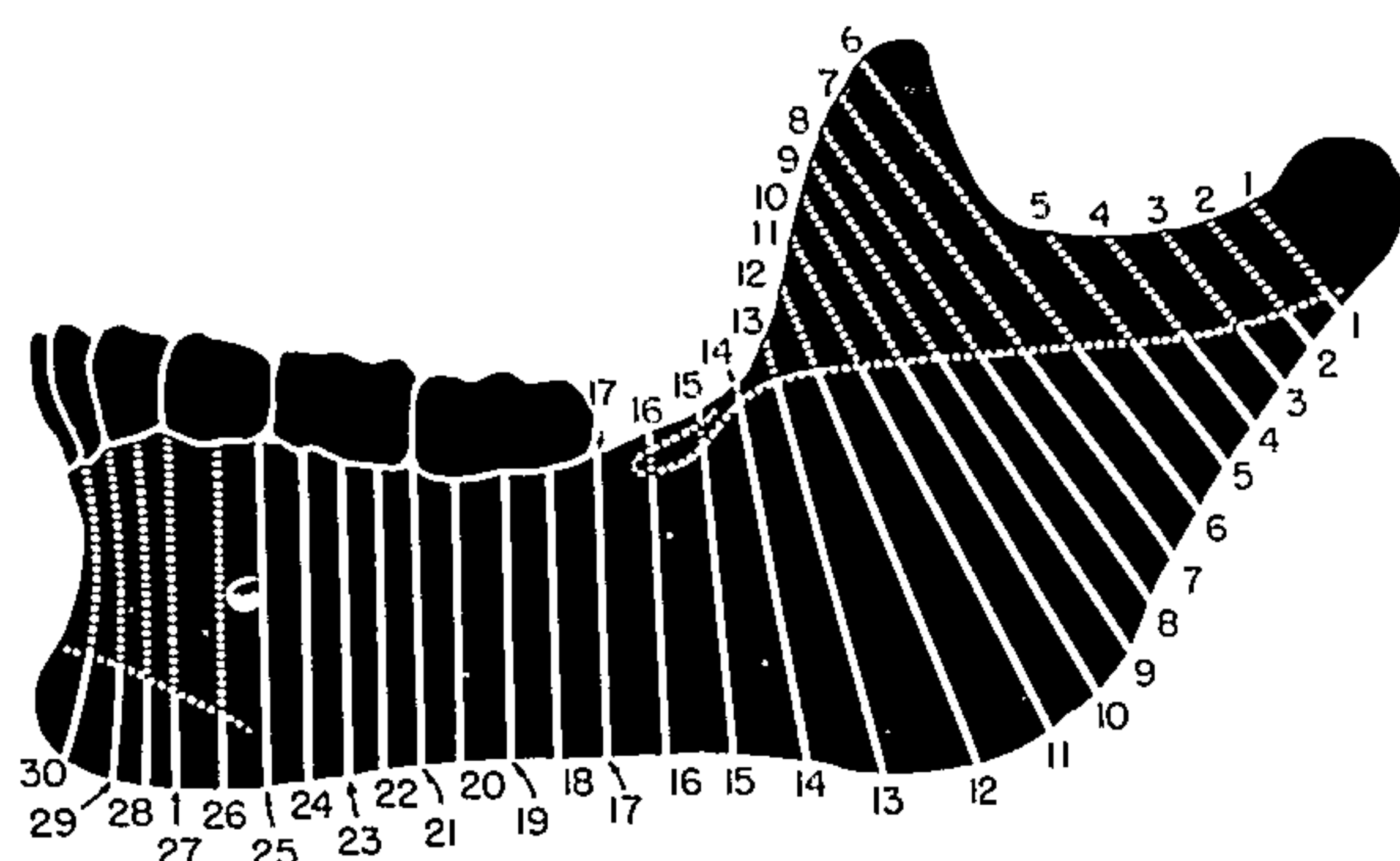


Fig. 23

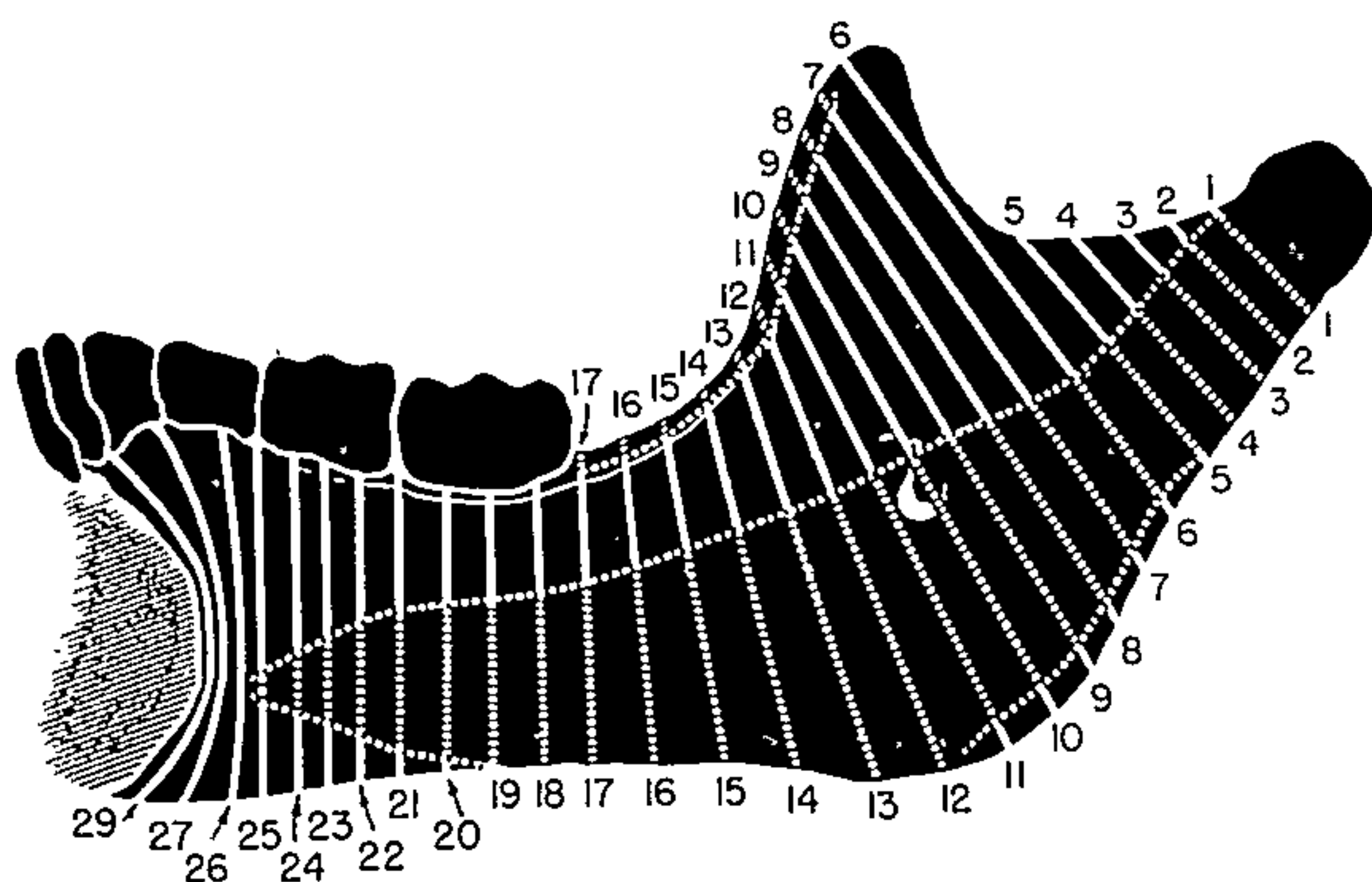


Fig. 24

Fig. 1. A composite figure based on twenty-five young human mandibles. The most frequently observed patterns of cortical structure in the various parts of the mandible are summarized in this diagram. Common variations are shown in Fig. 10. The numbered lines indicate the serial locations of entire transverse sections. Solid white lines represent cortical surfaces which have received periosteal deposits and which have grown in an outward or periosteal direction. Broken lines indicate resorptive surfaces with an underlying cortex composed of endosteal bone. The top figure represents the buccal side and the bottom figure the lingual side of the mandible.

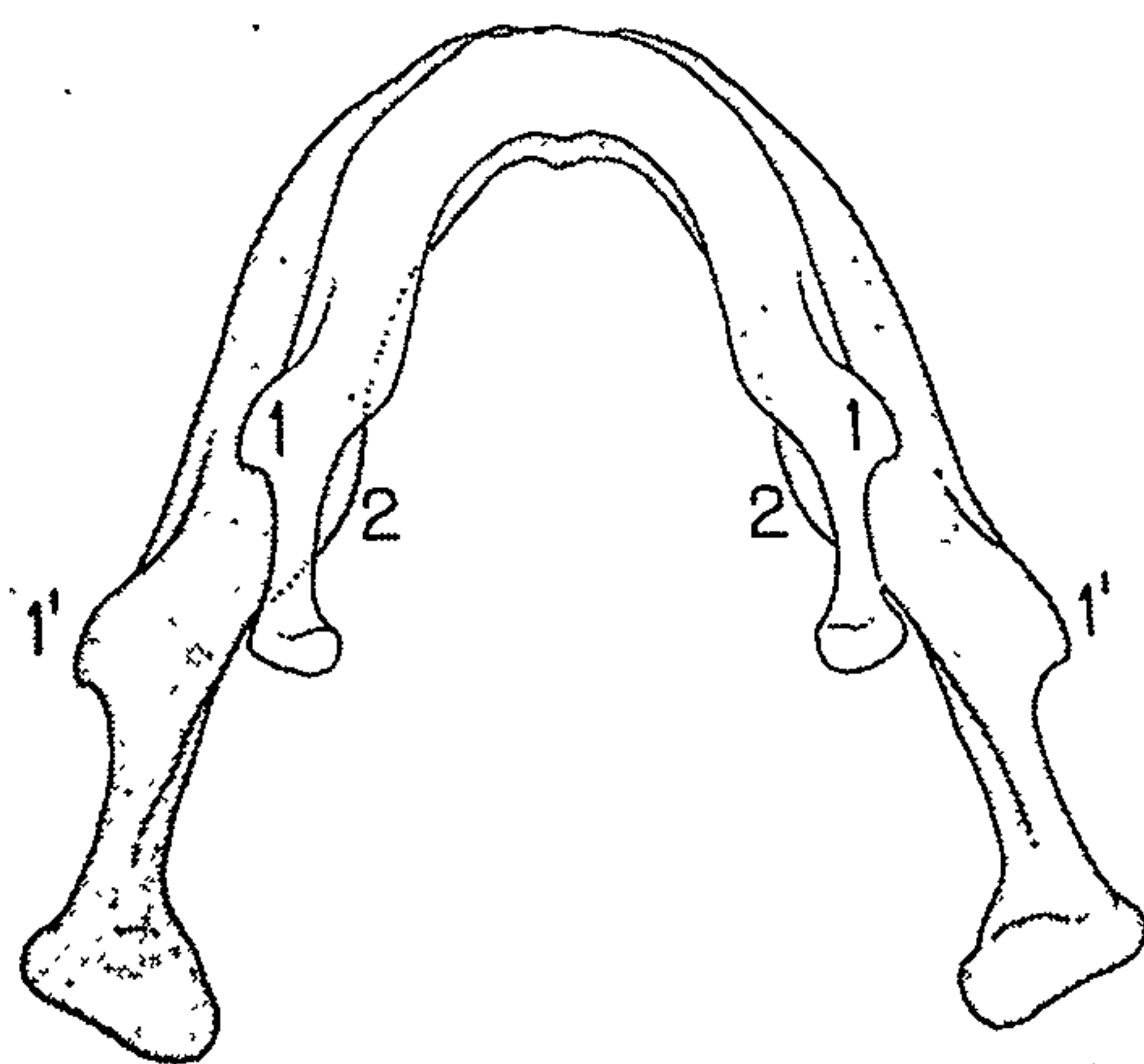


Fig. 25

over the whole chin button. Resorption occurred on the alveolar bone between the cuspids.

Bjork 1963 (10) found a wide individual variation in the growth of the mandible. He found no apposition or resorption on the anterior of the chin, but appositional growth occurred beneath the chin particularly during adolescence.

As reported for the maxilla the direction of growth was not necessarily linear and serial cephalometric x-rays are necessary to determine the direction of growth as shown in Fig. 26.

A - mean growth pattern

B - extreme vertical

C - extreme sagittal

Bjork also noted that the movement of the teeth in the alveolus followed a pattern which varied with the direction of condylar growth.

In a patient with bilateral hypoplasia of the mandibular condyles Bjork 1962 (9) found there was posterior rotation of the mandible about the first molar, increased ante-gonial notching and changed axial inclination of the teeth.

Bjork 1962 (9) says that alveolar prognathism was not shown by the implant study; he found distal tipping of the posterior teeth with no change in

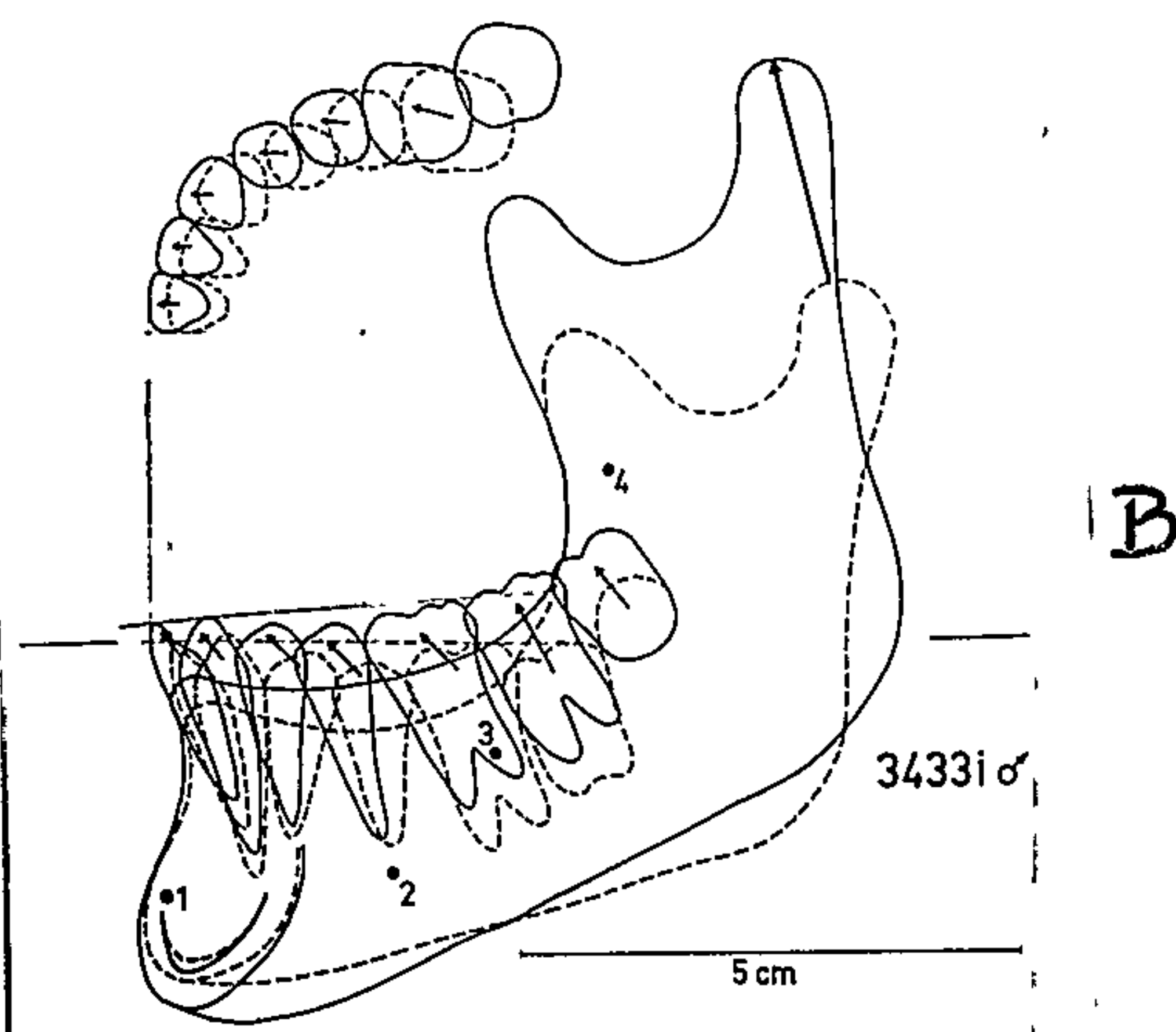
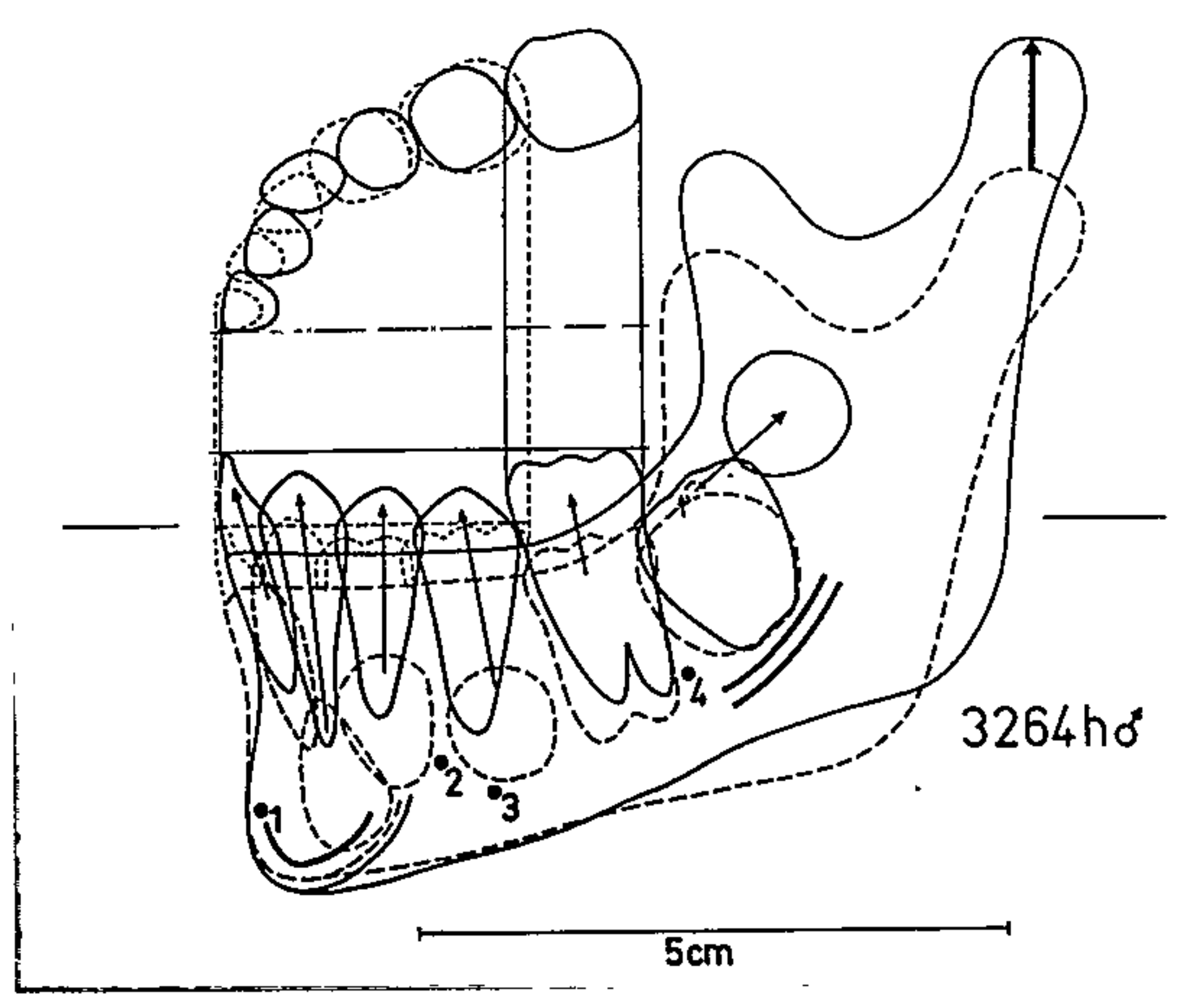
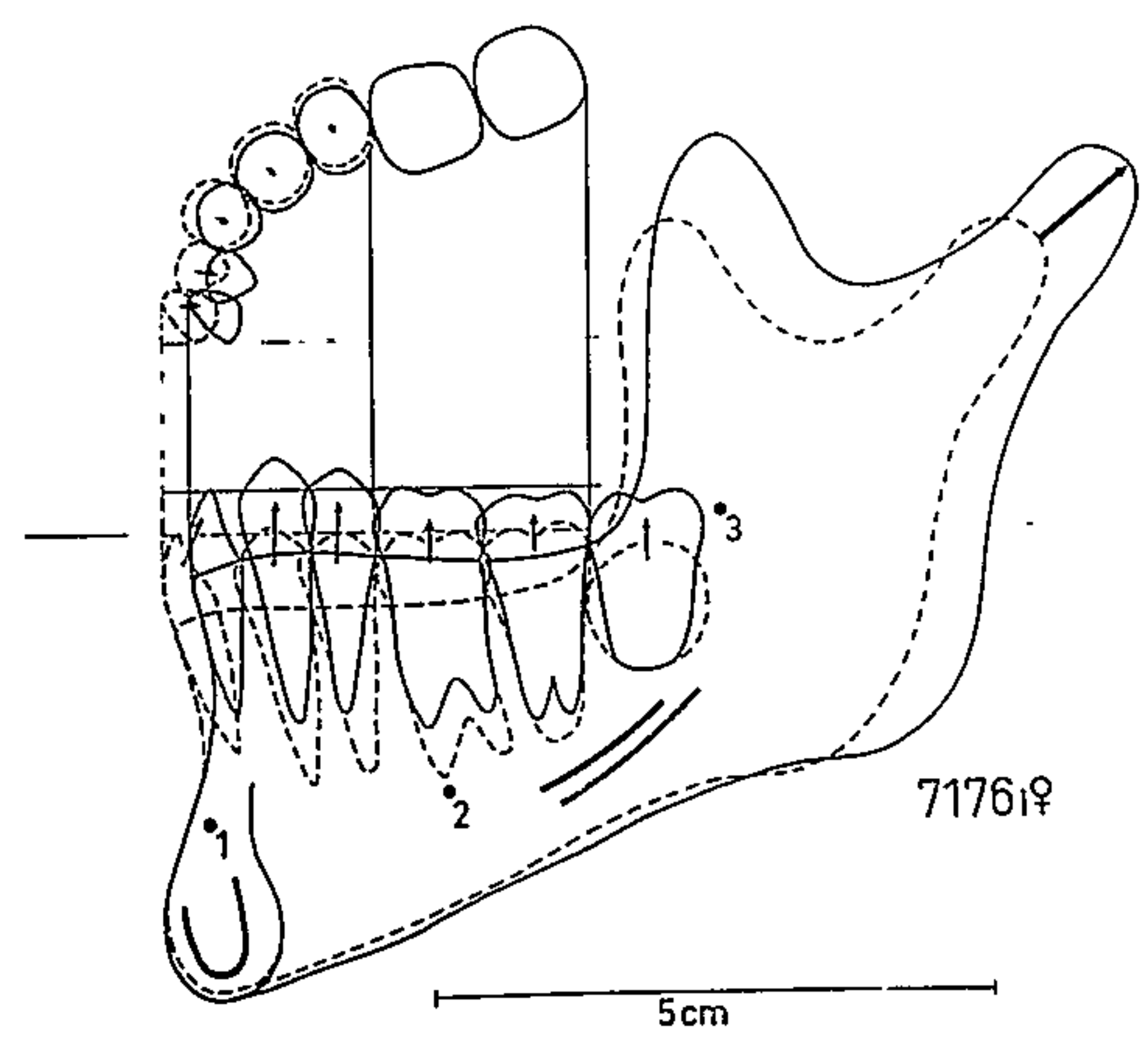


FIG. 7.—Case illustrating extreme direction of vertical growth at the condyles in the boy sample.
Broken line = age 11 years 7 months, solid line = age 17 years 7 months.



A

Fig. 26



C

the anterior teeth (Fig.27).

Ole Thrs 1964 (76) also demonstrated antegonial notching in the study of a patient wearing a Milwaukee-Brace. The brace had produced a reduction in facial height and apparent inhibition in growth of the condyle.

Moss 1964 (55) found that increase in facial height continues into the third decade and probably longer. Increases in upper facial height are associated with increased nasal height.

Lower facial height increases are closely related to increases in region of the mandibular symphysis.

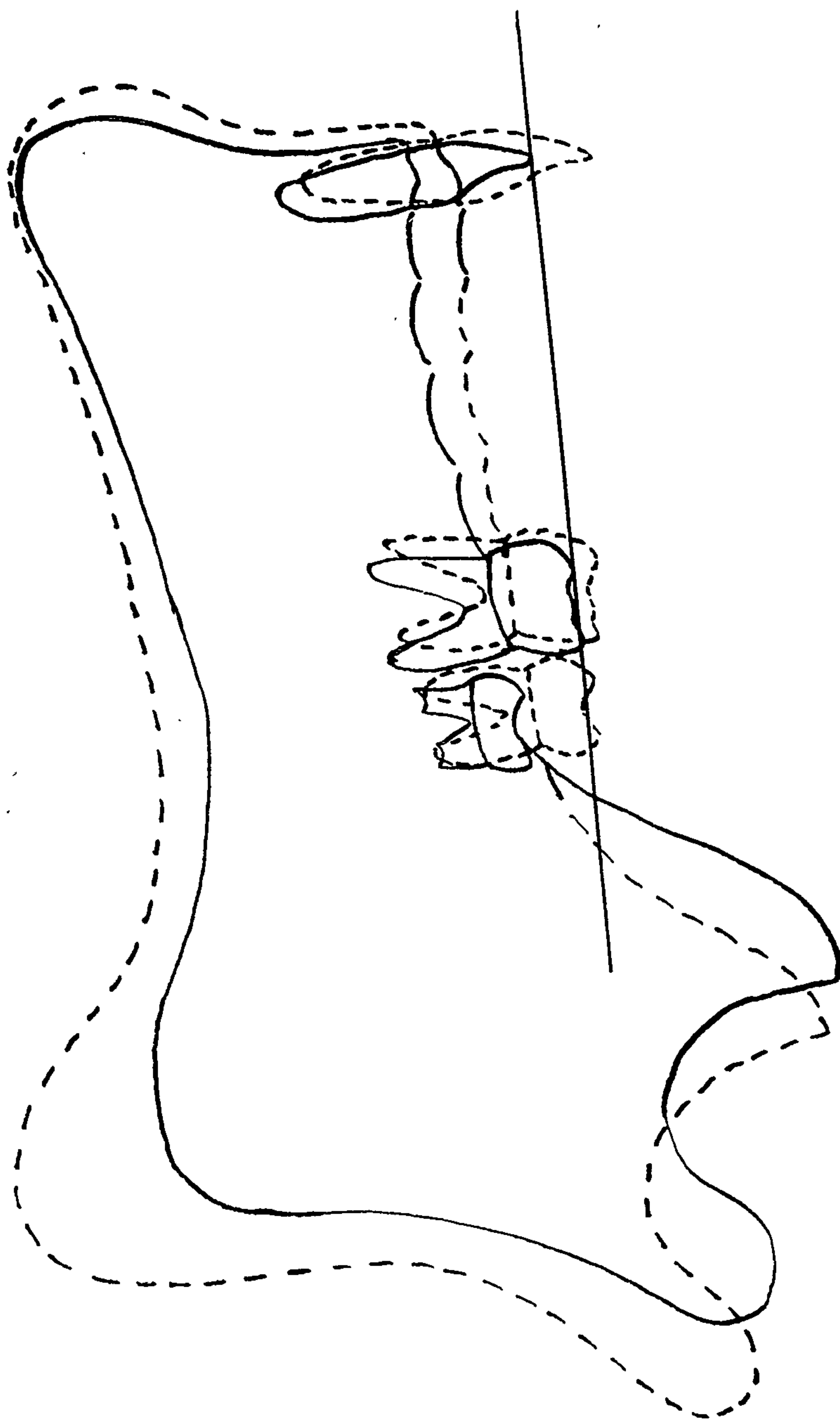


fig. 27

GONIAL ANGLE OF THE MANDIBLE

Schudy 1965 (64) states that an obtuse gonial angle in the mandible may compensate for a short body and ramus of the mandible. The gonial angle thus compensates for inharmonies in facial proportions. Schudy found a close relationship between the gonial angle and angle formed by S.N. and mandibular plane.

The author feels there has been insufficient study of the growth changes in the gonial angle and the significance of these changes.

Harvold 1960 (37) states that the gonial angle becomes more acute in the normal child between the ages of 3 and 12. Cleft palate cases who received orthodontic treatment also showed this pattern, but where no orthodontic treatment was provided Harvold did not find this normal reduction in the gonial angle. From this the author suggests that corrective orthodontic treatment in the maxilla can produce change in form of the mandible.

Krogman and Sassouni 1957 (47) found that the gonial angle was one of the most controversial measurements made in the mandible. The difference often arose on the points which should be used to

measure the angle. The most widely used method is to measure the angle formed by a tangent to the posterior border of the ramus and the condyle with the mandibular plane.

As an indication of the reported changes in this angle Krogman and Sassouni 1957 (47) cite the measurements reported by Izard. This author found the gonial angle was 150-135° at birth, 140-130° when the first dentition was complete, 130-120° at the stage of eruption of the 2nd permanent molars and 120° and less in old age.

Higley's 1957 (39) standard for the gonial angle in a 4 year old is $128^{\circ} \pm 4.5^{\circ}$ and in an 8 year old $127.2^{\circ} \pm 4.7^{\circ}$

Harris 1965 (33) found the gonial angle in 10 to 12 year old children with a class I occlusion was $127^{\circ} \pm 6^{\circ}$. In children of the same age with a mild class II div. I malocclusion he found the gonial angle was $125^{\circ} \pm 5^{\circ}$.

GROWTH OF THE CRANIUM

The cranial vault is made up of membrane bones. The bones are the frontal, the parietals, the squamous part of the temporals and part of the occipital and sphenoid bones.

The growth of the cranial vault is related to the growth of the brain.

The sutures between the bones of the cranial vault allow it to adapt readily to the rapidly growing brain of the young child. The suture is maintained by appositional bone growth in response to separation.

Apposition and resorption of bone across the individual bones between the sutures results in recontouring of the original cranial bones.

Reilly et. al. 1964 (61) found the time of closure of the cranial sutures very variable. They state that marginal sclerosis of the sutures normally commences after 9 years of age, and can go on for many years.

Pruzansky and Lis 1958 (60) state that craniosynostosis may result in facial malformations in two ways.

1. Changes in the neurocranium may produce

secondary changes in the facial skeleton.

or 2) Closure of the sutures may not be limited to the calvarium but may involve areas essential to facial development. Pruzansky says that synostosis of the coronal suture can result in shallow orbits, Kyphosis of the cranial base with reduction in the airway and arrested development of the maxilla resulting in open bite, and nasal atresia, which necessitates mouth breathing.

FUNCTIONAL CONSIDERATIONS IN CRANIOFACIAL GROWTH

Foster's 1965 (24) experience with a patient suffering from poliomyelitis emphasises the role that maintenance of the airway can play in the development of a malocclusion.

The patient had commenced treatment for a class III malocclusion before she suffered a very serious attack of poliomyelitis.

When she had recovered she returned for completion of the orthodontic treatment. The class III tendency had become much worse; the palate was almost flat and all teeth were extremely

tipped labially or buccally.

Eventually the underlying problem was detected. The cervical vertebrae had developed an anterior curvature, necessitating forward displacement of the tongue and mandible to maintain an airway.

The curvature was surgically corrected and mandibular posture improved spontaneously. Class I dental relationships were achieved following some extractions.

Whiteley 1966 (84) found that increased masticatory function could cause changes in the craniofacial area of the rat.

The overall size was not changed but areas of some muscle attachments changed. The zygomatic arch and coronoid process were enlarged, also the superior height of the skull was increased.

Increased function also resulted in enlargement of the masticatory muscles.

Moss 1962 (54) developed the idea of relating all growth to the requirements of function. His concept of the functional matrix appears to be winning increasing acceptance.

Graber et. al. 1967 (28) have used the functional matrix concept as the basis of methods of

treatment of so-called skeletal malocclusions. The authors' ideas are to change the functional matrix of growth by the application of heavy forces. The direction of application of the force is critical if the functional matrix is to be changed only in the area where unfavourable growth is occurring.

These authors' application to the functional matrix concept to treatment methods is a final step in the study of growth. In many areas of growth our knowledge is not yet sufficiently complete to enable the clinician to take this final step.

From Moss' original concept the first step must be to identify how the normal functional matrix exerts its controls on growth.

The second step should be to ascertain the way an abnormal functional matrix affects growth. This knowledge may then provide a basis for treatment methods. The final aim of the treatment is to restore the functional matrix to its normal condition as the ideal form of retention.

MATERIAL

The patients examined in this study were originally collected together and classified by Dr. S. Latham in 1965 at the Institute of Child Health, Royal Alexandra Hospital for Children, Camperdown, N.S.W. A dental examination was included with his original study.

Mr. K. Godfrey, as honorary orthodontist, at the Royal Alexandra Hospital for Children, became associated with the collection of dental records. Most of the patients were under medical care at this hospital and the dental records were collected there.

In the dental examination decayed, missing and filled teeth were recorded. The eruption stage of each tooth was recorded. The teeth were checked for enamel defects and these were recorded diagrammatically. Alginate impressions were taken of the teeth and plaster casts were poured from these and trimmed to a wax bite.

Cephalometric true lateral x-rays were taken of each patient and also of the parents and siblings when available. Familial characteristics in the occlusion were noted and the general dental

status of each member of the family was ascertained.

The medical records for each patient were examined, and the following information was obtained:

1. General clinical features in the patient at the time of diagnosis.
2. The family history of the patient.
The important points noted from the family history were reports of rickets, bony deformities, bone disease or marked reduction in stature in either maternal or paternal branches of the family.
3. A history of any serious or chronic illness suffered by the patient and the therapy instituted for this illness.
4. Serum levels of calcium, phosphate and alkaline phosphatase at the time of diagnosis, during active treatment and at subsequent follow-up appointments.
5. The presence and type of skeletal deformities, particularly of the legs and skull; the age at which any deformities were first noticed and any changes in deformities with growth or with treatment.

6. Height and weight measurements from birth.
These measurements were transferred to charts originally published by the National Health and Medical Research Council in 1957. These charts are marked in percentiles for height and weight compared with chronological age.
7. The general adequacy of the diet as assessed by the examining medical officer. The use of calcium and/or phosphate supplements to the diet was noted.
8. The state of muscle tissue. This information is based on tests for co-ordination, reflexes, and power, or on the qualitative assessment of the examining medical officers.
9. The mentality of the patient. Aptitude tests were performed in some cases but in general this information represents the opinions of the examining medical officers throughout treatment.
10. Vitamin D therapy prescribed throughout treatment. This includes the age at which vit. D therapy was commenced, the dosages administered throughout treatment and the total dose. It should be noted that not all cases received vit. D therapy.

11. Orthopedic operative procedures performed, the age at which they were undertaken and the results of the operations.

In 1968 during my study of these patients I was able to re-examine some of them. This second dental examination, approximately 2-1/2 years after the original one, resulted in two sets of dental models and two cephalometric lateral head x-rays being available for comparison in some cases and completion of the records in other cases.

The patients suffering from vit. D R.R. belong to 16 families. Twenty-three affected children and 12 affected parents are included in the material used in this thesis. Two cephalometric lateral head x-rays were available for five patients. These five patients are all children, as a second cephalometric lateral head x-ray was not taken for the adults. A total of 40 lateral head x-rays are included in the material of this study.

Parents and siblings in whom vit. D R.R. had not been diagnosed are not included in the material from which results are drawn in this thesis.

Plaster casts of the teeth of all the children included in the study were available. In 7 cases two sets of plaster models made approximately two years apart are included in the material studied.

Plaster casts were not made of the teeth of the adults. Five of the affected adults were wearing full upper and full lower dentures and four more had full upper dentures over their natural lower teeth - at least six lower anterior teeth being present.

METHOD OF EXAMINATION OF MATERIAL

As previously noted in the review of the literature on craniofacial abnormalities found in association with vit. D R.R. there is a paucity of quantitative results.

My methods of examination have been aimed at supplying quantitative results, wherever possible, to bridge this gap. By doing this it is hoped that any future studies in this field may be able to make direct comparisons with the results obtained in this study.

My examination has been concentrated on the lateral head cephalometric x-ray as I feel this can frequently and accurately show peculiarities of craniofacial growth.

The study models are essentially important when the attempt is made to relate the observations on craniofacial growth to effects in the dental structures.

Using a sharp 2H "Goldfaber" pencil, tracings of the lateral head cephalometric x-rays were made onto "Kodatracer". This was done in a semi-darkened room over an x-ray viewbox, where unnecessary light was excluded.

The points used in the subsequent analysis are shown on Fig. 28 which was reproduced from a tracing of one of the patients studied.

The planes used and the relationship of these planes to the points on the tracing are also shown in Fig. 28.

Complete definitions and discussions of the cephalometric landmarks and planes used are to be found in the Syllabus compiled by Krogman and Sassouni 1957 (48). A list of the points and reference planes used is presented below with an abridged definition of each point from the Syllabus of Krogman and Sassouni.

Nasion, Na

The most anterior point of the naso-frontal suture seen on the lateral head x-ray.

Anterior nasal spine, ANS

This refers to the tip of the anterior nasal spine, as it appears on the lateral head x-ray.

Subspinale, A

This is taken as the deepest midline point on the premaxilla between the anterior nasal spine and prosthion. (Prosthion is the most anterior point

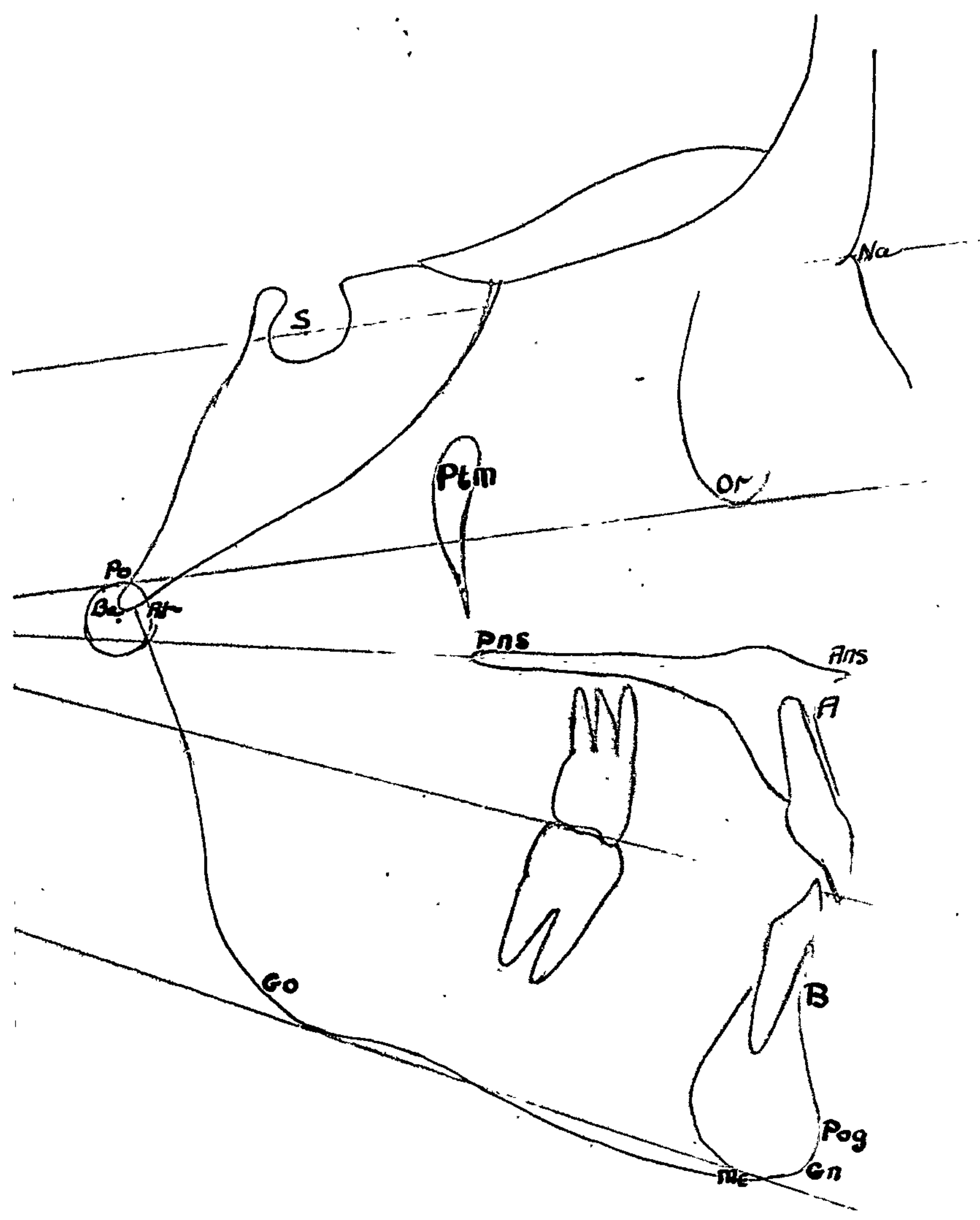


Fig. 28

on the alveolar portion of the maxillary bone and is usually between the central incisors).

Supramentale, B

The most posterior point on the outer anterior contour of the mandibular alveolar process.

Pogonion, Pog.

The most anterior point on the bony chin as seen in the lateral head x-ray.

Gnathion, Gn

A point on the chin, found by bisecting the angle formed by the facial and mandibular planes.

Menton, Me

The lowermost point on the symphysis of the mandible, as seen in the lateral head x-ray.

Sella, S

The mid-point of the sella turcia, determined by inspection.

Basion, Ba

The midpoint of the anterior margin of the foramen magnum.

Posterior nasal spine, PNS

The tip of the posterior spine of the palatine bone in the hard palate.

Gonion, Go

This point is found by bisecting the angle formed by the tangents to the lower and posterior borders of the mandible.

Articulare, Ar

The point at the contour of the external cranial base and the dorsal contour of the condylar process.

Porion, Po

The centre of the top of the ear-rods. This is 4 mm. above the centre of the ear-rods in the cephalostat used.

Ptyergomaxillary fissure, Ptm.

This is not a point. It is the projected contour of the fissure.

Orbitale, Or

The deepest point on the infraorbital margin.

Occlusal Plane

For this plane the depth of overbite in the anterior teeth was bisected and the cusp height of the first permanent molars was bisected for the posterior point.

Mandibular plane, M.P.

This was drawn as a tangent to the lower border of the mandibular symphysis, at Menton, and a tangent to the lower border of the mandible at the gonial angle.

The first method of examination of the lateral head cephalometric x-rays involved superimposing the age-standard transparencies* compiled by Sassouni 1960 (63) over the tracings.

Sassouni 1960 (63) presented his composite tracings to provide a method of evaluation of facial balance during development. When used in this way the results obtained are chiefly qualitative. By assessing 10 area, detailed below, I have attempted to produce more quantitative results.

Although the results of this analysis are not linear or angular measurements, which can be assessed in relation to a mean with standard deviations, they do provide age comparisons.

These age comparisons provide quantitative results in two ways.

1. They indicate the degree of advancement or retardation in development by comparison with the age of the patient.

* The transparencies used were of white Americans, at the ages of 4 years, 8 years, 12 years, 16 years and adult.

2. The assessed age standard for each area can be superimposed on the transparency showing the average development for the age of the patient. In this way both linear and angular variations can be seen simultaneously.

The ten areas selected for comparison with the age standard transparencies, and the method of superimposition for each area are presented below.

1. Cranial base angle, Fig. 29.

Superimposition of the transparencies is done on the outline of the anterior and posterior cranial base only. Nasion is not considered. In the above illustration the angle would be recorded as flat. Where a transparency fitted the angle more accurately - independent of the length - then the age standard of the transparency is recorded.

2. The horizontal length of the anterior cranial base. Superimposition for this measurement was on S and Na. points. The age standard which fitted most closely was recorded.
3. The horizontal length of the naso-maxillary area, Fig. 30.

WHITE: ADULT, Mal

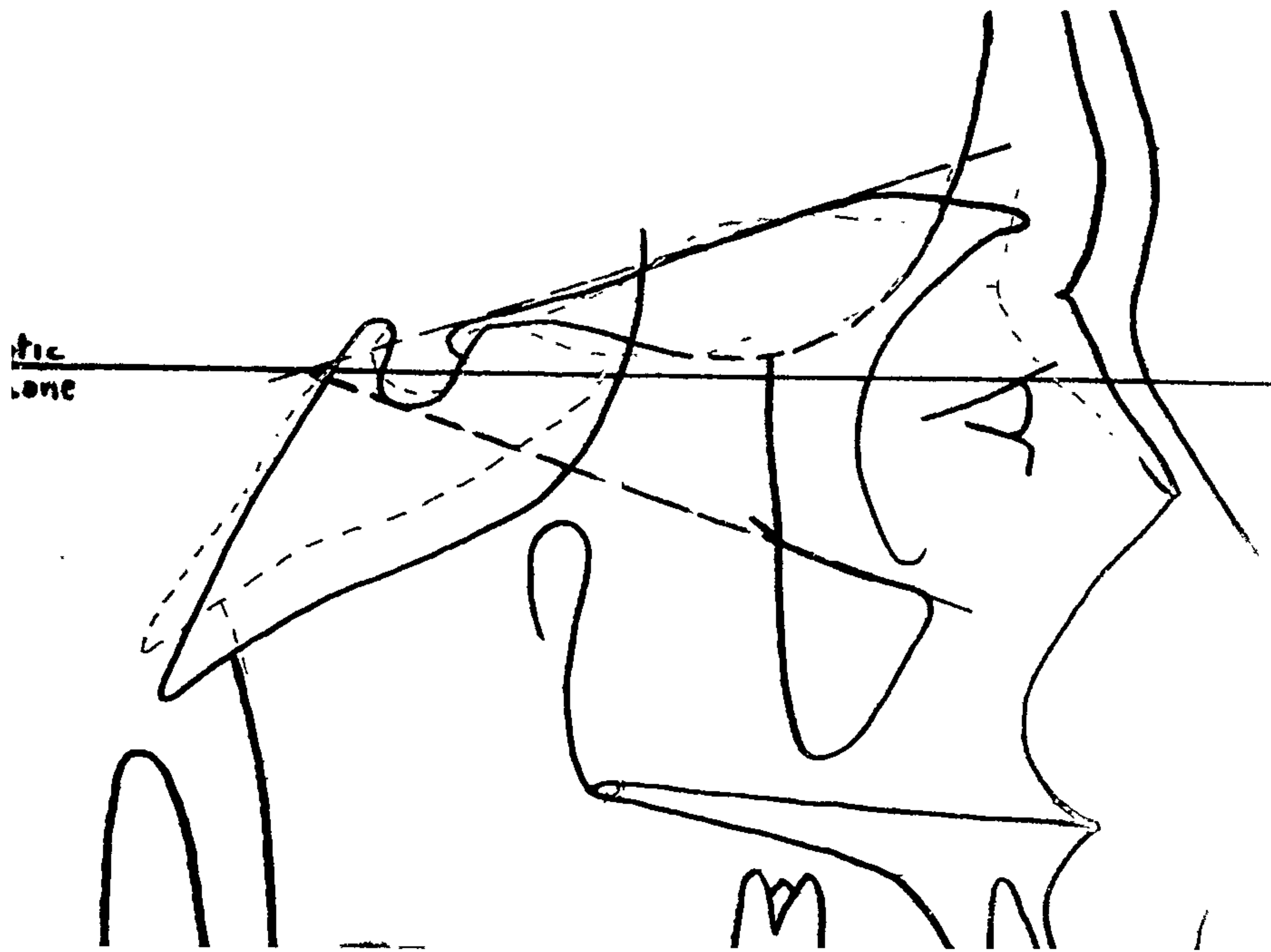


Fig. 29

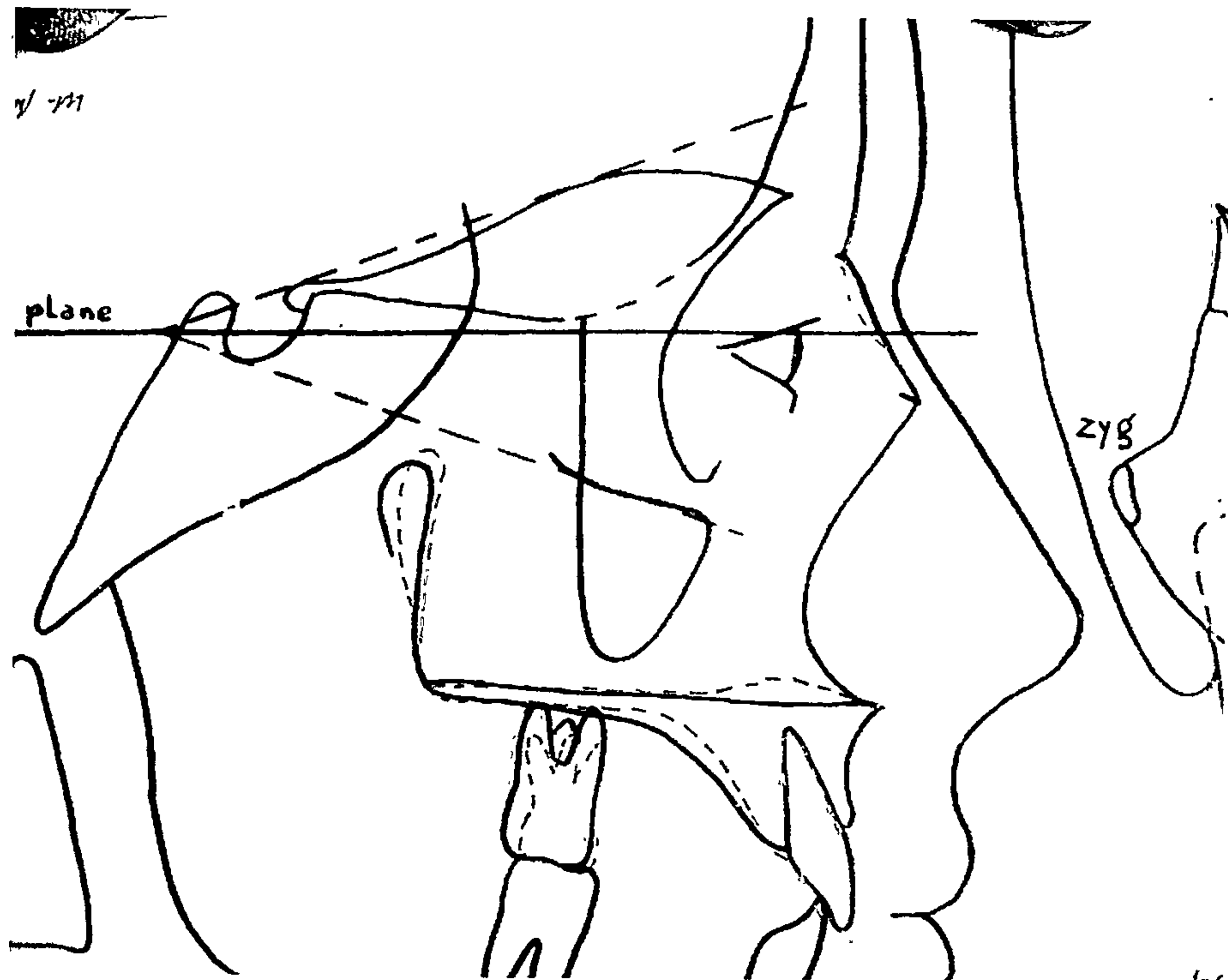


Fig. 30

Superimposition was on anterior nasal spine, posterior nasal spine, and the lower limit of the pterygomaxillary fissure.

4. The horizontal length of the corpus of the mandible.

Superimposition was on the anterior outline of the symphysis of the mandible and the posterior portion of the gonial angle.

5. Posterior cranial base.

This length was assessed by superimposing on S and basion. No recording was made where basion was not located.

6. Vertical nasal height, Fig. 31.

Superimposition is on nasion and the outline of the hard palate. This is a measurement of height and anteroposterior positions of ANS and PNS are not considered.

7. Height of the body of the maxilla, Fig. 32.

Superimposition is on the superior border of the pterygomaxillary fissure and the outline of the palate.

8. Alveolar process of the maxilla.

This is assessed by superimposing on the outline of the palate and occlusal plane of the teeth.

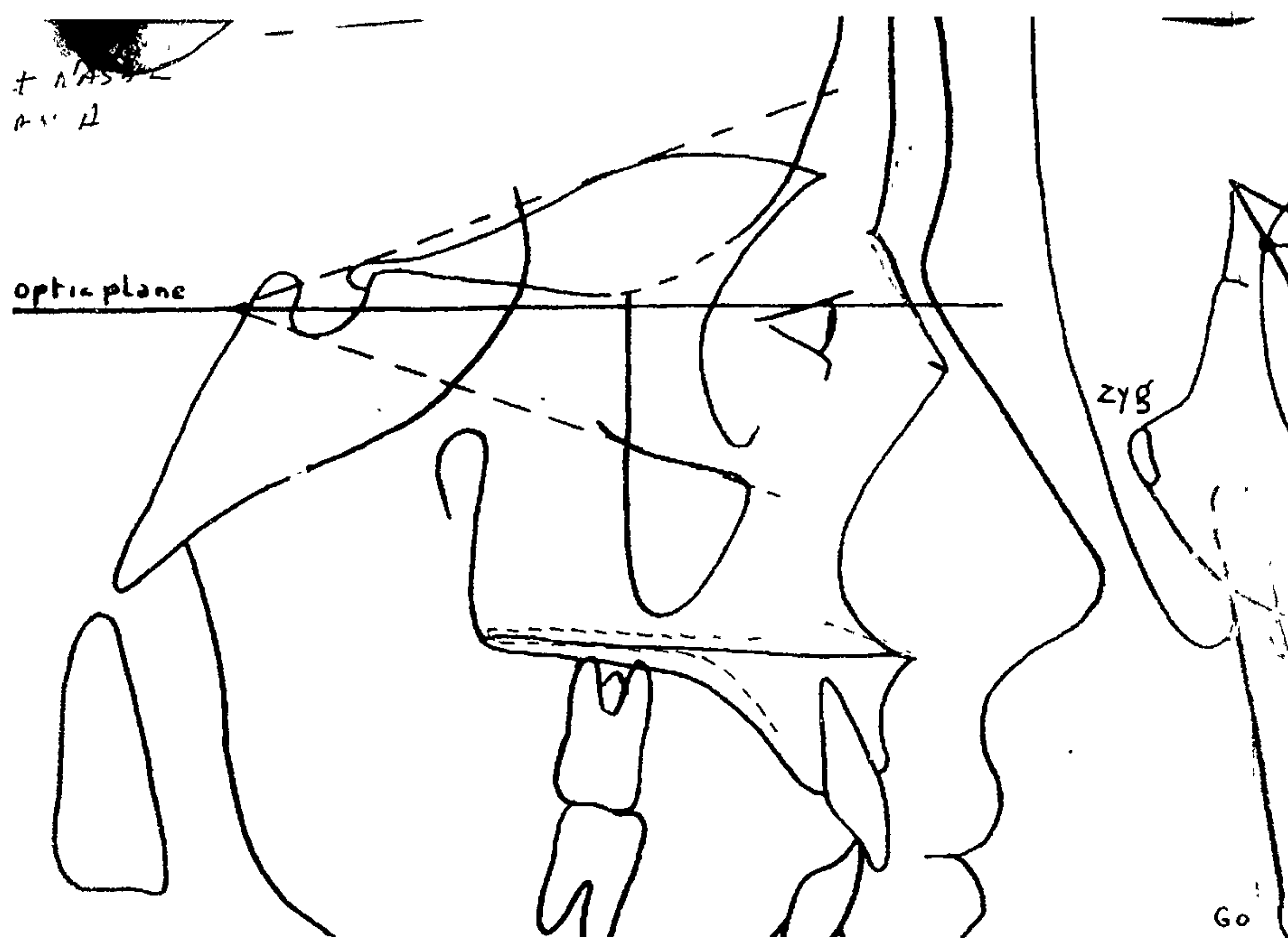


Fig. 31

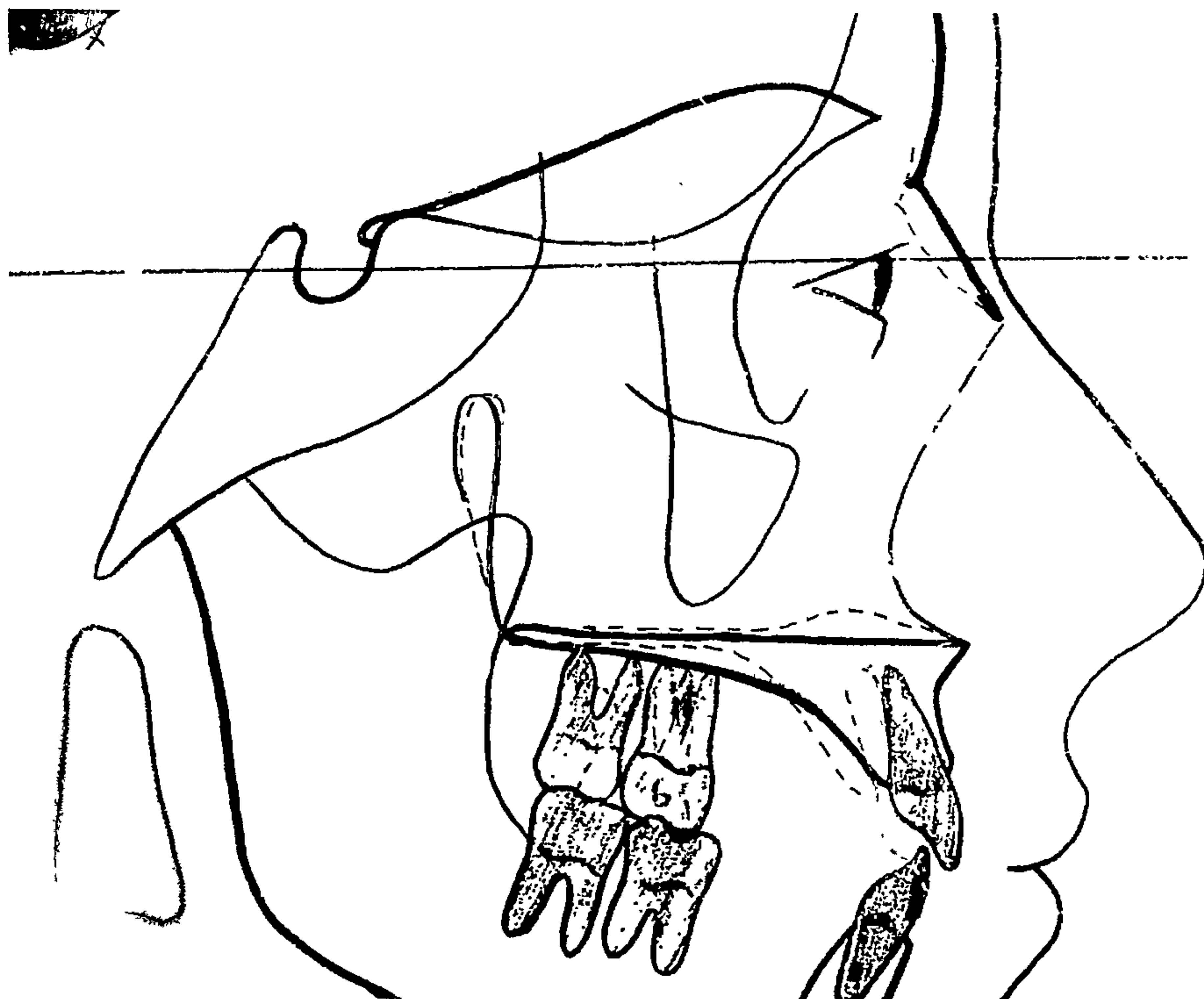


Fig. 32

9. Height of the mandibular ramus.

This is measured by superimposing on articulare and the lower border of the gonial angle of the mandible.

10. Height of the body of the mandible.

This is assessed by superimposing on the lower border of the body of the mandible and on the occlusal plane.

An analysis of vertical development was made from the lateral head cephalometric x-rays of the patients affected by vit. D R.R.

Sassouni's 1960 (63) standards were used for comparison. These standards were derived to assess the proportional vertical development of the anterior and posterior regions of the craniofacial structures.

The measurements compared were:

1. Sella to gonion in the posterior region as a percentage of nasion to menton in the anterior.
2. ANS to menton - lower facial height - as a percentage of the total anterior facial height of nasion to menton.

As an assessment of horizontal development the following measurements were made:

1. Y axis to Frankfort horizontal.

2. Y axis to SN.
3. The angle SNA.
4. The angle SNB.

These angular measurements are compared to the standards derived in the "Alabama Analysis", of Taylor and Hitchcock 1966 (75).

A direct measurement was made of the gonial angle in each patient. This measurement will be compared to the pattern of change of the gonial angle described in the literature review.

The facial profile can also be quantitatively assessed from the lateral head cephalometrix x-rays. To make this analysis I have used some of the measurements suggested by Downs 1948 (19).

The measurements which were made and the significance which Downs attributes to each measurement are given below:

1. Facial Angle, Fig. 33.

Downs found that this angle was characteristic of the facial type. Prognathism and retrognathism could be identified by their facial angles.

2. Angle of convexity, Fig. 34.

This is a measure of the protruberance of the maxilla.

3. AB to facial plane (N-Pog), Fig. 35.

Downs used this angle to assess the anterior limits of the denture base to each other and to the profile.

The analyses used in the examination of the lateral head cephalometric x-rays are designed to show:

1. The general balance in facial development for ten selected areas by comparison with Sassouni's composite tracings.
2. The relationship in vertical development of the anterior and posterior regions of the craniofacial skeleton.
3. Horizontal development, and the relationship between horizontal development in the cranial base and horizontal position of the jaws.
4. Characteristics of the facial profile.

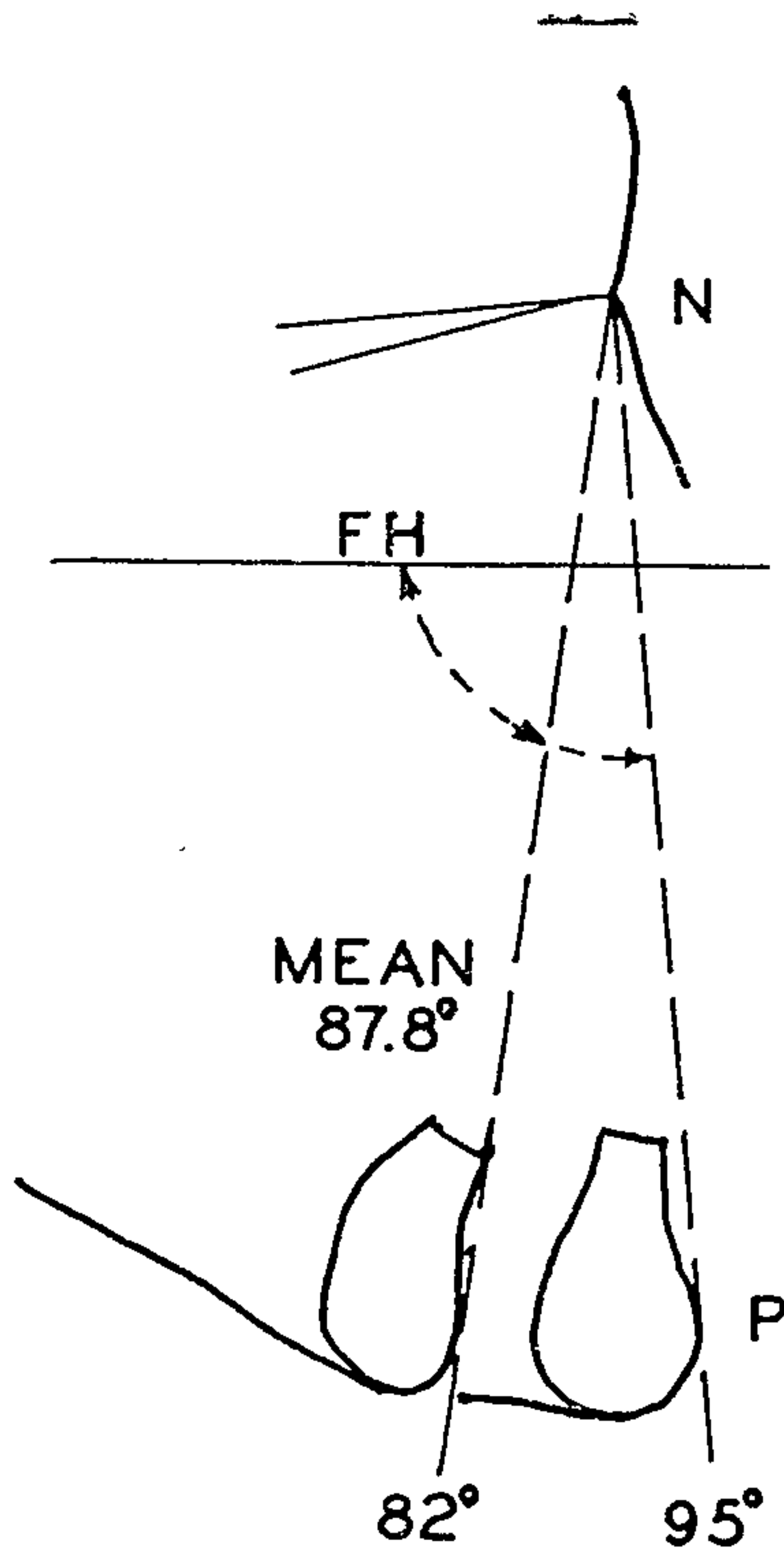


Fig. 33

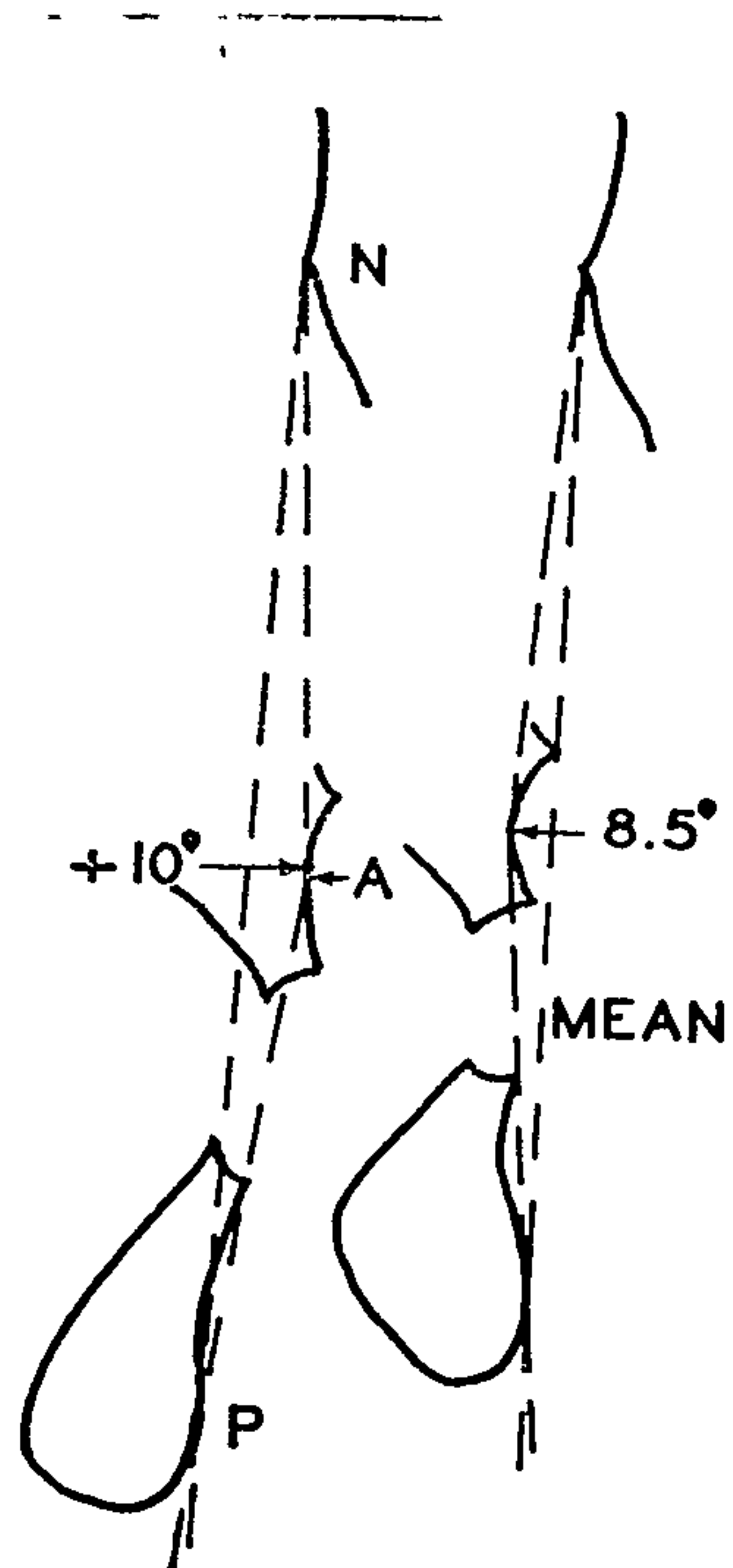


Fig. 34

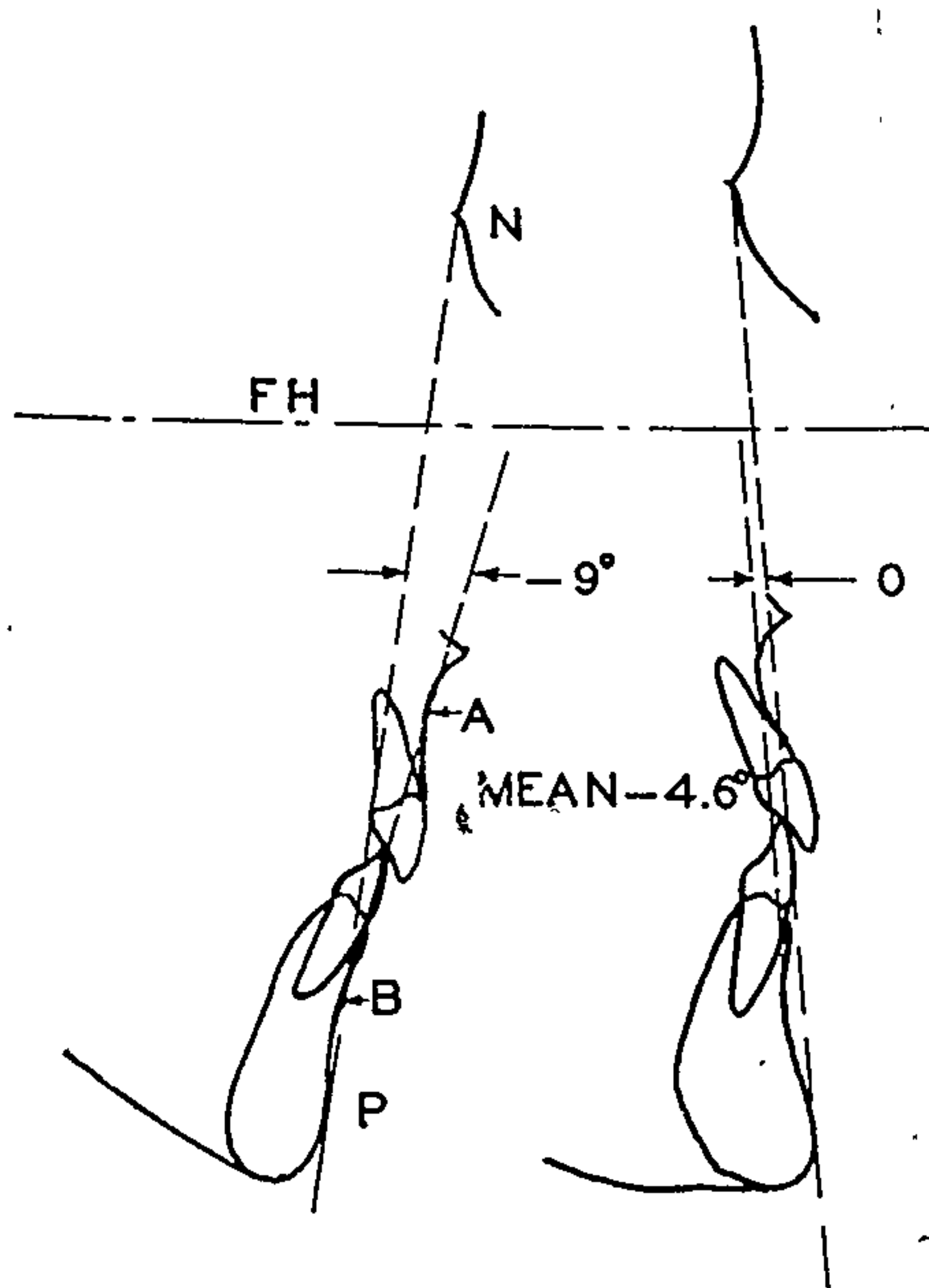


Fig. 35

Fig. 6.—The angle of convexity.

EXAMINATION OF THE PLASTER MODELS

1. Classification of the occlusion into normal (good) occlusion. Angle Class I, or Class II (div. 1 or 2), or Class III malocclusions.
2. Arch form and upper and lower arch coordination. Where a cross bite was present it was described as unilateral or bilateral and the extent was judged by the teeth involved in cross bite.
3. Shape of the palatal vault.
4. Incisor relationships; this includes an assessment of the vertical and horizontal relationships of the upper and lower incisors, and the mesiodistal relationships of the incisors in each arch - this involves an assessment of crowding or spacing of the incisors.
5. Mutilation of the occlusion due to premature loss of teeth. This was noted where deciduous and/or permanent teeth were missing.
6. Caries activity. As the dental examinations were carried out under varying conditions and by different operators the only level of caries activity recorded in Table 9 is where

gross caries was present. gross caries
could be seen in the plaster models of the
teeth, and extraction of the involved
teeth would probably be necessary.

FINDINGS AND RESULTS

Findings from Medical Records

1. General Clinical Features

At the time of diagnosis the only common clinical feature was deformities of the legs. The leg deformities which had been noticed by the parents or the family doctor, were the reason for seeking treatment for the child.

Abnormalities in the shape of the head were reported in some cases, but no particular shape was found to be characteristic.

2. Family History - Inheritance Pattern

A family history compatible with an x-linked mode of inheritance, as described by Winters et. al, was found in all cases except one. The one exception was patient No. 11, G.S-S., a male. In this case bow legs were reported in the paternal grandmother and four paternal aunts. The father showed no bowing of the legs and no abnormalities of serum chemistry. The mother was tall, with normal legs, and normal serum chemistry. The legs of the maternal grandmother and grandfather were normal.

From the family history patient G. S-S. appears to be an example of male-to-male transmission and this is not compatible with an x-linked inheritance pattern. This patients kindred is shown in Fig. 36. In the children examined there are 10 affected males and 13 affected females. Due to the small sample size, 23, it can only be stated that this male to female ratio of affected children is compatible with an x-linked dominant inheritance pattern.

3. Other serious or chronic illnesses

The affected children, as a group, appeared to be quite free of serious or chronic illnesses other than vit. D R.R. No allergies were noticed in the children, however one child, David C. No.4, suffered severe asthmatic attacks.

4. Serum levels of calcium, phosphate and alkaline phosphatase

The serum levels of calcium, phosphate and alkaline phosphatase at the time of diagnosis are shown in Table 6.

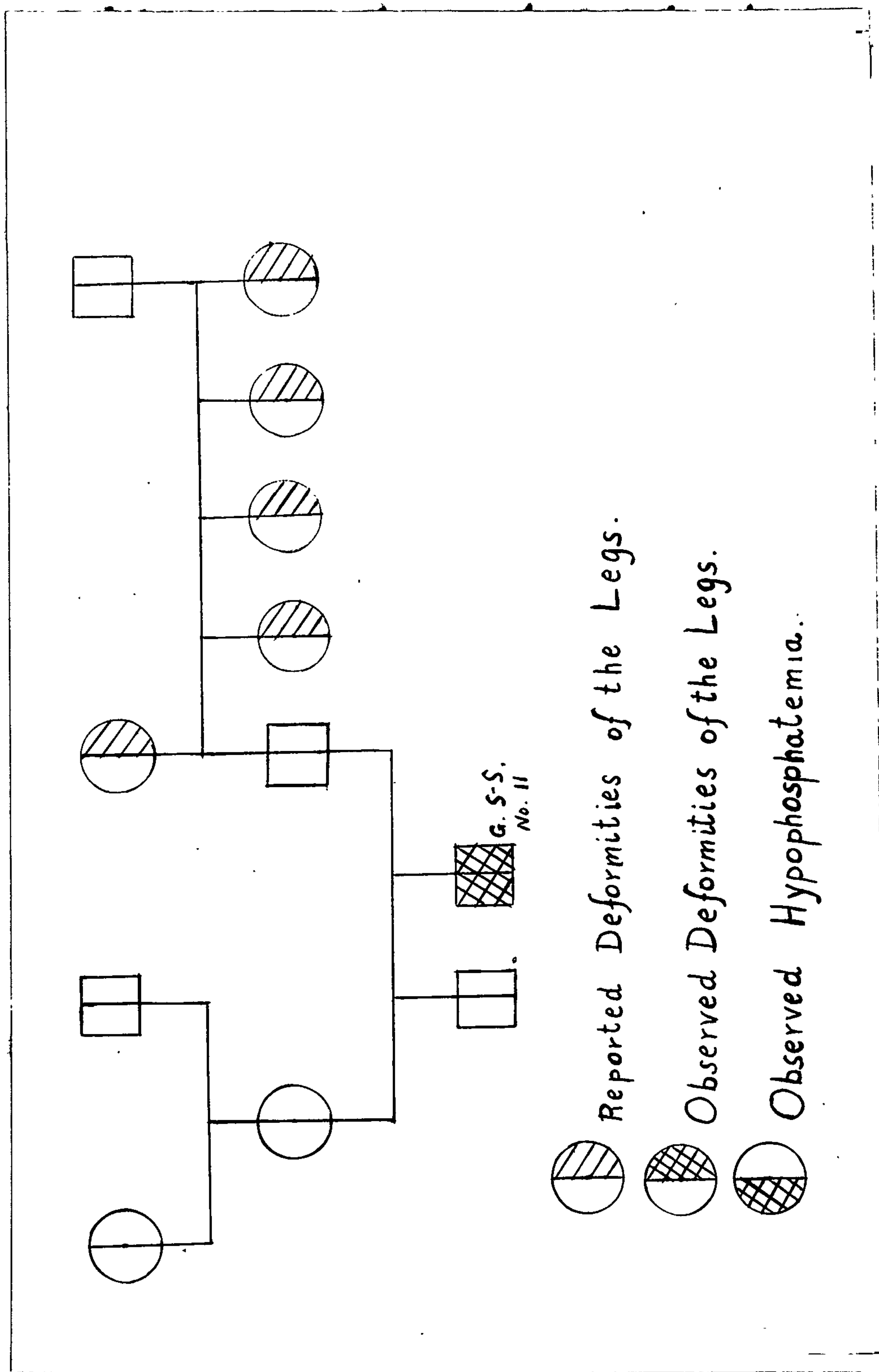


Fig. 36

Any changes which occurred during treatment in these levels have also been indicated in Table 6.

5. Deformities

Deformities of the legs were routinely present at the time of diagnosis. Generally the parents had noticed leg deformities at the time the child commenced walking or shortly after this stage. In two cases the leg deformities were not noticed when the child commenced walking but became apparent some years later.

Deformities of the skull were reported in only nine of the twenty-three children. Two of these 9 children had extremely abnormal tower-shaped skulls. These two were from the same family; their family history showed their father and a paternal uncle had the same shaped skull. This was diagnosed as acrocephaly. The mother of this family had a history of rickets and seems to have been the carrier of the vit. D R.R.

Table 6 gives the results of treatment, medical and surgical on the deformities of the legs. Table 6 also gives the procedures undertaken for direct treatment of the deformities. This includes one operation undertaken to relieve

increased intercranial pressure. This operation was performed on patient No.2, Rodney B, who was referred to in the preceeding paragraph as suffering from arocephaly; his sister Gail B., patient No.8, did not develop sufficiently increased intercranial pressure to require cranial surgery.

6. Height and Weight Measurements

The height and weight measurements shown in Table 6 are the most recent measurements available for each child. Height and weight charts are presented where measurements were taken over an extended period.

7. Diet

The examining medical officers found the general diet of all the patients was adequate. A phosphate supplement was added to the diet of patient No.5, G.A.

8. Muscle Tissue

The tests performed for muscle co-ordination, reflex, and power produced normal responses. The

116-117

(170)

No. 2

R. B.

NAME

Ward

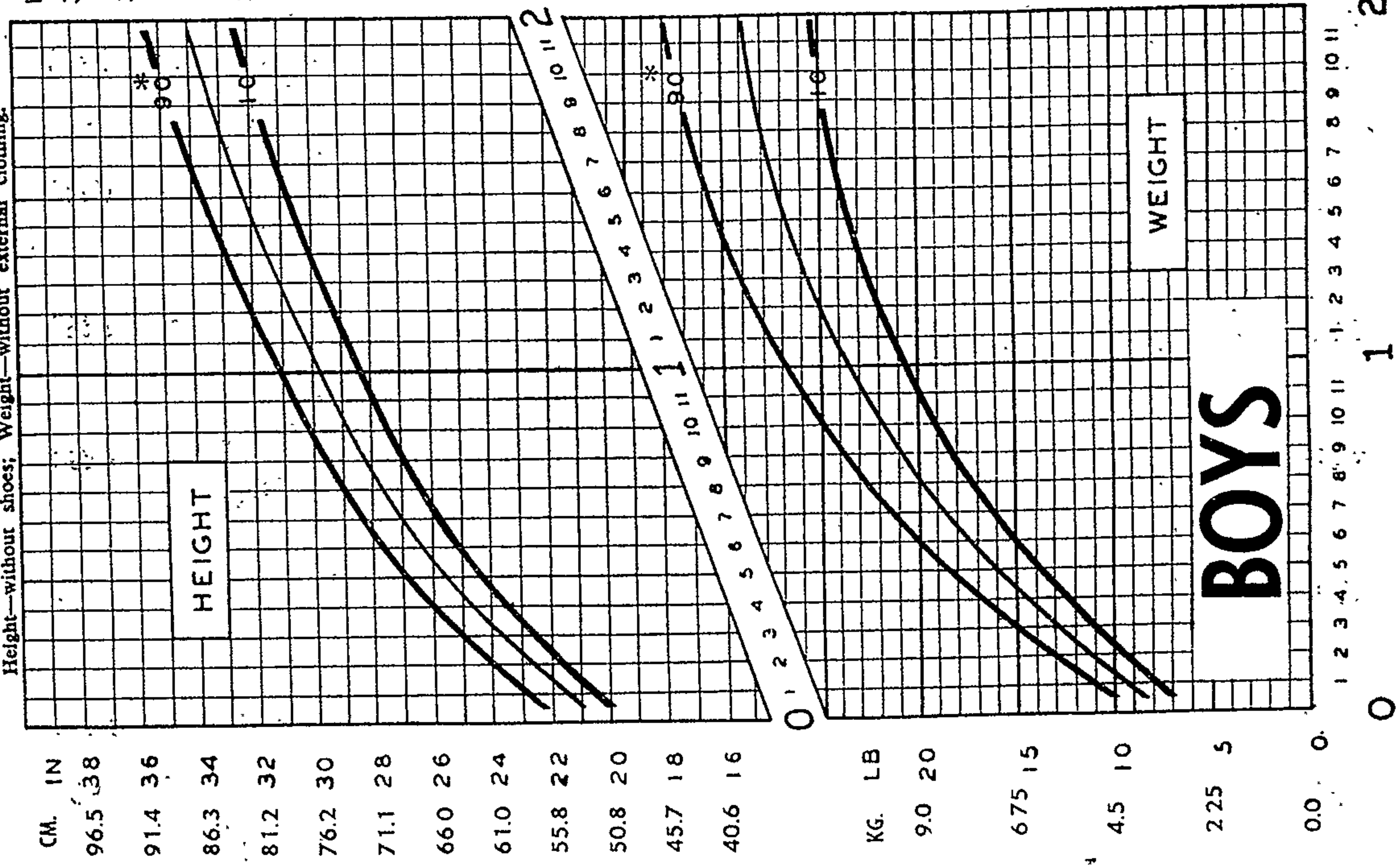
Age

Date of Admission

H.M.O.

BOYS 0-2 YEARS

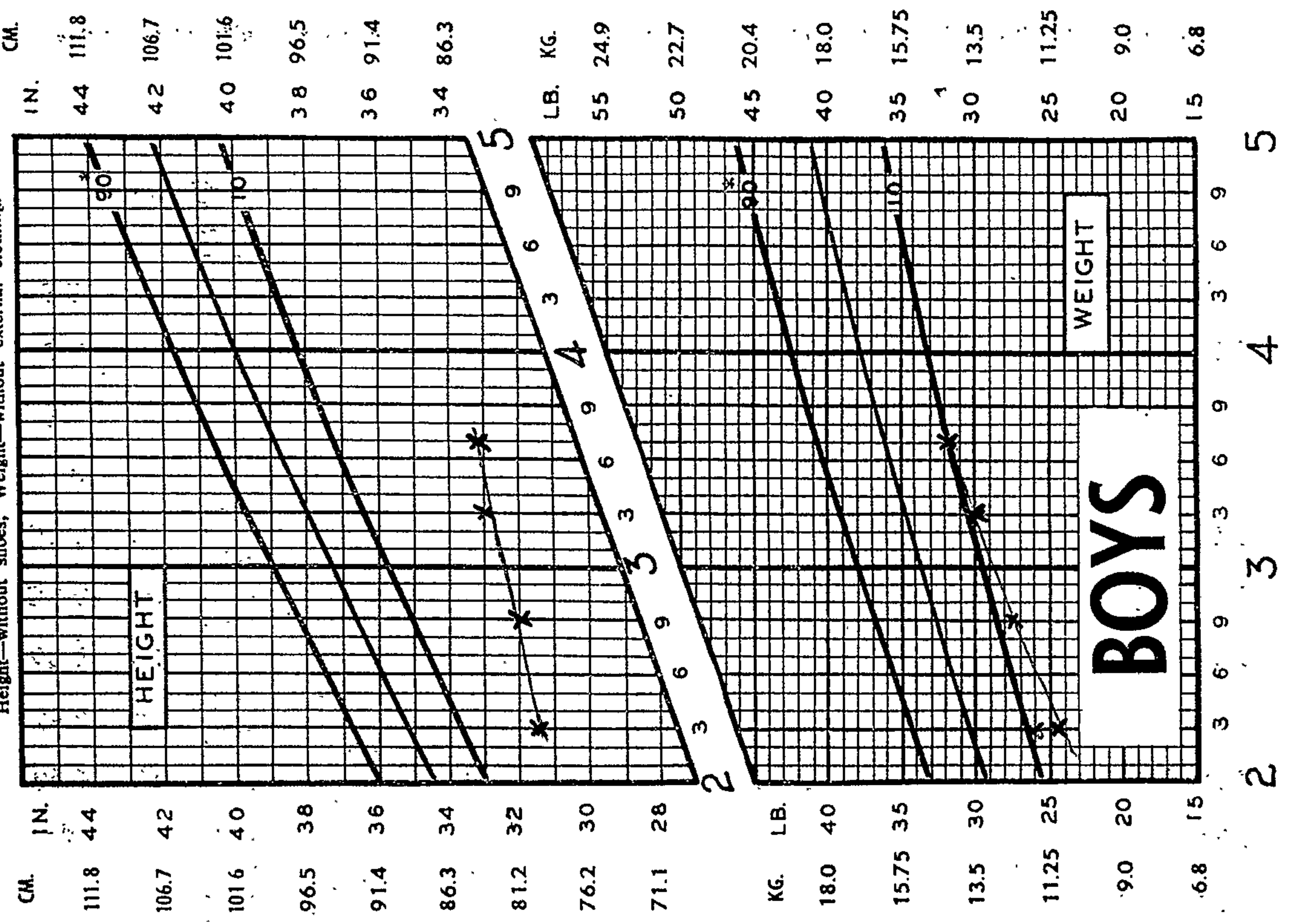
Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

BOYS 2-5 YEARS

Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

No. 2. R. B.

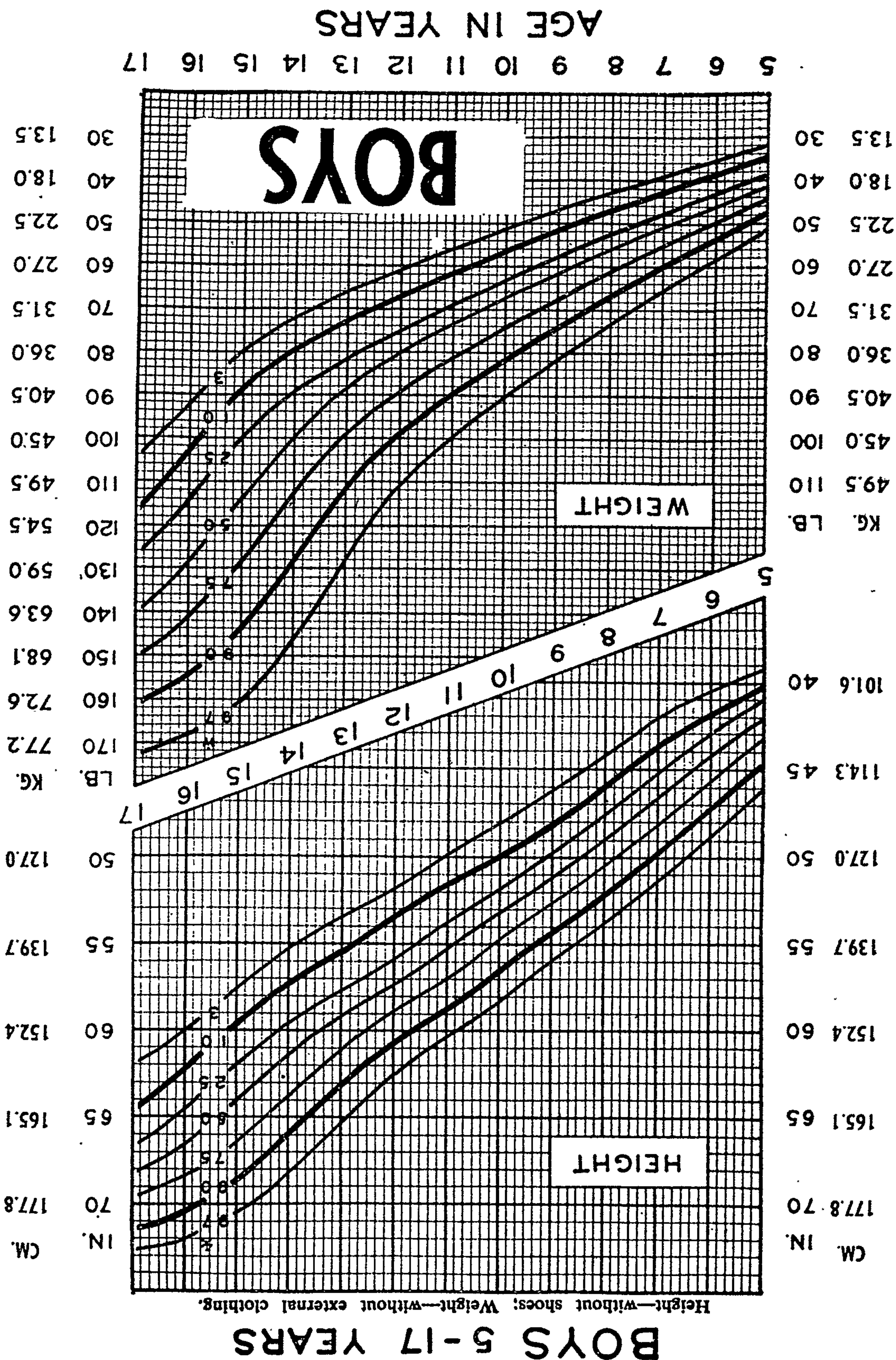
150

150

HEIGHT / WEIGHT CHART - BOYS

MR - 44

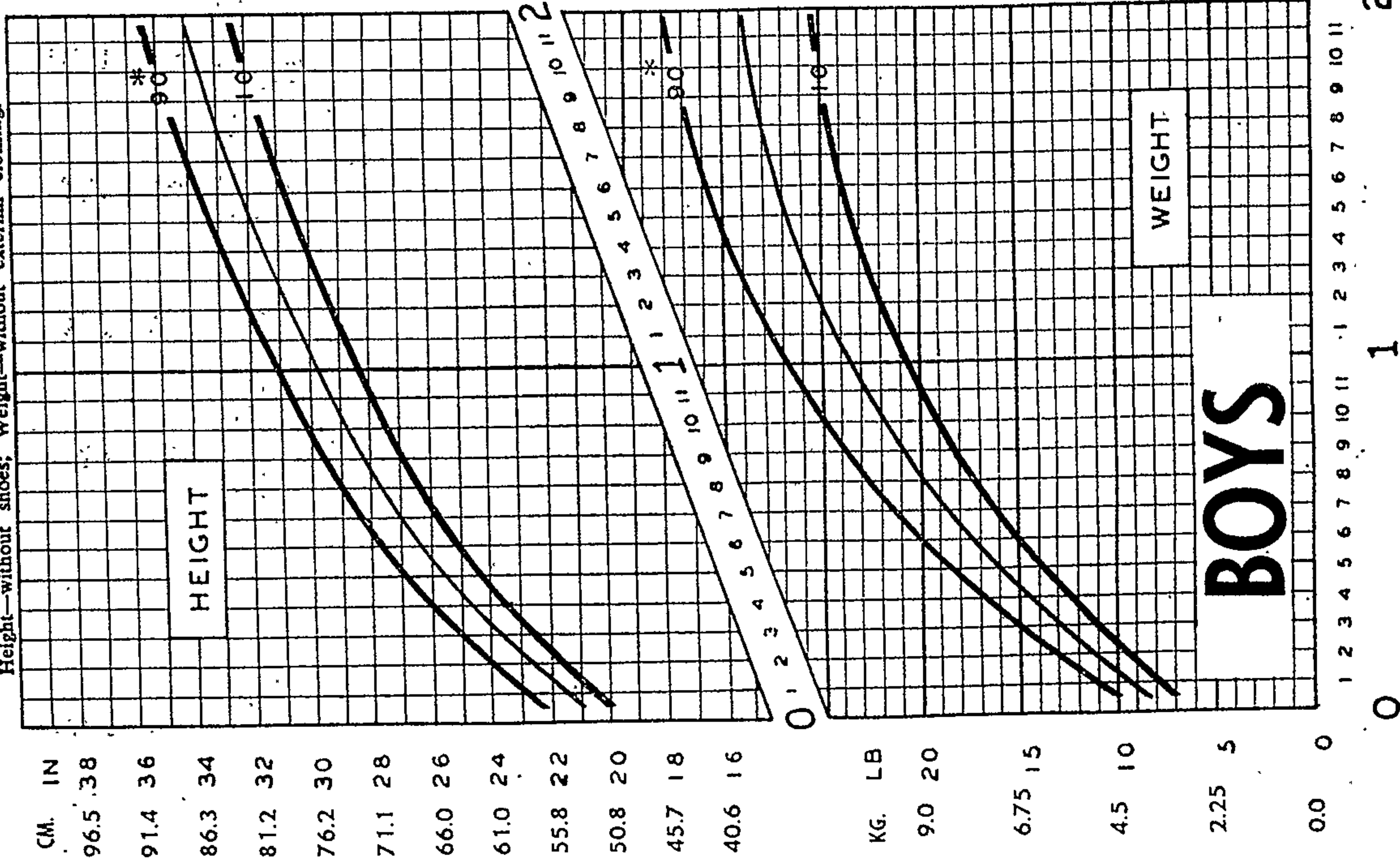
This chart was originally published by the Nutrition Committee of the National Health & Medical Research Council, 1957.



NAME.....Age.....Ward.....H.M.O.....
Date of Admission.....

BOYS 0-2 YEARS

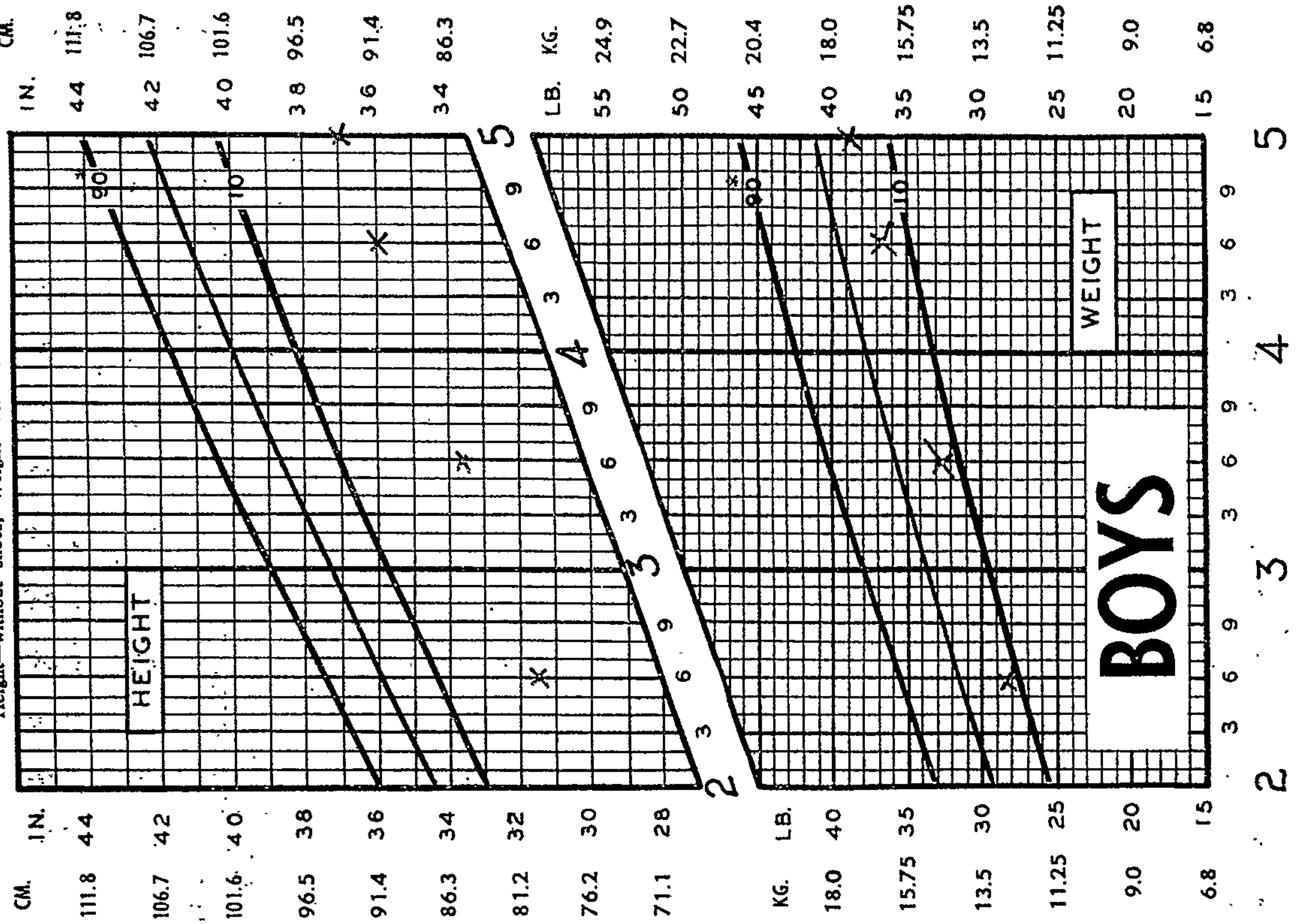
Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

BOYS 2-5 YEARS

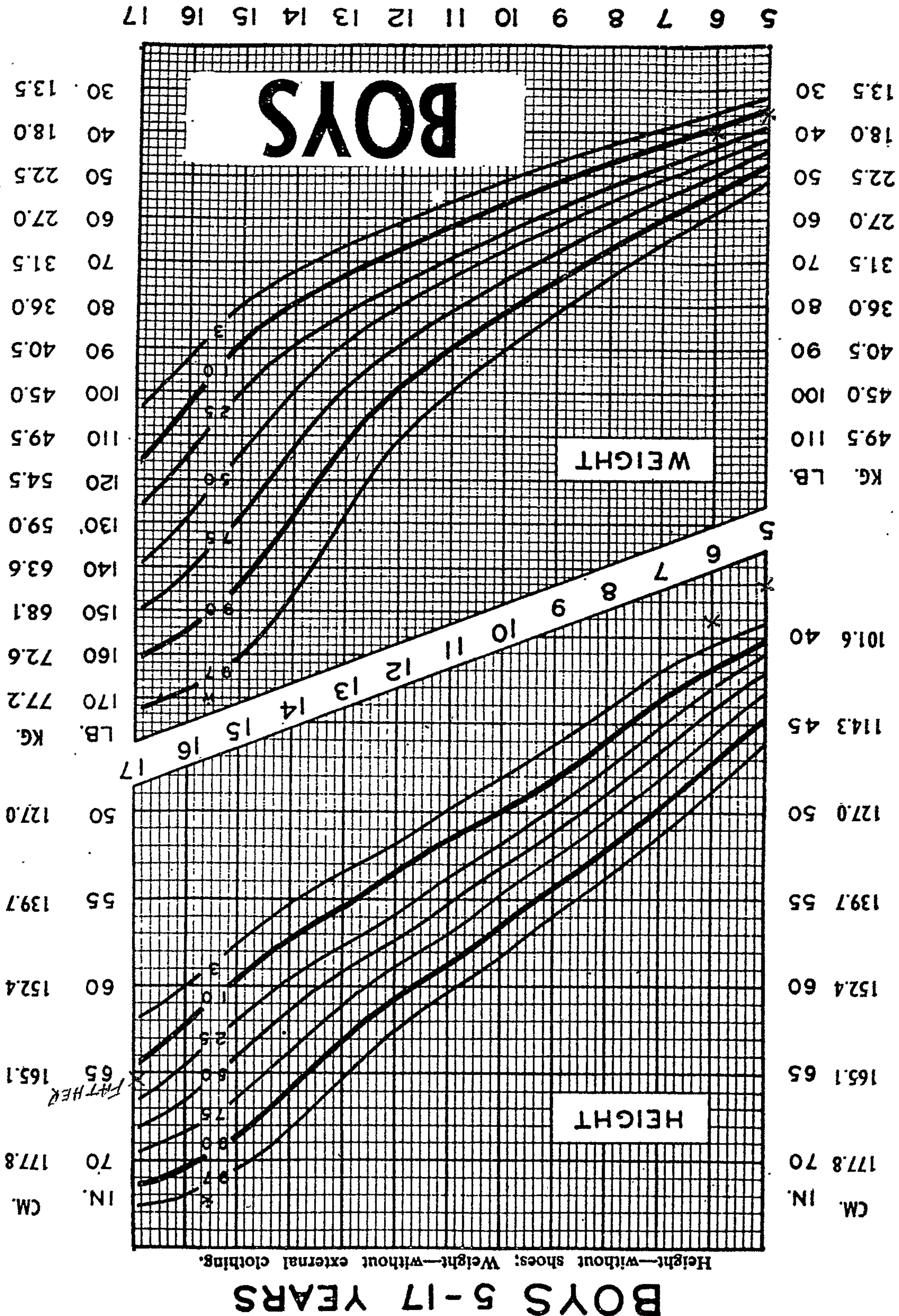
Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

HEIGHT / WEIGHT CHART — BOYS

MR — 44



This chart was originally published by the Nutrition Committee of the National Health & Medical Research Council, 1957.

(251)

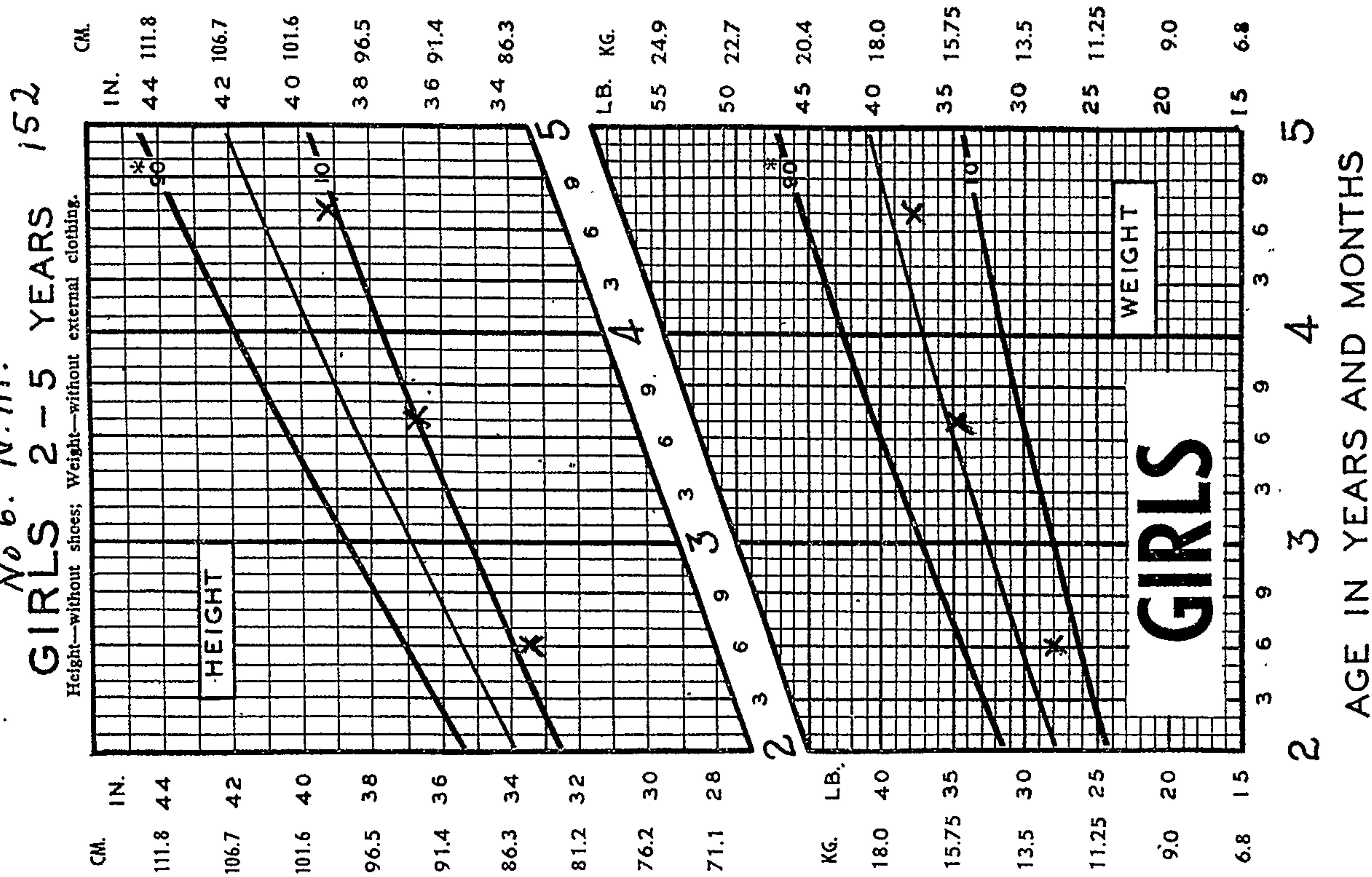
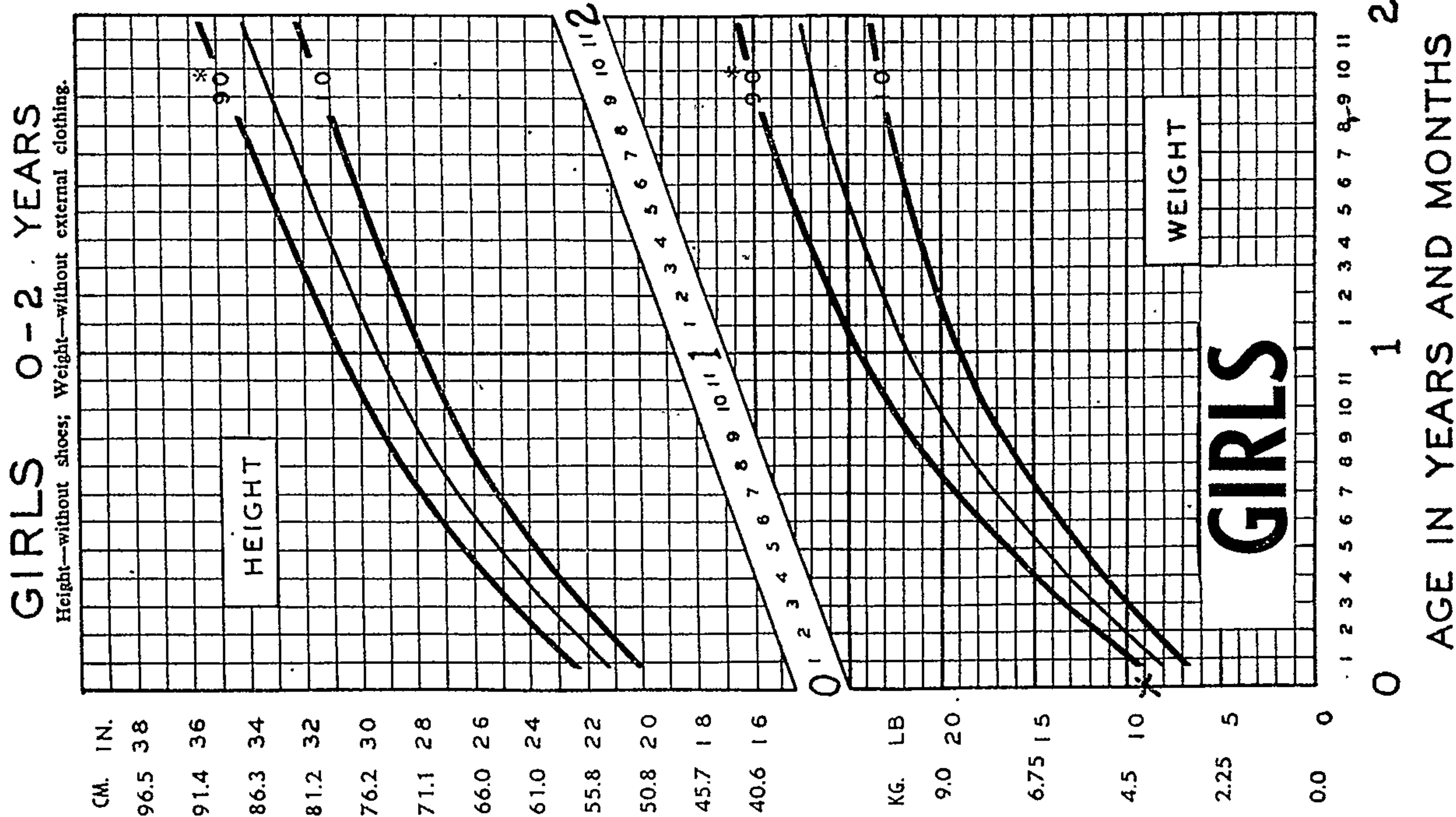
NAME.

Age

ward

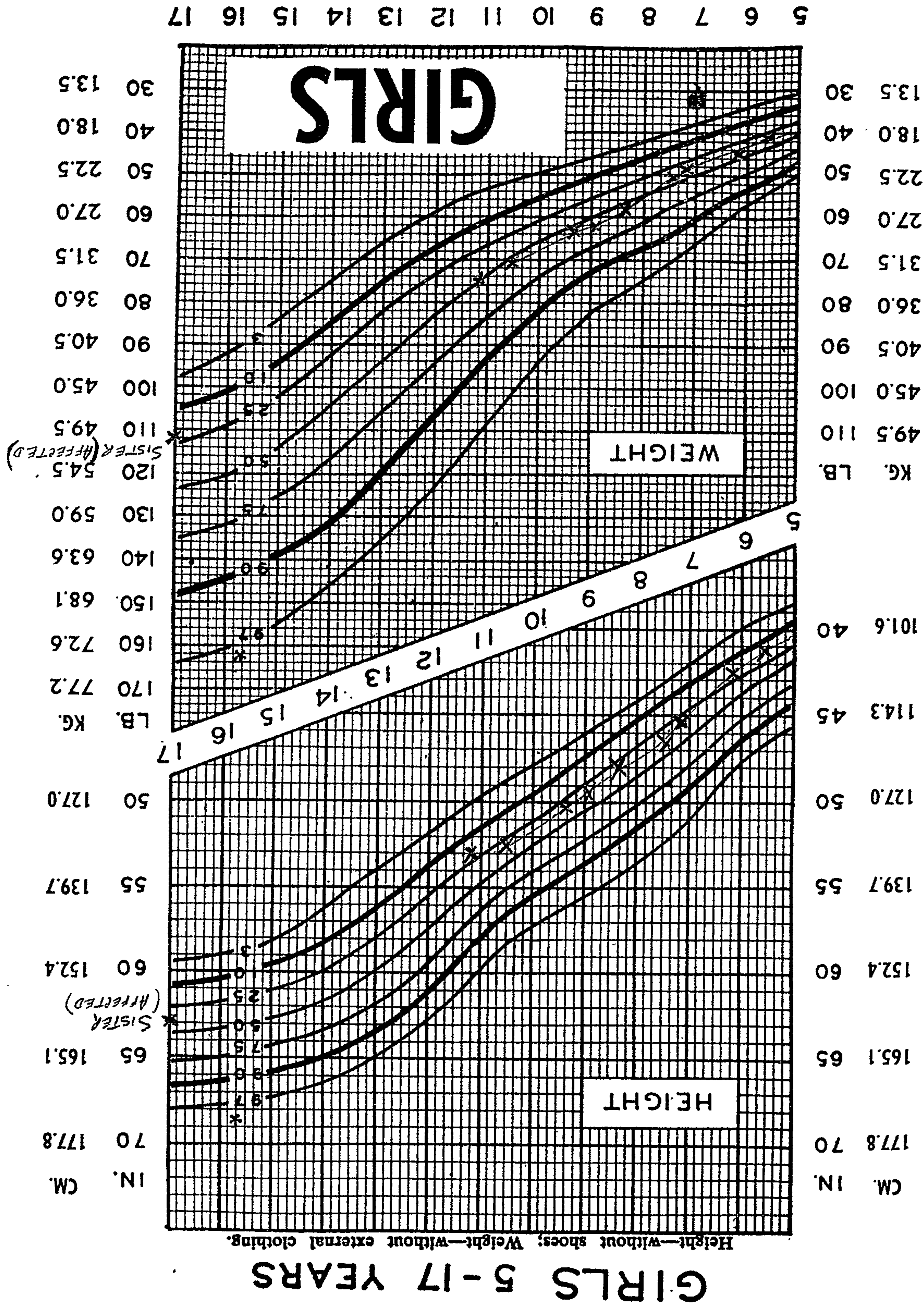
O.W.H.

Date of Admission.



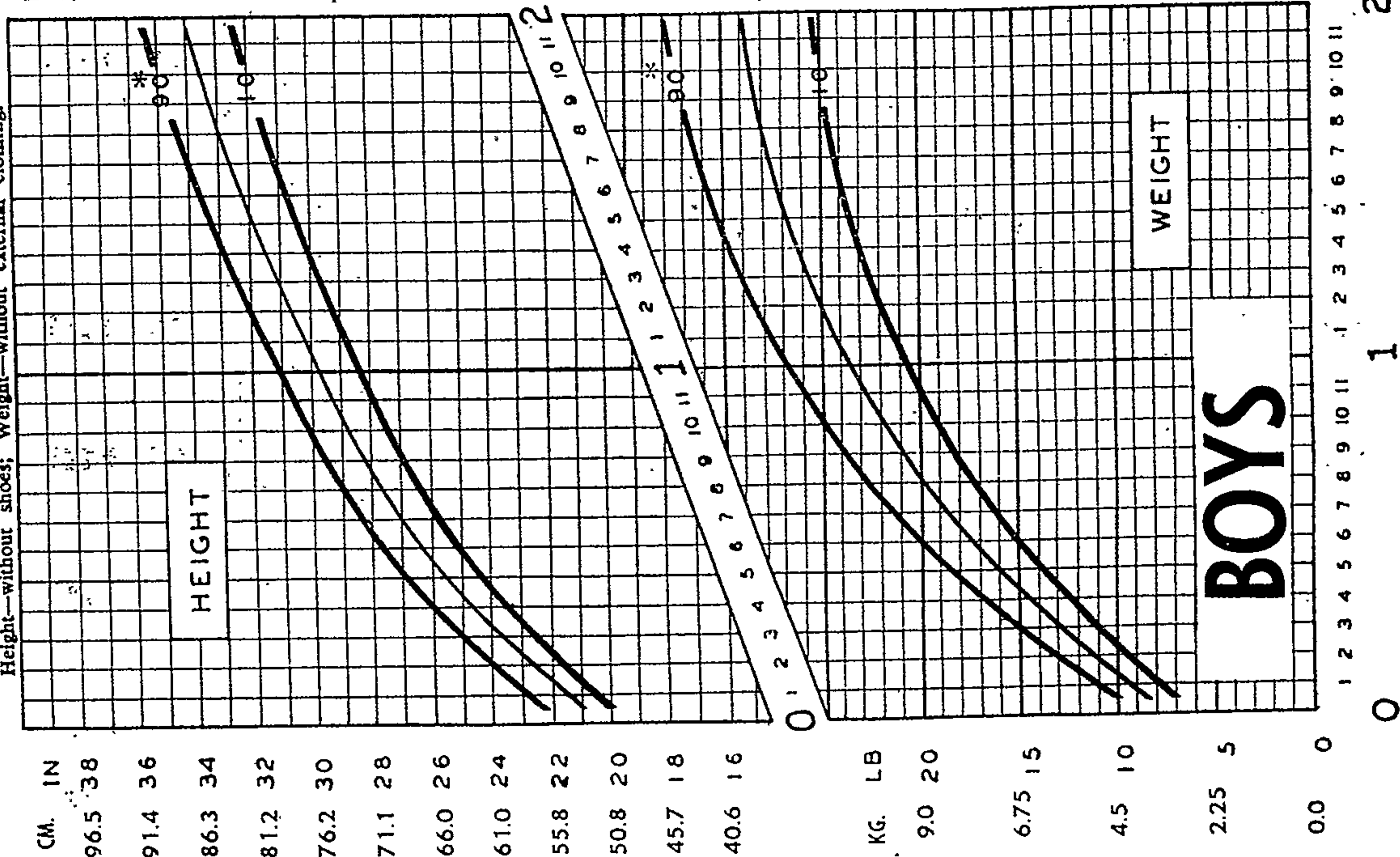
HEIGHT / WEIGHT CHART - GIRLS

MR - 45



BOYS 0 - 2 YEARS

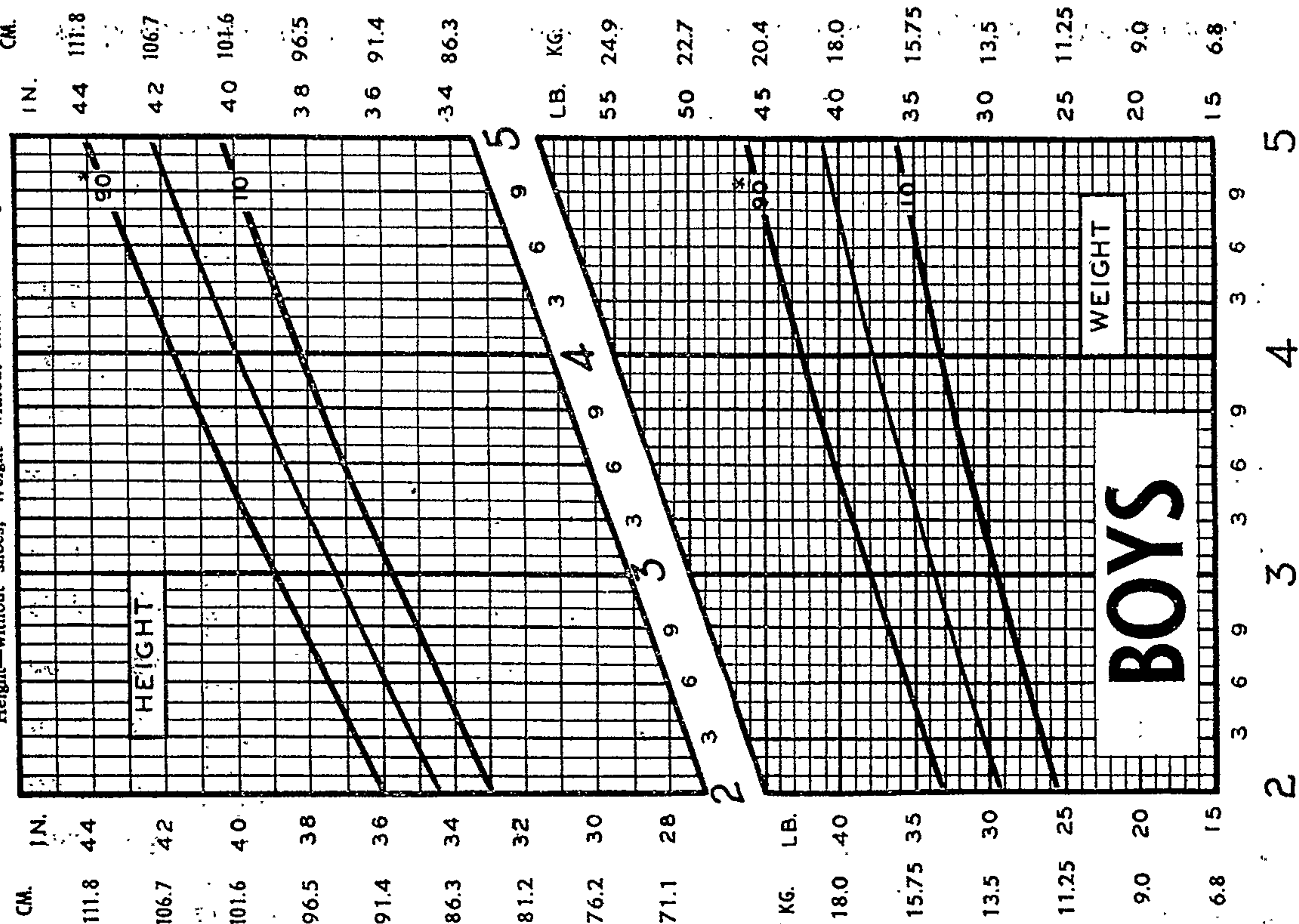
Height—without shoes: Weight—without external clothing.



AGE IN YEARS AND MONTHS

BOYS 2-5 YEARS 153.

Height—without shoes; Weight—without external clothing.

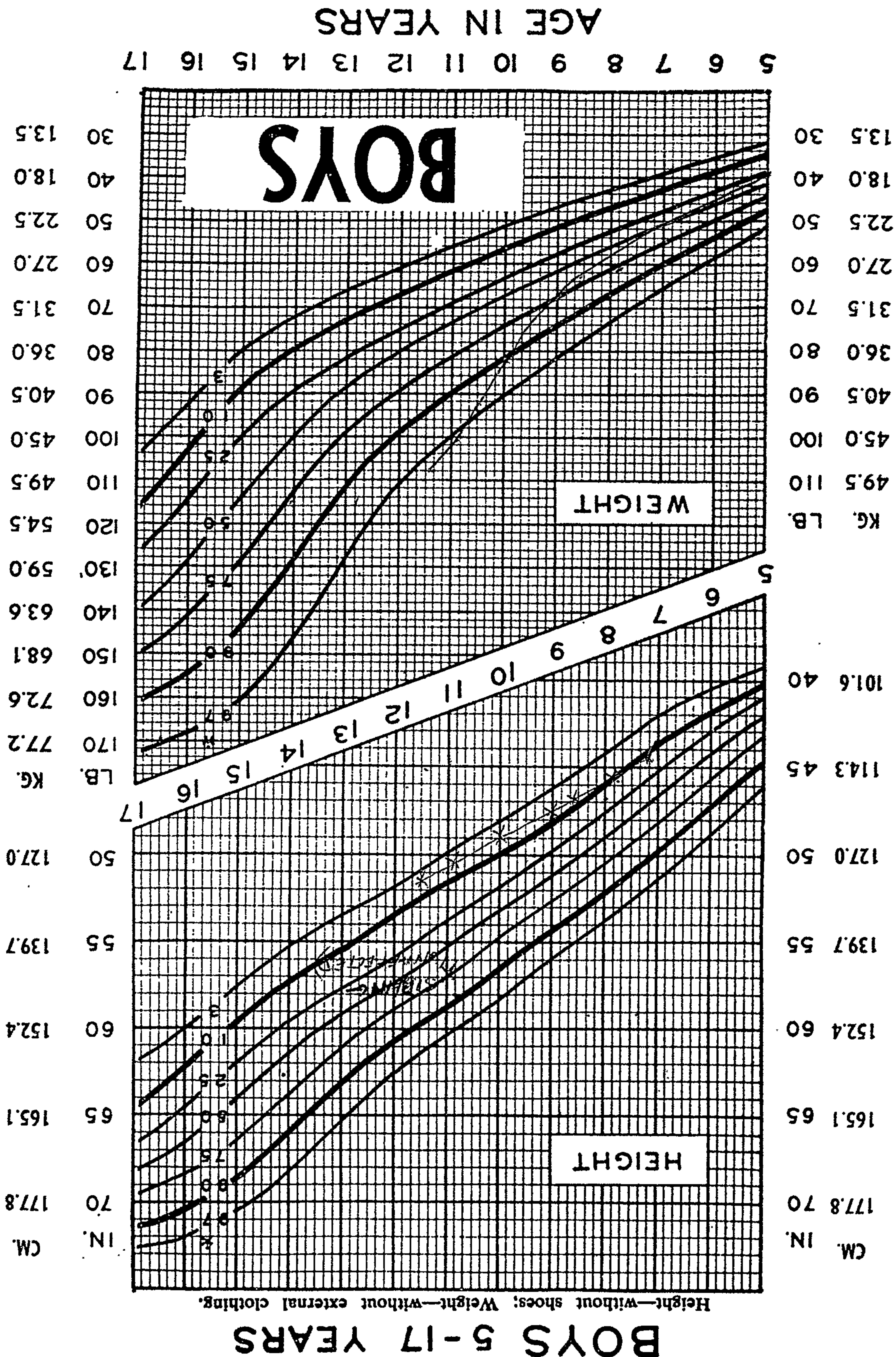


AGE IN YEARS AND MONTHS

HEIGHT / WEIGHT CHART - BOYS

MR - 44

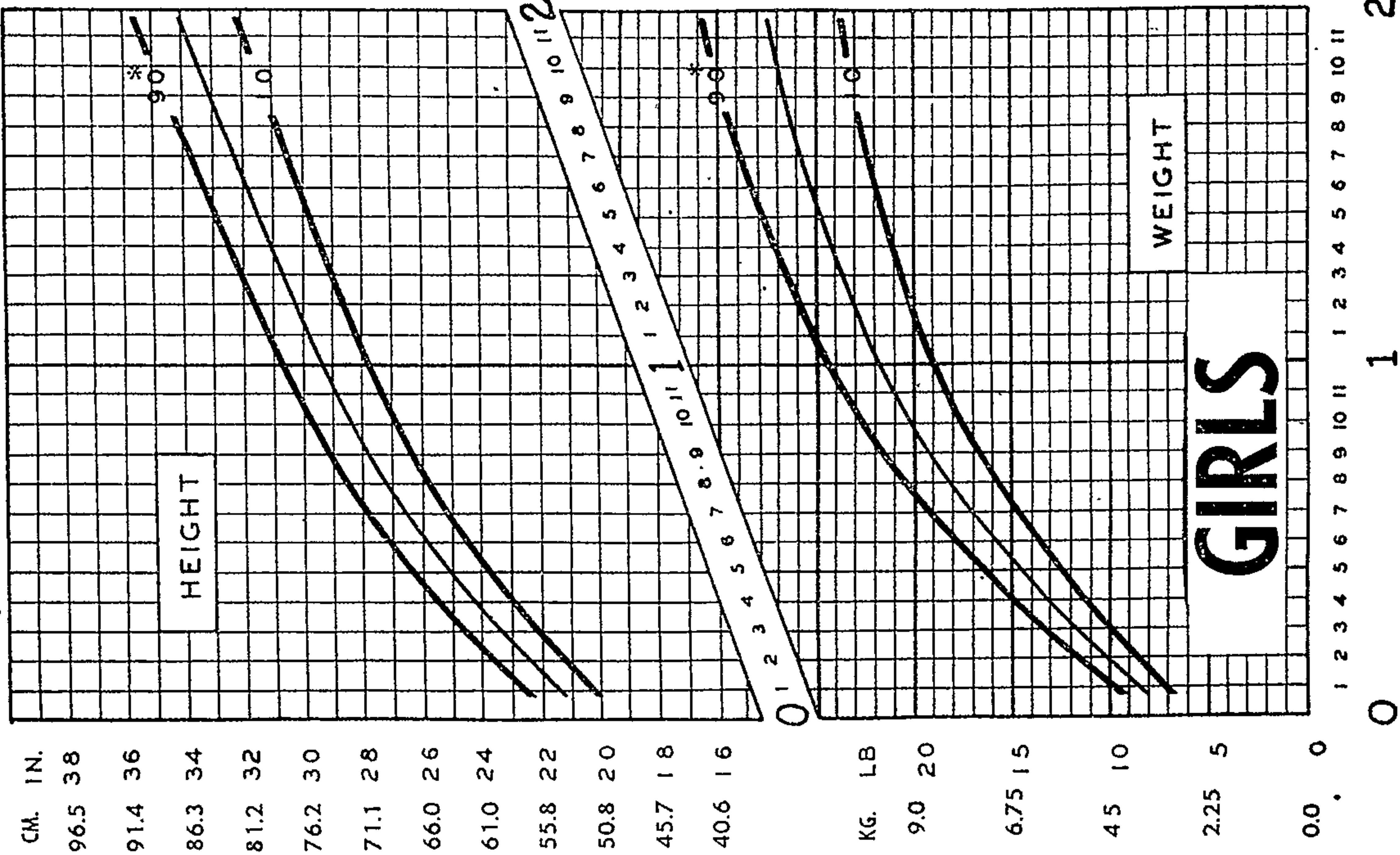
This chart was originally published by the Nutrition Committee of the National Health & Medical Research Council, 1957.



NAME.....Age.....Ward.....H.M.O.....
Date of Admission.....

GIRLS 0-2 YEARS

Height—without shoes; Weight—without external clothing.

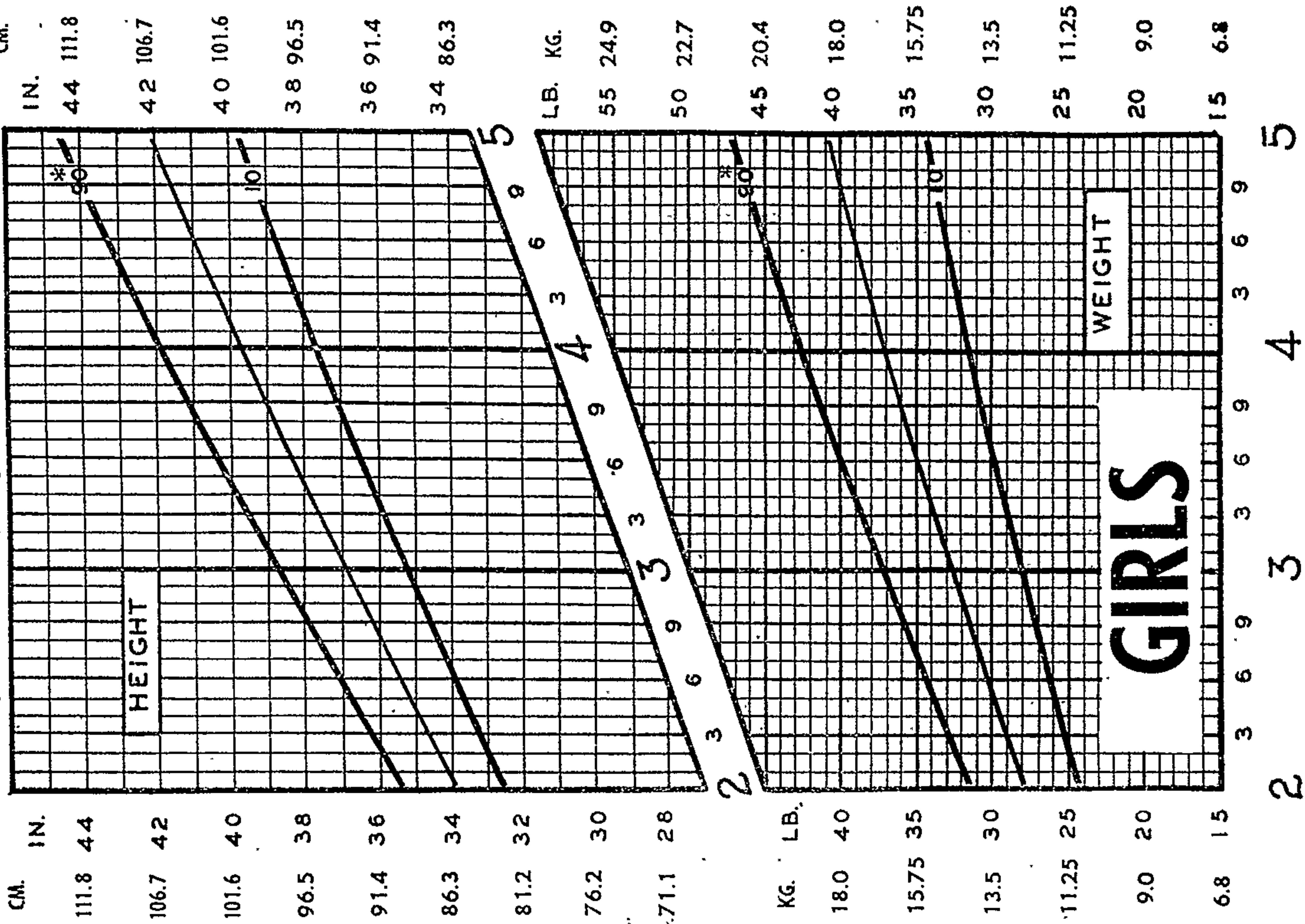


AGE IN YEARS AND MONTHS

No 12 c.D

GIRLS 2-5 YEARS

Height—without shoes; Weight—without external clothing.

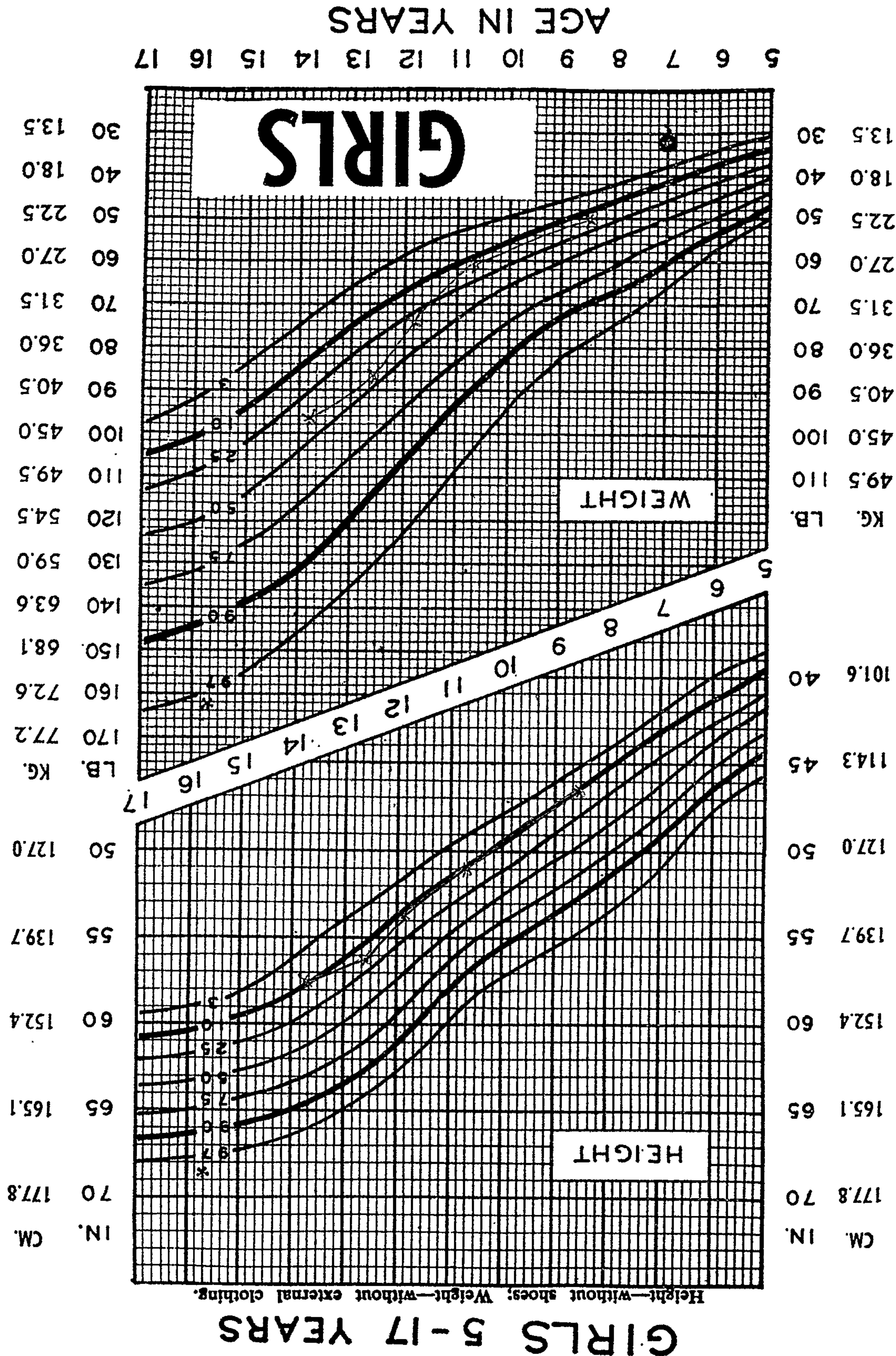


AGE IN YEARS AND MONTHS

SEE OVER

HEIGHT / WEIGHT CHART - GIRLS

MR - 45

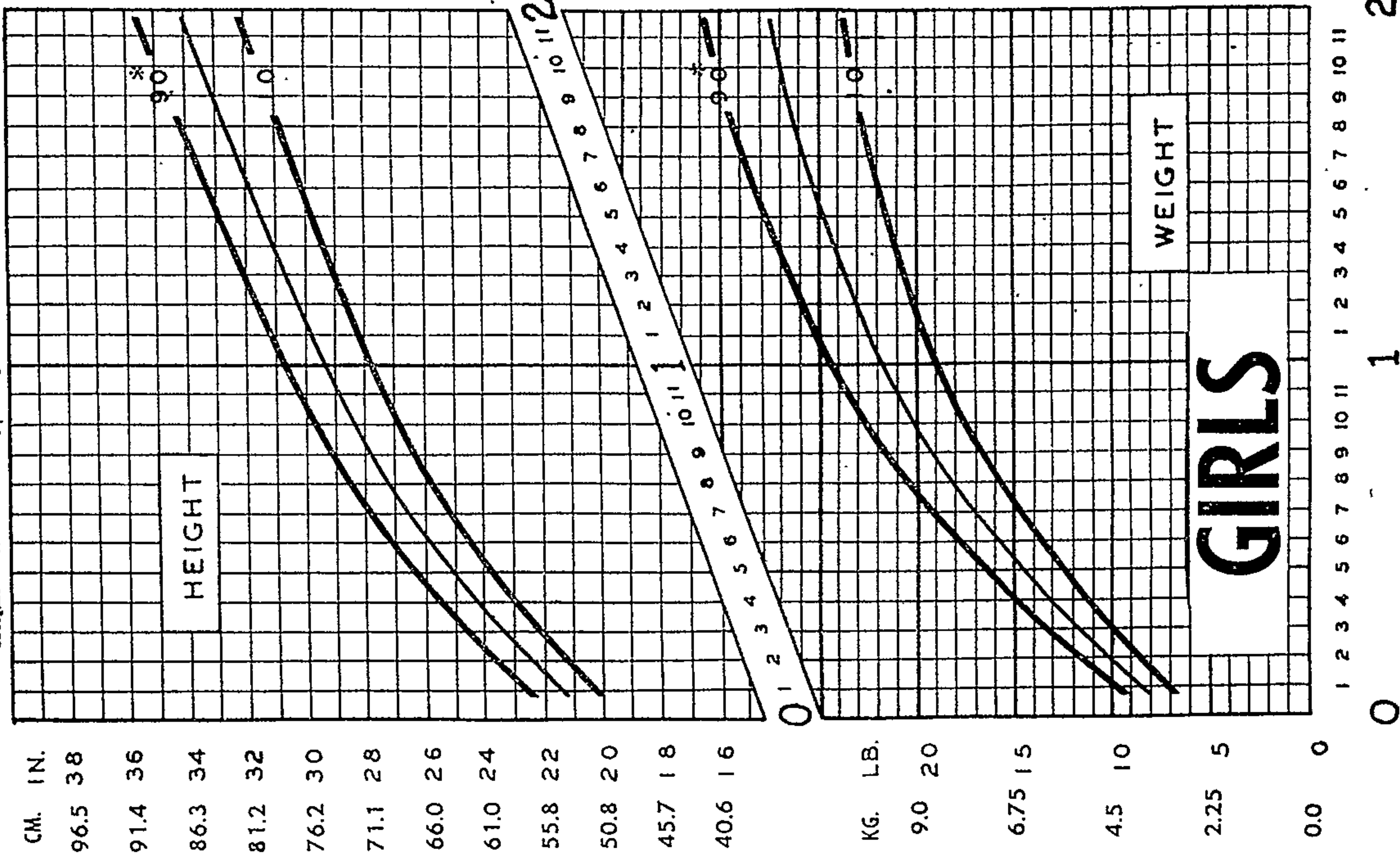


This chart was originally published by the Nutrition Committee of the National Health & Medical Research Council, 1957.

NAME.....Age.....Ward.....H.M.O.....
Date of Admission.....

GIRLS 0-2 YEARS

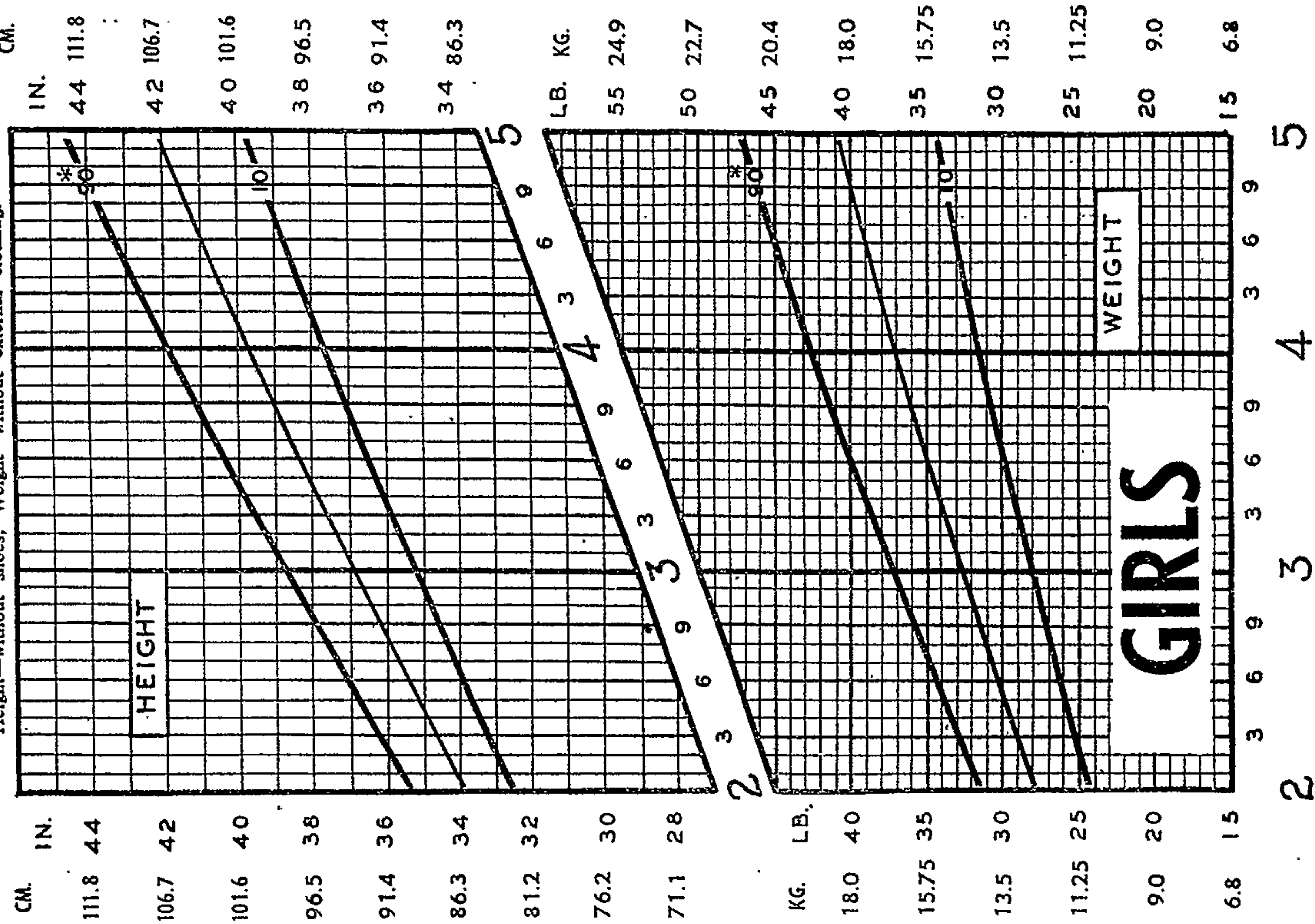
Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

No. 16, U.S. GIRLS 2-5 YEARS

Height—without shoes; Weight—without external clothing.

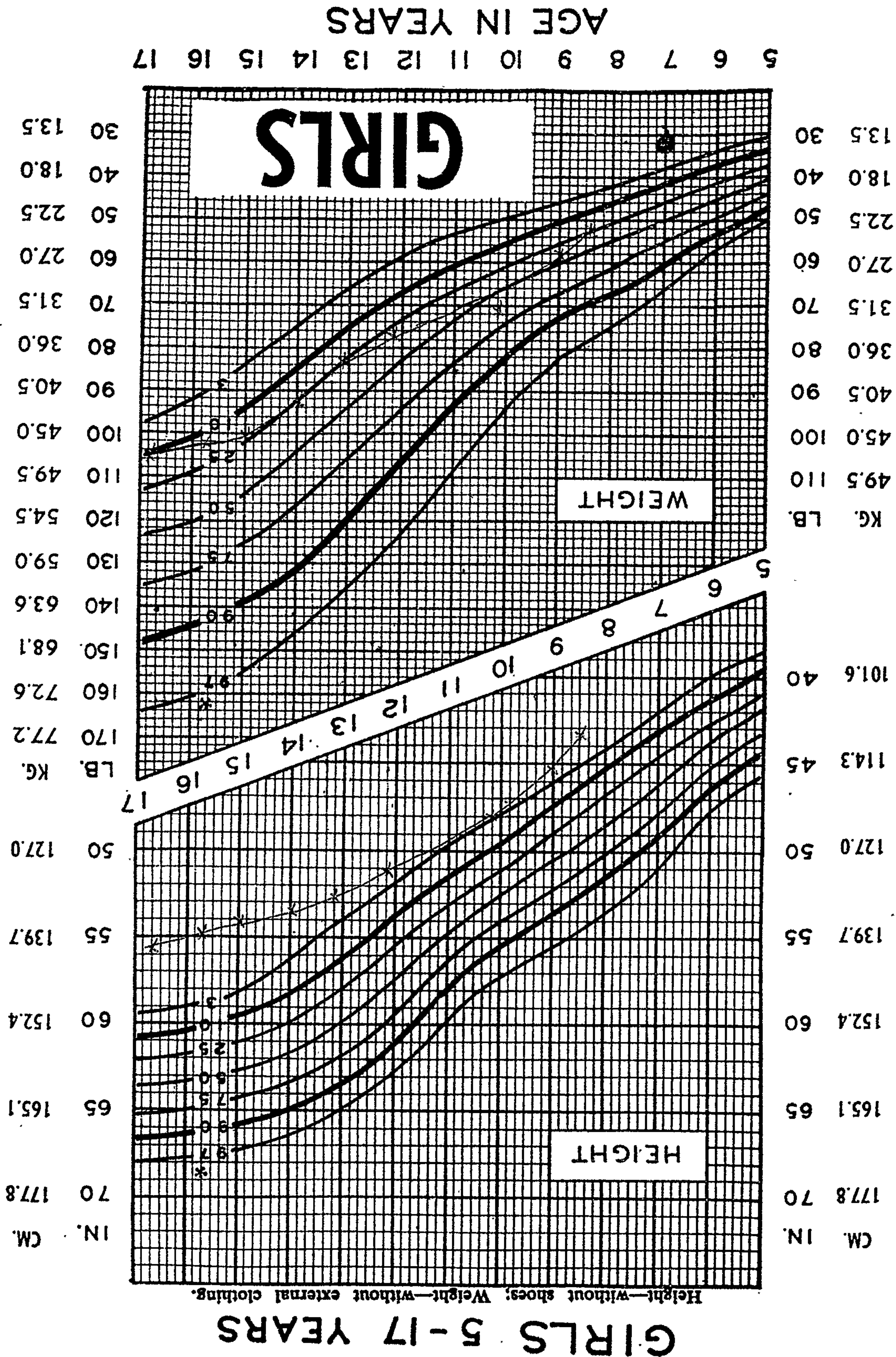


AGE IN YEARS AND MONTHS

HEIGHT / WEIGHT CHART - GIRLS

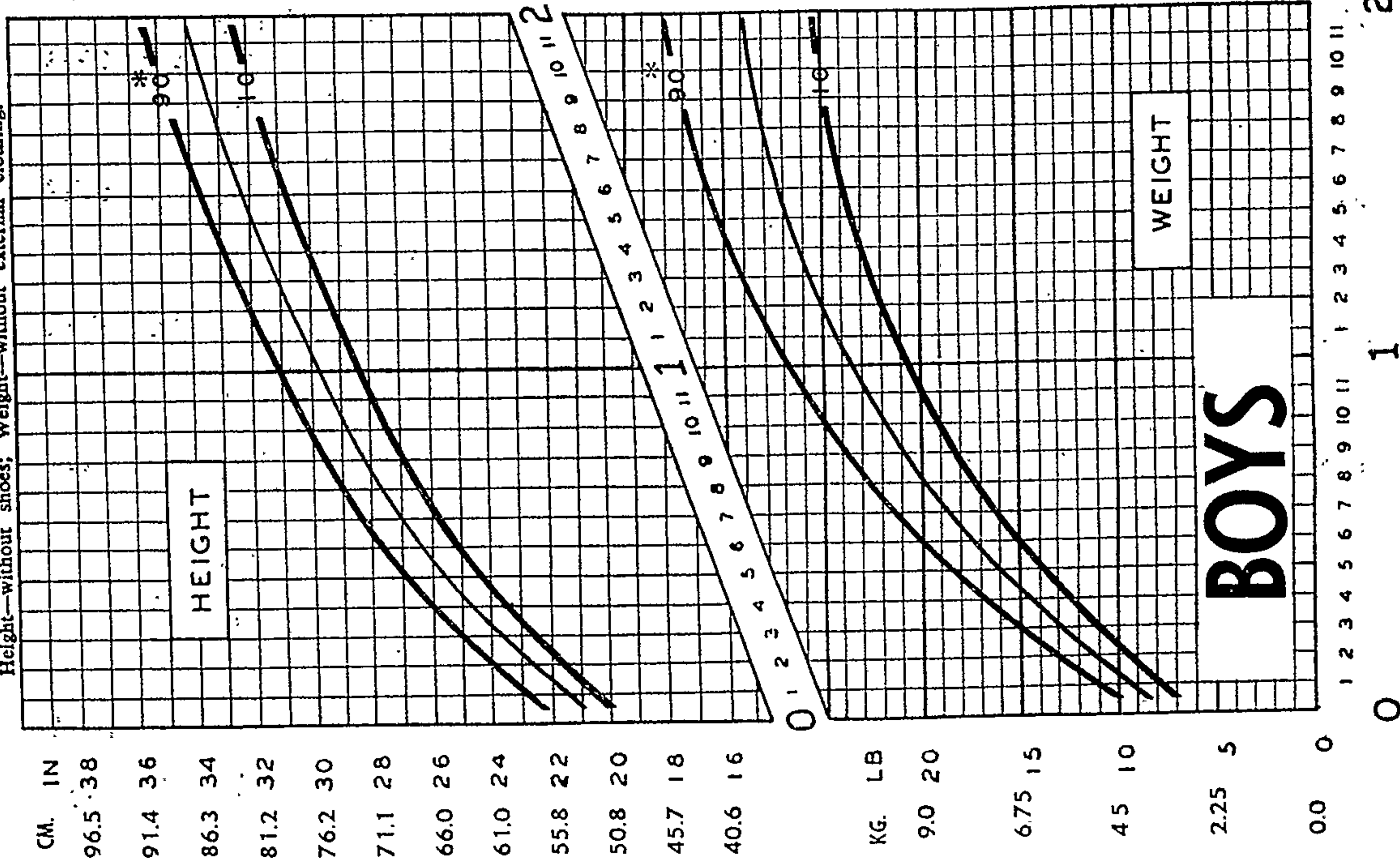
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This chart was originally published by the Nutrition Committee of the National Health & Medical Research Council, 1957.



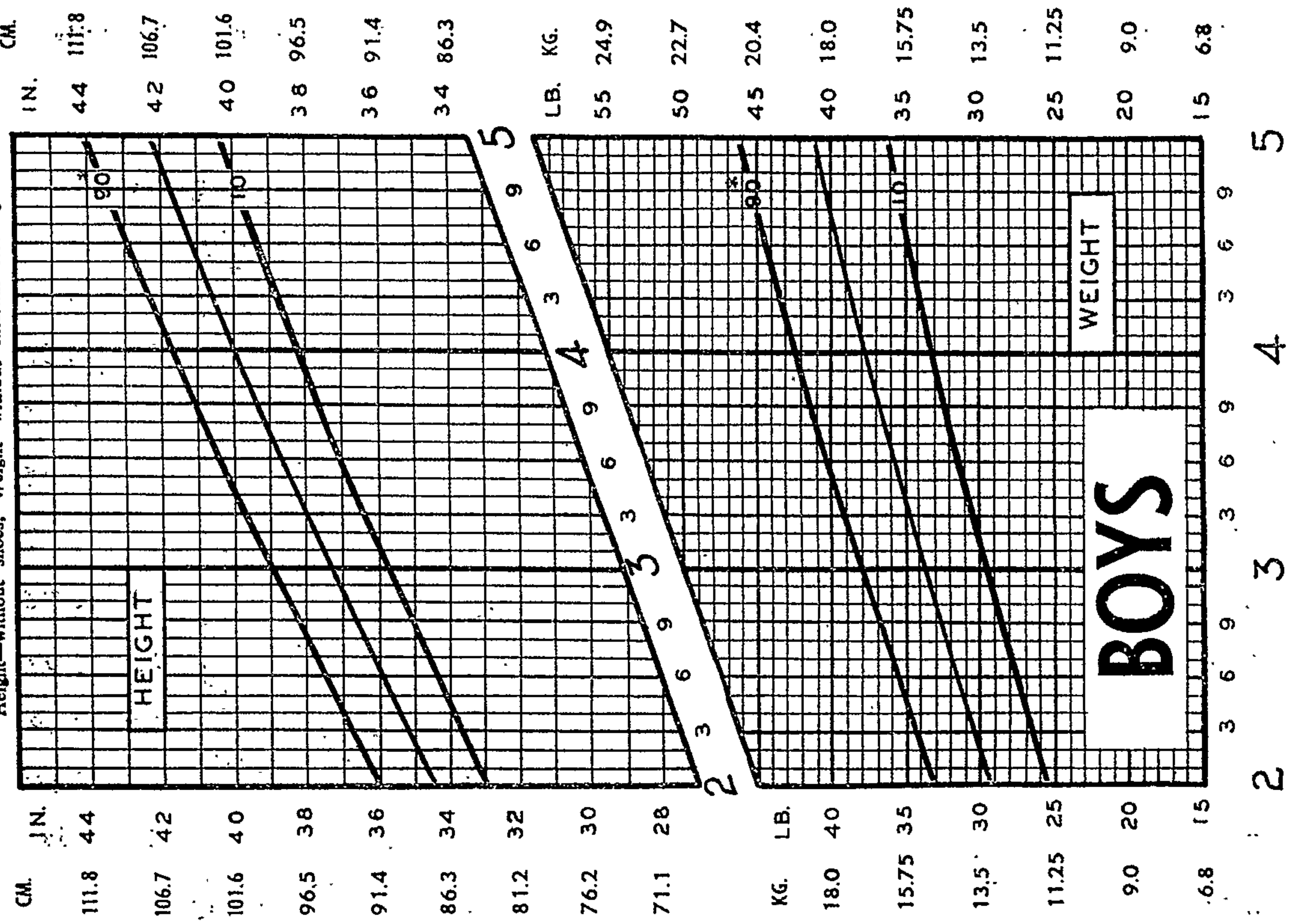
BOYS 0-2 YEARS

Height—without shoes; Weight—without external clothing.



BOYS 2-5 YEARS

Height—without shoes; Weight—without external clothing.



NAME

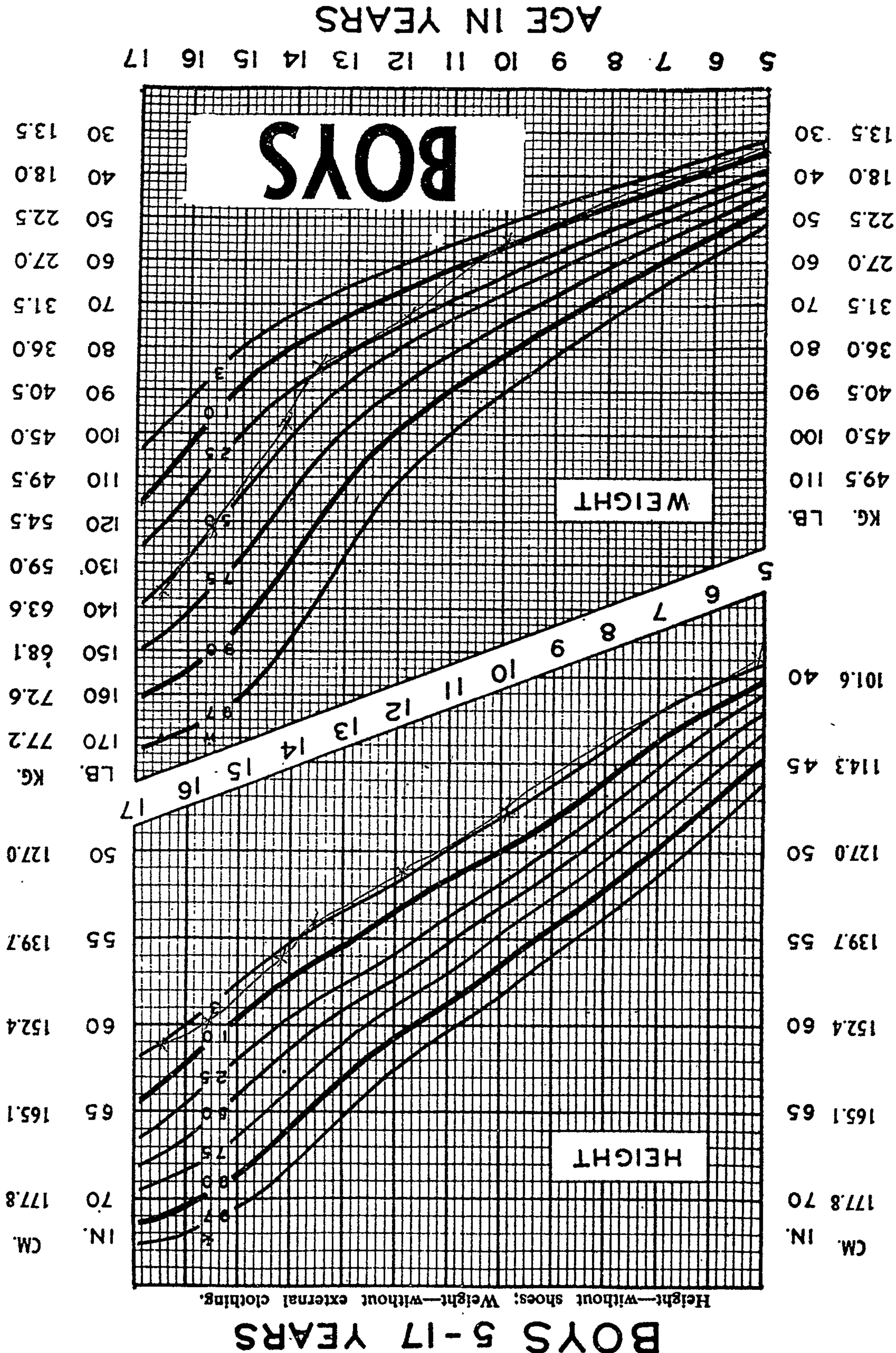
Age

Date of Admission

H.M.O.

HEIGHT / WEIGHT CHART - BOYS

MR - 44

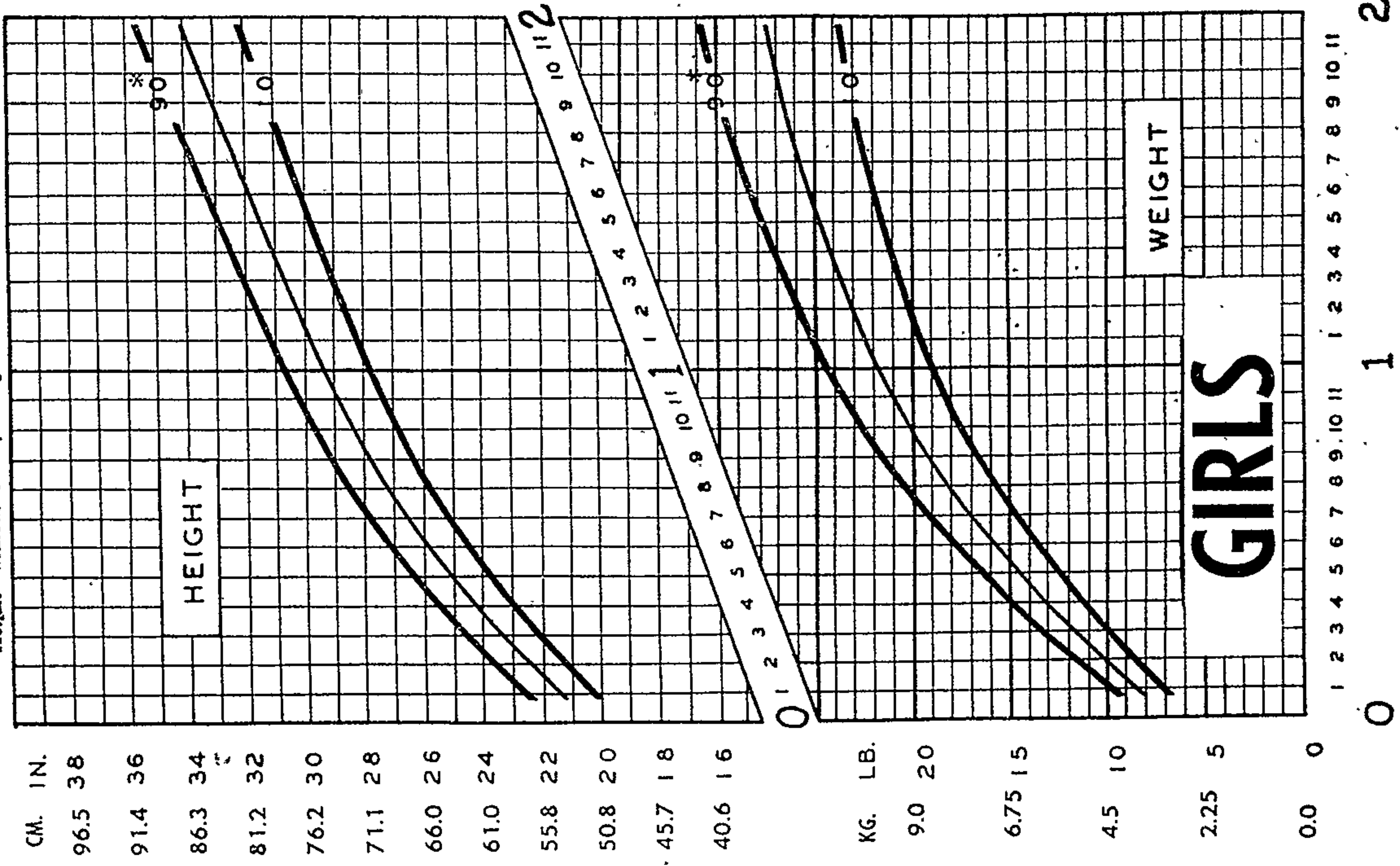


This chart was originally published by the Nutrition Committee of the National Health & Medical Research Council, 1957.

NAME Lynette U No 18 Ward 154 Date of Admission 1/5/57 H.M.O. SEE OVER

GIRLS 0-2 YEARS

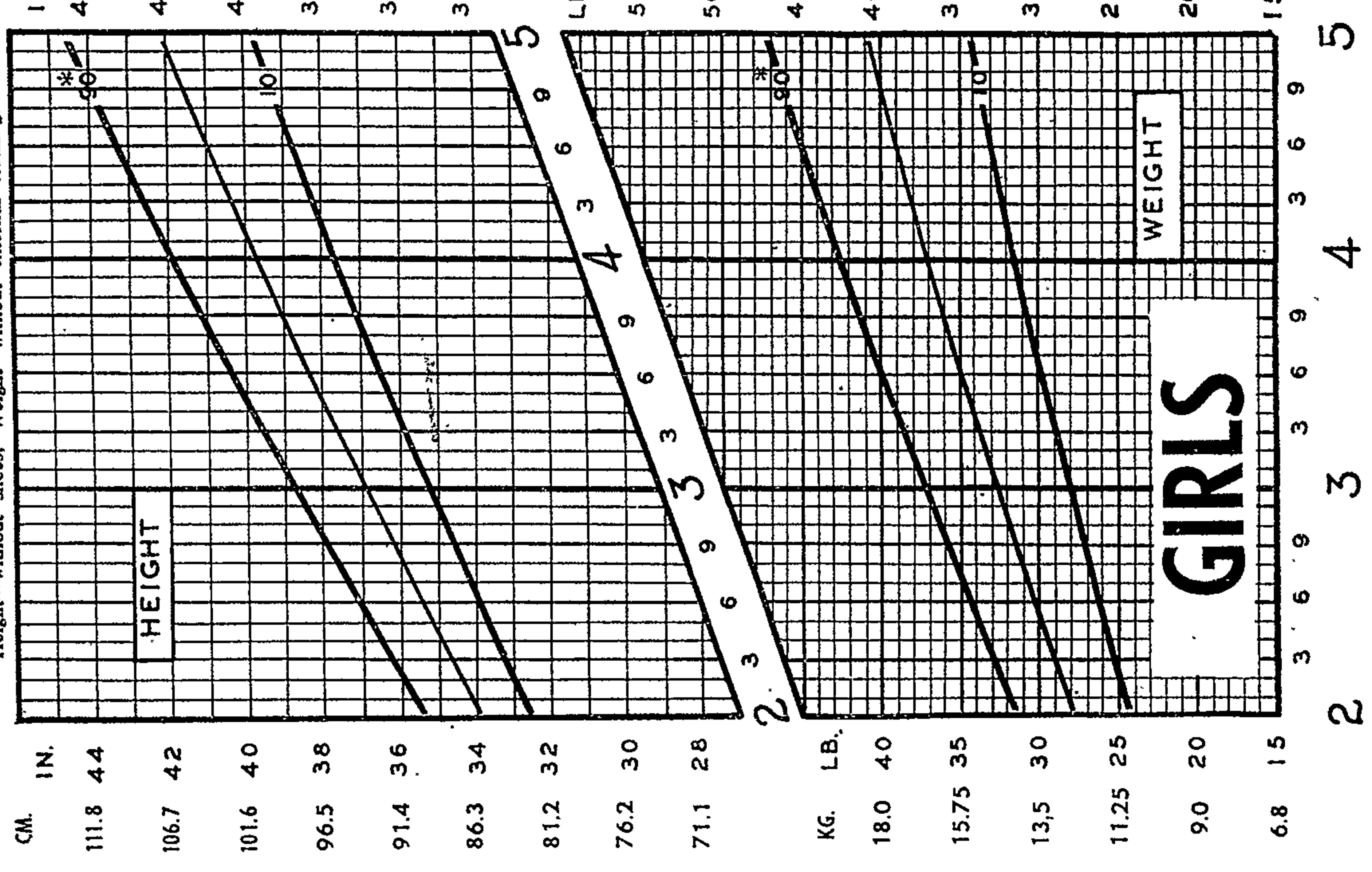
Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

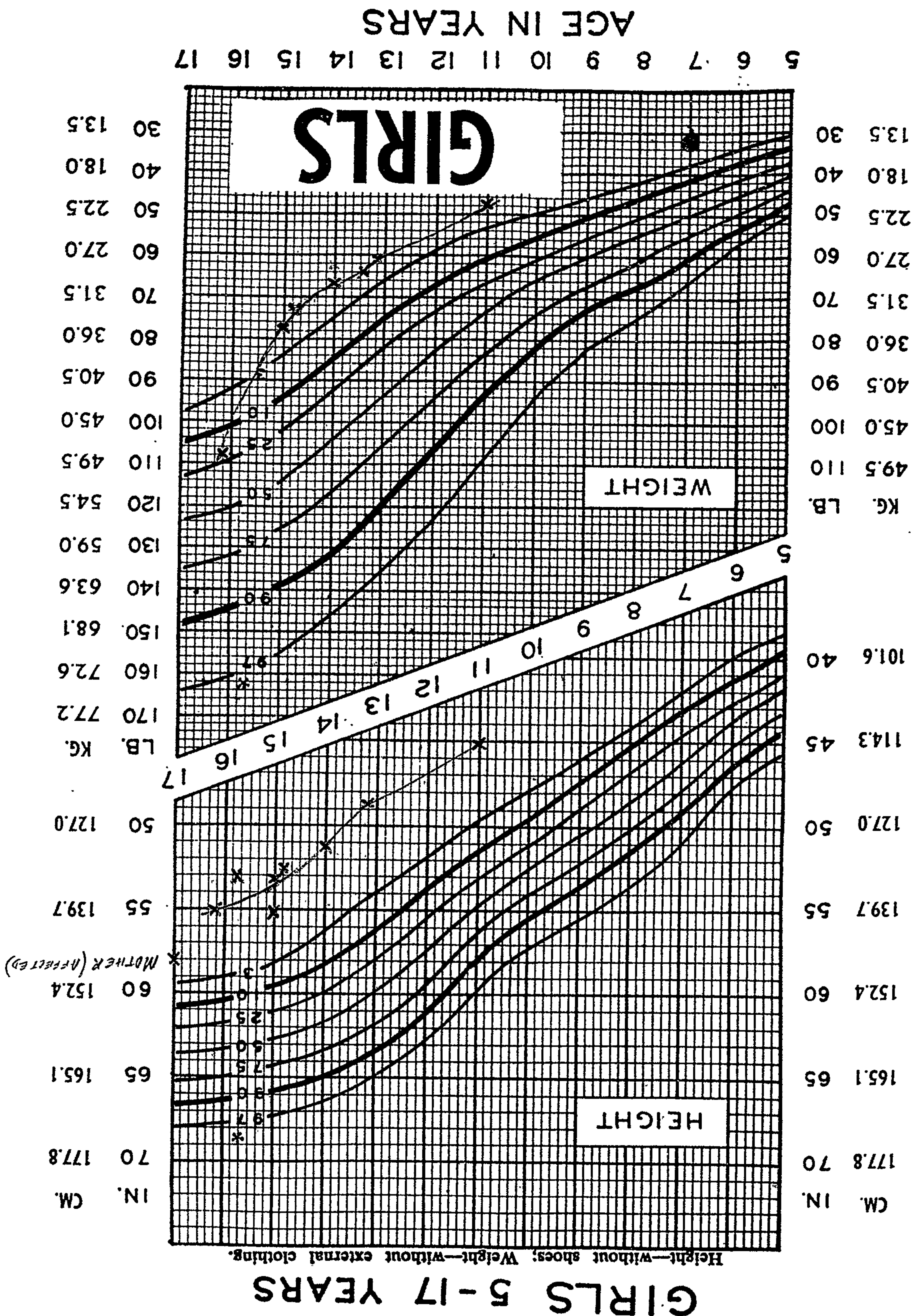
GIRLS 2-5 YEARS

Height—without shoes; Weight—without external clothing.



AGE IN YEARS AND MONTHS

MR - 45



examining medical officers did not report any abnormalities in muscle function.

9. Mentality

The aptitude tests and the assessments of examining medical officers indicated the patients are of normal mentality.

10. Vitamin D therapy

The details of vit. D therapy are included in Table 6.

11. Orthopedic Operative Procedures

All orthopedic procedures are shown for each patient in Table 6 under the treatment of deformities. The results of these procedures can be ascertained from the third column in Table 6 which gives the effects of treatment, both medical and surgical, on the deformities.

FINDINGS FROM CEPHALOMETRIC TRUE LATERAL
X-RAYS AND PLASTER MODELS

Table 7 presents the findings from the cephalometric lateral x-rays when compared with the composite transparencies of Sassouni.

Table 8 contains the results of the vertical and horizontal analysis of the craniofacial region from the lateral x-rays. The measurement of the gonial angle is also included in this table.

Table 8 is the analysis of the facial profile using three of the measurements suggested by Downs.

The measurements used for the analysis of vertical, horizontal and facial profile development shown in Table 8 have been located in each column by their degree of deviation from the mean value.

Measurements within one standard deviation of, above or below, the mean value occupy the centre position in each column. Results greater than 1 standard deviation below the mean are placed to the left of the column and results greater than 1 standard deviation above the mean are placed to the right side of the column.

The results from the examination of the plaster models, which were made for each child in this study, are presented in Table 9.

DISCUSSION OF RESULTS

THE CRANIUM

Cranial abnormalities were not found in as many cases as expected from the reports in the literature.

Winters et. al. 1958 (68) found that skull deformities recorded in 39 of the 65 patients which had been reported in the literature before their study.

Marks et. al. 1965 (50) found abnormalities of the skull in all of their patients for whom a cephalometric lateral head x-ray was available - the x-ray was available for 8 out of the 9 patients in their study.

A possible explanation for the lower reported incidence of cranial abnormalities in my material could be that the original study did not concentrate on this facet of the problem. The full extent of the cranium is not visible on the lateral head x-rays.

In all patients the examining medical officers had reported the skull shape to be normal or abnormal. However, measurements of cranial circumference on the patients, or measurements of

anteroposition length on the lateral head x-rays may have indicated abnormalities which were not obvious on general clinical examination.

The results of this study do indicate that a clinically obvious abnormality of the cranium will not be found routinely in patients suffering from vit. D R.R.

The cranial base angle, given in Table 7 was "flat" in 7 of the 9 patients with an abnormal cranial shape. This is approximately the same incidence of a flat cranial base angle as found for all the children in this study. Sixteen of the 23 children examined showed a flat cranial base angle.

HEIGHT AND WEIGHT MEASUREMENTS

The measurements of height and weight show that height is routinely more retarded than weight.

This suggests that growth of the soft tissues is not as severely affected by vit. D R.R. as is bone growth.

No direct relationship can be seen, from Table 6, between the amount of orthopedic surgery

required for individual patients and the difference found between growth in height and growth in weight.

VITAMIN D THERAPY

Using the methods suggested by Tapia et. al. for assessment of the varying requirements of vit.D it may be possible to achieve more uniformly satisfactory results and to reduce the amount of orthopedic surgery required. However as Tapia et. al. 1964 (74) found, full patient co-operation is essential over the complete period of treatment.

Many of the patients examined for this thesis lived in country areas and the time and expense involved for them in travelling to hospital for routine checks must be considered.

DISCUSSION OF CEPHALOMETRIC FINDINGS

The abnormality which appears most consistently in the cephalometric x-rays is flattening of the cranial base angle. This angle was recorded as "flat" in 20 of the 34 patients. (The method of assessment is given earlier.) In one patient the

posterior cranial base was not visible on the lateral head x-ray.

No patient showed a marked decrease in the cranial base angle.

The horizontal length of the anterior cranial base, as assessed in Table 7, shows some decrease in most cases.

The vertical development of the posterior cranial base, shown in Table 7, is fairly normal.

The horizontal development of the nasomaxillary region as shown in Table 7, is satisfactory. However, when the results for the nasomaxillary region are compared with the results for horizontal development of the mandible, in Table 7, it is seen that horizontal mandibular development is often in advance of it by one age group of the standards used, - i.e., 4 years.

Vertical and horizontal mandibular development, as shown in Table 7, are quite normal.

The results in Table 7 indicate that vertical development in the alveolar process of the maxilla was often more advanced than the vertical development of the body of the maxilla. The reverse situation where vertical development in the body

of the maxilla was in advance of vertical development of the alveolar process of the maxilla occurred in only 5 of the forty cephalometric x-rays.

In Table 8 the vertical development in the posterior craniofacial region (S-Go.) is compared to vertical development in the anterior craniofacial region (Na-Me.). The results routinely come within a normal range of $\pm$ one standard deviation of the mean value. A possible exception to this appears in youngest children. In the group of five children who were under 5 years of age when examined, the results for three children are greater than 1 standard deviation below the mean value.

The comparisons of vertical development in the lower face (ANS-Me.) to vertical development in total facial height (Na-Me.) indicates abnormal development, particularly in the children. These results are given in Table 8.

The results for the children are routinely greater than one standard deviation above the mean value.

The measurement of the Y axis to Frankfort horizontal shown in Table 8 does not indicate an obvious pattern of development. The results are extremely variable.

The measurement of the Y axis to the S-N plane does bring out a pattern of development. These results are shown in Table 8. Four of the children in the under 5 year old group show results greater than one standard deviation above the mean value. The rest of the children show results closer to the mean value; the oldest child in the study was the only one to give a result greater than one standard deviation below the mean value.

In the adults the measurement of the Y axis to the S-N plane indicated a different pattern to that seen in the children. Four out of 12 adults gave results greater than one standard deviation below the mean value.

The Y axis is used to indicate the position of gnathion and so the anterior border of the mandible. Measurement of the angle between the Y axis and S-N plane indicate a tendency towards a retrognathic position of the mandible where this angle is high and a tendency towards a prognathic position of the mandible where the angle is low.

From the results of the measurements of the Y axis to S-N plane the young children - under 5 years of age - as a group exhibit a tendency towards a retrognathic position of the mandible. The Y axis to S-N plane in the adults indicates that the mandible is in a normal position. The older children exhibit an in between stage with the mandible being in a normal position with a slight tendency towards the retrognathic position.

The angles SNA and SNB shown in Table 8 do not illustrate any pattern of development. The angle ANB, which equals SNA minus SNB, does show a regular change throughout. ANB angle is high in the patients under five, becomes lower for the older children and is negative in five of the adults.

In the angle classification of malocclusion a high ANB angle is used as an indicator of a skeletal Class II malocclusion. A negative value for the ANB angle is an indicator of a skeletal Class III malocclusion.

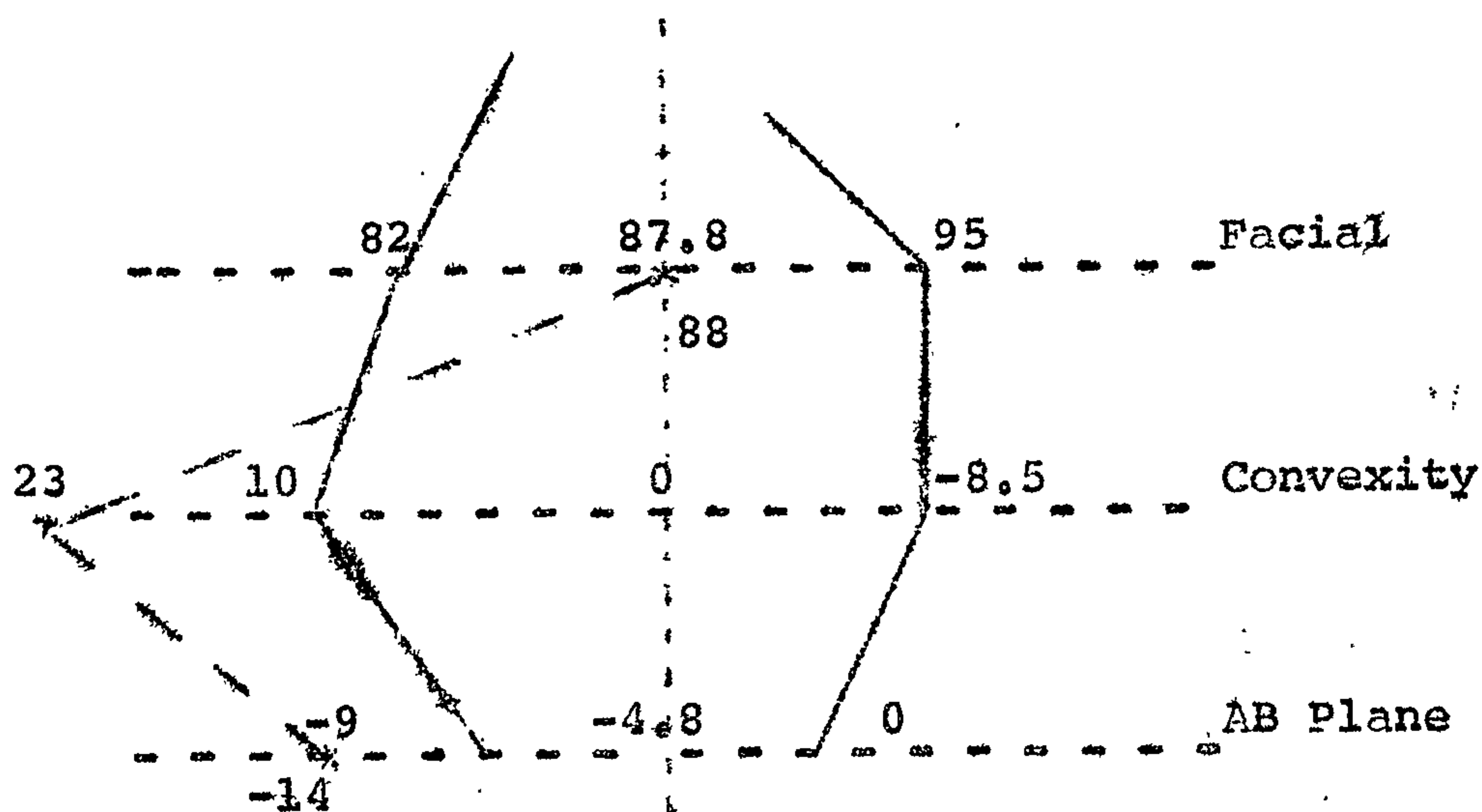
The measurement of the gonial angle is shown in Table 8. The normal pattern of change in the gonial angle reported in the literature is pro-

gressive reduction from birth to adulthood. The children suffering from vit. D R.R. fit into this pattern. The gonial angle for the group under 5 years old has an average value of 136° . The average for the gonial angle in the rest of the children is 126° . However the adults, affected by vit. D R.R. have an average gonial angle of 129° . This increase in the adults represents a reversal of the normal pattern of change in the gonial angle. To assess the importance of the variation in the gonial angle serial cephalometric x-ray examination over a long period is really necessary.

The measurements of the facial profile are given in Table 8.

A section of Downs' 1948 (19) facial diagram is presented below.* The limits suggested by Downs for the facial angle, the angle of convexity and AB to facial plane are shown.

* The facial diagram, or cephalometric polygon, was originally constructed by Vorhies and Adams in 1951. Vorhies and Adams used the measurements from Downs' facial analysis in drawing up the polygon.



Retrognathic to
the Left

Prognathic to
the Right

The measurements for patient No. 1 are shown on the facial diagram.

By comparison with the measurements in the facial diagram the direction of Class II and Class III variations for each angle have been indicated in Table 8. The results under the headings of Class II and Class III only indicate a tendency in the direction of column heading.

By inspection, the facial angle in all the children is more often on the Class II side of the mean value than on the Class III side of the mean. This changes in the adults to the extent that five measurements are in the Class III direction and only two measurements are in the Class II direction.

The angle of convexity in the young children is strongly in the direction of a Class II development. In the older children approximately one-third of the results are on the Class II side of the mean value and no results are in the Class III direction.

This situation is again reversed in the adults. One-third of the adults show results in the Class III direction, and no adult patients show results in the Class II direction.

The measurement of the AB plane to the facial plane, as shown in Table 8, varies in a similar way to the angle of convexity.

The AB to facial plane measurement shows a strong Class II tendency in the children under 5 years of age. The tendency in the direction of a Class II is reduced in the older children and in the adults the tendency is reversed. Five of the adults show a marked Class III tendency and only two show the Class II tendency which predominated in the children.

PLASTER DENTAL MODELS

As shown in Table 9, four of the five children under five years of age showed a Class II mal-

occlusion. After that age most of the children showed a normal occlusion or a Class I malocclusion.

Two sets of models were available for patient No. 8 (G.B.); the first set was made in August, 1965 and the second set was made in July, 1968. In the three year period between the models the occlusion had changed from an angle Class II to a Class I malocclusion.

Two sets of models were made for patient No. 7 (S.H.); the models were made about 2-1/2 years apart. He exhibited an angle Class I malocclusion in both sets of models. Any other changes were difficult to assess due to exfoliation of some teeth and the loss of others as a result of caries. Spacing of the lower anterior teeth was seen in both sets of models. The lower anterior teeth did not appear to have suffered any lingual collapse as a result of premature loss of the deciduous molars. There had been an increase of 2 mm. in maxillary molar width during the 2-1/2 years between the models; however the arch form still appeared normal. This increase in molar width and the continued spacing of the lower incisors could indicate that the tongue was

exerting a strong influence on the dentition in this case.

Two sets of models, made six months apart, were available for patient No.12 (C.D.). An angle Class III dental relationship in the buccal teeth was present when the first set of models was made. In the short period between the models the Class III relationship of the buccal teeth had become more pronounced, a slight spacing between the upper central incisors had increased and a positive overbite of one-third of a lower incisor had changed to an edge to edge anterior relationship.

Patient No.17 (R.N.) had two sets of models made of his teeth. The first set was made some time after orthodontic treatment. The orthodontic treatment consisted of removal of two upper first bicusps and retraction of the six anterior teeth. The original malocclusion was almost certainly angle Class II division 1 with an anterior open bite. The molars remained in a Class II relationship.

The second set of models, made 2-1/2 years later, show a good deal of relapse. The overjet has increased to 7 mm. and the canine relationship

is tending towards Class II. The overbite is still 0 mm.

Two sets of models were made for patient No.18 (Lyn. U.), and patient No.22 (M.E.) also. Neither of these patients showed any significant change in occlusal relations in the 2-1/2 year period between the models.

ARCH FORM

The arch form in the older children appears to be abnormal. A constricted upper arch, particularly in the anterior, was present in many of the older children. Crossbites were often found in association with the constricted upper arches. The form of the lower arch was usually normal, and in one patient it appeared broad.

In comparison to this the arch form in the younger children was consistently good and no crossbites were present.

The palatal contour in these patients did not show any consistent abnormalities.

INCISOR RELATIONSHIPS

The incisor relationship in the younger children was typical of Class II division 1 malocclusions. In patient No.1 (P.H.) the $\underline{A_1A}$ had exfoliated but the position of the $\underline{B_1B}$ indicated that a wide overjet and no overbite would have been the relationship when the $\underline{A_1A}$ were present.

Of the children in the under 5 years of age group only one patient did not suffer from a Class II division 1 malocclusion. This patient had an angle Class I occlusion.

The vertical overbite and horizontal overjet relationships of the incisors are shown in Table 9. In the older children these relationships are quite variable and do not exhibit any obvious pattern.

The presence of crowding or spacing appears variable in both arches.

UNDERLYING PROBLEMS IN VITAMIN D RESISTANT
RICKETS

The material examined for this thesis reveals a changing pattern in the occlusion of the patients affected by vit. D R.R. Broadly stated, there is a class II malocclusion in the younger children particularly in those under the age of 5 years - which changes to a class I occlusion in the older children - often with constriction of the upper arch. By adult life the occlusion shows a class III tendency.

From this thesis no single factor can be advanced in explanation of the changes reported in the occlusal relationships.

The factors which I feel could play a part in craniofacial development in patients affected by vit. D R.R. are discussed below:

A. DECREASED CARTILAGE GROWTH

Abnormalities in cartilage growth are a most consistent finding in all forms of rickets. Statural height of patients affected by vit. D R.R. is consistently reduced. This indicates that cartilage growth is not only abnormal but is actually decreased.

The areas in which cartilage growth is most important in the craniofacial region are:

1. The cranial base

This area develops from cartilage.

The results shown in table 7 indicate that the length of the anterior section of the cranial base is reduced in many patients.

I did not find any reduction in the posterior part of the cranial base.

2. The nasal region

The assessment of horizontal growth in this region, shown in table 7, did not reveal any abnormalities. However it should be noted that this assessment was made of the inferior surface of the nasal cavity, represented approximately by the distance from ANS to PNS. If the superior surface of the nasal cavity is taken as the anterior cranial base, then there is reduction in the horizontal development of the nasal region.

My assessment of vertical nasal development relies on the comparisons of vertical development shown in table 8.

Total anterior facial height is in proportion to posterior craniofacial height but lower anterior facial height is proportionally

greater than total anterior facial height.

This indicates a reduction in the height of the nasal cavity in the anterior region.

3. The mandible

The overall development of the mandible has been quite normal. This suggests either cartilage growth is not a primary factor in mandibular development or that cartilage growth is not affected by vit. D. R.R. in this region.

B. DECREASED RATE OF BONE FORMATION

The rate of bone formation at the osteon level has been reported to be severely reduced in people affected by vit. D R.R.

If this reduced rate of bone formation does occur in the cases examined it would be most noticeable in the areas where growth is most active. All areas would take longer to reach their final proportions although the final result may not be changed.

I feel this type of growth reduction would only be detected by linear measurements compared with a carefully derived age standard.

C. DEFORMATION OF THE CRANIAL BASE

Table 7 shows there is consistent flattening of the cranial base in the children and the adults examined for this thesis.

I have not been able to identify the mechanisms which could be responsible for the flattening of the cranial base.

Pruzansky 1958 (60) has suggested flattening of the cranial base is associated with reduction in the dimensions of the airway.

D. FUNCTIONAL DEMANDS FOR OROPHARYNGEAL SPACE

According to Moss's 1962 (54) theory of the functional matrix, functional requirements will be the final factors controlling growth.

For function to produce the abnormal patterns of development found in the patients with vit. D R.R. an abnormality must exist in the functional matrix.

My study suggests that one abnormality in these patients is deficient cartilage growth.

Deficient cartilage growth in the anterior cranial base, and in the nasal capsule could place a limitation on the capacity of the nasal airway.

The case report by Foster 1965 (24), discussed in my literature review, showed that the jaws must adapt to allow the maintenance of the airway.

HYPOTHESIS ON THE PRODUCTION OF THE ABNORMAL-
ITIES FOUND.

METHODS OF JAW ADAPTION TO ABNORMAL FUNCTIONAL
REQUIREMENTS.

The possible ways by which the jaws can adapt to altered functional demands have never been determined. Following the work of Moss 1962 (54) many research workers studying growth and development must be very conscious of the important role which function has in their particular field. For this reason I feel that future research in craniofacial development will point out the mechanisms by which the jaws can adapt to altered functional demands. It is essential for a more complete understanding of craniofacial development that these mechanisms of adaptation be identified.

Although this thesis must stop at the point of detecting an unusual pattern of craniofacial development in patients affected by vit. D R.R, I feel this must not be regarded as the final stage in a study of this nature. A further study should be made to attempt to identify the way in which this unusual pattern of development takes place.

I would like to present my ideas on the

possible mechanisms underlying the developmental pattern of the patients observed in this thesis. These ideas should provide pointers to possible future study.

I have previously suggested that there is a decrease in the capacity of the nasal airway, due chiefly to deficient cartilage growth, caused by the disease of vit. D R.R.

The body must compensate for a limitation in the essential function of respiration.

COMPENSATORY GROWTH

Initial compensation may be achieved by posturing the mandible - and the tongue - to facilitate respiration.

I suggest that this continual position of the mandible reduces the functional forces on the teeth. The teeth then continue to erupt and alveolar bone continues to grow until the functional load on the teeth is sufficient to stop this process. The jaws remain in the position where the most basic functional demands - respiration and deglutination - are being satisfied.

The process of adaptation and compensatory growth outlined above would commence as soon as a deficiency in cartilage growth developed. Growth is usually retarded from a very early age.

RESULTS OF COMPENSATORY GROWTH

The children under 5 years of age in this study exhibit class II malocclusions in 4 out of 5 cases.

My measurements of vertical growth indicate deficient anterior nasal height and an excess in lower anterior facial height. Table 7 indicates that the increased lower facial height may be associated with increased alveolar growth, at least in the maxilla.

Schudy 1965 (64) has shown the greatest difference between class I and class II occlusions is the greater amount of alveolar growth which has occurred in the class II cases.

SPECIAL CONSIDERATIONS IN PATIENTS WITH VITAMIN D R.R.

A. Flattening of the cranial base.

The distal position of the mandible may be

associated with the observed flattening of the cranial base. The flattening of the cranial base could produce a distal positioning of the glenoid fossa, and so the temporomandibular articulation, in relation to the upper face. The flattening of the cranial base is still present in the adult patients in this study although the class II malocclusion has changed.

B. Decreased rate of bone formation.

Decreased rate of bone formation at the level of the osteon may not affect the growth response of alveolar bone. If the trabecular pattern is changed to a more coarse structure - as has been noted in other areas of bone - growth may extend over the same distance with less actual bone formation.

The decreased rate of bone formation may retard growth which relies on apposition and resorption without the presence of much trabecular bone.

PATTERN OF DEVELOPMENT IN OLDER PATIENTS

As described previously the craniofacial development changes to class I in the older children and a class III tendency is present in the adults.

My hypothesis on the development of a class II malocclusion in the young patients relies on a response to functional demands. When the demands of function are met in the older patients - this may be achieved by the continued predominance of appositional growth over cartilage growth - there is a reversal from abnormal growth towards normal growth.

I feel this situation of balance, between craniofacial growth and functional demand, is reached in the older children in this study.

Then in the adult, any malocclusion seen is a true manifestation of the results of rickets; it is no longer masked by the compensatory growth which produced the class II malocclusion in the young children. In the adult there is a deficiency in the nasomaxillary development and normal development in the mandible. This gives the class III tendency.

SUMMARY AND CONCLUSIONS

The disturbance in vit. D metabolism present in vit. D R.R. results in the failure of normal calcification during endochondrial ossification. The failure in calcification is related to the production of an abnormal matrix by the cartilage cells.

It is thought that the disturbance in vit. D metabolism affects the transcription of D.N.A. into messenger R.N.A. within the collagen-producing cells. The collagen fibres formed as a product of the affected cells do not achieve the exact orientation necessary to allow initial mineralisation to occur.

The disturbance in mineralisation is also present in lamella bone formation, resulting in wide, unmineralised osteoid borders.

The result of the massive doses of vit.D used in the treatment of vit. D R.R. is to improve mineralisation. Unfortunately, the mineralisation never becomes completely normal.

The optimal dosage of vit. D, which must be accurately assessed, can produce improved growth in the patient and minimise the deformities

which are associated with vit. D R.R. For the best results the vit. D therapy should be commenced very early, probably before the patient is one year old.

The measurements taken over a period of time indicate that both height and weight are routinely retarded. On closer examination of these measurements it was found that height was more severely retarded than weight in each patient.

The family history of each patient was examined to ascertain whether a pattern of inheritance could be detected in the patients in this study.

My findings support the theory of an X-linked mode of inheritance of the disease. However, it must be noted that one patient did not fit into this pattern of inheritance.

The development of the cranium, faces and jaws was studied and comparisons were made with normal standards. Abnormal cranial morphology was not noted routinely in this study, whereas some craniofacial abnormalities were detected quite routinely. The review of the literature revealed that very few quantitative measurements of craniofacial development in patients with vit. D

R.R. had been made.

In this thesis the analyses of the cephalometric x-rays, viewed in conjunction with the plaster dental models of the vit. D R.R. patients, revealed a surprisingly consistent pattern of development from childhood to adult maturity.

The children under 5 years of age suffering from vit. D R.R. showed an angle Class II malocclusion. The older children generally showed an angle Class I occlusion. The adults in this study exhibited a tendency towards an angle Class III malocclusion.

This abnormal pattern of development led to an hypothesis of the mechanisms which could be involved in the production of the abnormality.

It is suggested that a constriction of the nasal airway is caused by deficient cartilaginous growth as a result of the vit. D R.R.

This constriction of the airway has its greatest effect in the young children and results in the production of an angle Class II malocclusion.

It is hypothesised that the Class III tendency in the adult patients is the ultimate effect of

vit. D R.R. The disease has resulted in a deficiency in maxillary growth but has not disturbed mandibular growth.

The adults in this study did not receive adequate vit.D therapy, by present day standards. If the children in this study are receiving adequate vit. D therapy early enough to limit craniofacial malformations, then the malocclusions in the children should not progress to the Class III tendency found in the adults in this study.

As abnormalities in craniofacial growth have been found in the children under 5 years of age in this study, a long term follow-up study is necessary to assess how effective treatment has been in limiting the development of craniofacial abnormalities.

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MEDICAL RECORDS

TABLE 6

No.	PATIENT	AGE EXAMINED	BIRTH	SEX	MEDICAL TREATMENT
1	Peter H.	3	1/63	M	Vit.D:20,000 i.u. daily since Feb. 67.
2	Rodney B.	3-8/12	11/64	M	Vit.D 10,000 i.u. daily May 67, 20,000 i.u. daily Feb. 68.
3.	Debra M.	4-3/12	9/61	F	Vit.D; 25,000 i.u. daily Sept.64 to March, 65
4	David C.	4-5/12	8/61	M	Vit.D:100,000 i.u. daily April 64 50,000 i.u. daily Jan 66 for 12 m., 100,000 i.u. daily Feb.67 75,000 i.u. daily Oct.67
5	Graham A.	4-10/12	7/63	M	Vit.D:75,000 i.u. daily July 66, Phosphate: up to 125 ml. units per day "Bacilic"
6	Nerida M.	8-6/12		F	Vit.D:7,500 i.u. daily Feb.1960 20,000 i.u. May 60, 50,000 i.u. Sept. 61 75,000 i.u. Sept.62, 100,000 i.u. March, 63 50,000 i.u. Sept.64
7	Stephen H.	9-3/12	5/57	M	Vit.D: Diagnosis Nov.61 20,000 i.u. daily Feb.66
8	Gail B.	9-8/12	11/58	F	Vit.D: 20,000 i.u. daily Mch, 63 40,000 i.u. daily Sep.63
9	Gail N.	9-11/12	1/56	F	Vit.D: up to 200,000 i.u. daily at 6 months of age 100,000 i.u. daily July 67 for 5 years
10	Cheryl M	10-6/12	6/55	F	Vit.D: low dose commenced 6/59 high dose (25,000 i.u. daily) 6/63
11	Graham S.	10-11/12	2/53	M	Vit.D: 50,000 i.u. daily from 1960 100,000 i.u. daily from 1961
12	Christine D.	11	12/52	F	Vit.D: low dosage until 1960 50,000 to 100,000 for 2 years, then 150,000 i.u. daily
13	Cheryl G.	11-6/12	9/52	F	Vit.D: 50,000 i.u. daily Sep.57 75,000 i.u. daily Sept.58 continued on this dose
14	Gregory U.	11-9/12	4/54	M	Vit.D: 200,000 to 230,000 i.u. daily, commenced early '62 80,000 i.u. daily early '66.
15	Alan A.	13-6/12	6/52	M	Vit D: none
16	Marion S.	13-6/12	6/51	F	Vit D: 25,000 i.u. daily at 7 yrs old,50,000i.u. at 8 yrs. 100,000 i.u. at 9 yrs old, 150,000 i.u. at 11 yrs decreased to 100,000 i.u. daily for 2 yrs then 50,000 i.u. daily

MEDICAL RECORDS

TABLE 6

No.	PATIENT	AGE EXAMINED	BIRTH	SEX	MEDICAL TREATMENT
17	Robert N.	13-10/12	3/52	M	Vit.D: 200,000 i.u. daily at 2 yrs old 100,000 i.u. daily 1957, 50,000 i.u. daily '59 for 2 years
18	Lynette U.	13-10/12	3/52	F	Vit.D: 50,000 i.u. daily 3/63, 200,000 i.u. daily 10/65 Ca: 700 mg. daily
19	Robyn B.	14	1/52	F	Vit.D: 75,000 i.u. daily 2 yrs commenced July, 1954 25,000 i.u. daily commenced 1/62, 50,000 to 200,000 i.u. from 1964.
20	Laurence U.				Vit.D: 50,000 i.u. daily 4/57, this was not continued 80,000 i.u. daily 9/66.
21	Yolanda C.	18	2/48	F	Vit.D: no record of administration
22	Merryn E.	19-2/12	12/46	F	Vit.D: none
23	Leonie M.	18-1/12	7/50	F	Vit.D: None

MEDICAL RECORDS

TABLE 6

No.	PATIENT	TREATMENT OF DEFORMITIES	RESULTS OF TREATMENT
1	Peter H.	Bilat-roational tibial osteotomies Feb.66	Surgical corrections
2	Rodney B.	Leg irons 6/68; cranioplasty 1967, no osteotomis	Legs not improved
3	Debra M	Bilateral osteotomies tibial 6/65 Calipers from 15 months	Surgical correction
4	David C.	No osteotomies, No splints	
5	Graham A.	None	Still present
6	Nerida M.	No surgery, built up shoes when young - before 1960	Marked bowing 2/60, bowing decreased 4/65; legs good; slight anterior bowing of femora 5/68.
7	Stephen H.	Bilateral femoral osteotomies 2/62; Rotational osteotomy L tibia 11/62; Osteotomy R tibia 12/62; Bilateral tibial osteotomies 8/67.	Surgically corrected.
8	Gail B.	Bilateral femoral osteotomies 9/61	
9	Gail N.	Bilateral tibial osteotomies 9/61	Surgically corrected. Legs good 8/68
10	Cheryl M.	None recorded	No improvement recorded
11	Graham S.	None	Bowing from 15/12 months. Still present 1960; separation of knees gone by 1963; leg bowing still present
12	Christine D	6 corrective osteotomies - 4 on R. leg, first op.1957. Splints tried 1954.	Surgical correction.
13	Cheryl G	Bilateral tibial osteotomies 1/68, Splints at 2-3/12 yrs. old	No improvement observed with splints. Jan 66 bowing has diminished. Knee separation diminished from 14 cm. Jan.60 to 5 cm. Jan.66, surgical correction
14	Gregory U	Bilateral tibial osteotomies 10/65, leg irons to be worn from Jan.60	Knock kneed since standing, no improvement by 1962.
15	Alan A.	Bilateral tibial osteotomies 1960, L tibial osteotomies 1961; bilateral femoral osteotomies 1962	Legs bowed since 2-1/2 yrs old

MEDICAL RECORDS

TABLE 6

No.	PATIENT	TREATMENT OF DEFORMITIES	RESULTS OF TREATMENT
16	Marion S.	R tibial osteotomy at 11 yrs old R " " " 13 " " L " " " 14 " " Calipers worn throughout. Repair to cleft of soft palate 1954, cleft of bony palate repaired some years later.	Cleft palate <i>repaired</i>
17	Robert N.	R tibial osteotomy 10/62, Bilateral tibial osteotomies 6/63	Bowing had decreased a lot by 4/57.
18	Lynette U.	R tibial osteotomy 8/67, L " " 2/68	Legs straight until 8 yrs old, then developed knock knees. Felt deform- ity not getting worse 10/65, X-ray review showed striking improvement 11/66.
19	Robyn B.	No surgery, wore splints when young	No record of changes from original bowing.
20	Laurence U.	Bilateral tibial osteotomies 4/57, " femoral " 2/60 Further orthopedic operation '64 Leg brace, June 65.	Leg deformities present at 3 yrs. 1962/65 both knees had moved from varus to valgus position. June 1965 leg brace & weight lifting each leg. Oct. 65 no further deformities.
21	Yolanda C.	Bilateral tibial osteotomies 11/59 History of earlier osteotomies in Italy	R leg 1-1/2 inches shorter than L leg
22	Merryn E.	Stapling of lower femoral epiphysis, bilateral tibial osteotomies Jan. 57, Osteotomy L femur 8/58; osteotomy R femur 9/58, bilateral tibial osteo- tomies 11/58.	Legs normal 6/68
23	Leonie M.	None	Slight bowing of legs first noticed at 16 yrs old.

MEDICAL RECORDS					TABLE 6	
No.	PATIENT	RELATION TO PERCENTILES HEIGHT WEIGHT		SERUM Ca. NORMAL 9-11	SERUM PHOS. NORMAL 4-6	SERUM ALK. PHOS. NORMAL 10-25 KA
1	Peter H.	<3	3-10	N	L	H
2	Rodney B.	<3	10	N	L	N
3	Debra M.	10-25	25	N	L	H
4	David C.	<3	10-25	N	L (fluctuation)	H
5	Graham A.	<10	10	N	L	Slightly H
6	Nerida M.	25	50	N	Improved almost N	Improved almost N
7	Stephen H.	10	10	N	L	H
8	Gail B.	25	25	N	L	H
9	Gail N.	25-50	≈90	N hyper-calcemic 5/57	L	Slightly H
10	Cheryl M.				4/59	
				10.3	3.0	30 K A units
11	Graham S.	3-10	≈97	N	Improved with treatment 3.0	Lowered to N when radio- graphic healing seen
12	Christine D	≈10	25-50	N	L	H often very H
13	Cheryl G.	3	25	N	L	H
14	Gregory U.	≪ 3	3	N	L	H (variable)
15	Alan A.	3	3	N	L	H

MEDICAL RECORDS						TABLE 6
No.	PATIENT	RELATION TO PERCENTILES HEIGHT WEIGHT		SERUM Ca. NORMAL 9-11	SERUM PHOS. NORMAL 4-6	SERUM ALK. PHOS. NORMAL 10-25 KA
16	Marion S.	« 3	10-25	N hypercal on 3 occasions	L	H earlier N 3/68
17	Robert N.	3-10	50	N	L	H
18	Lynette U.	« 3	10-25	N	L	H
19	Robyn B.	25-50	50	N	improved to slightly L	H
20	Laurence U.	< 3	≈10	N	L	H
21	Yolanda C.	< 3	10	N	L	H
22	Merryn E.					
23	Leonie M.	25	25			

TABLE 7

	1	2	3	4	5	6		7	8	9		10	11	12	13
	Peter H.	Rodney B.	Debra M.	David C.	Grahame A.	I. Nerida M.		Stephen H.	Gail B.	1. Gail N.		Cheryl M.	Graham S.	Christine D.	Cheryl G.
Age at examination	3	3 ⁸ ₁₂	4 ³ ₁₂	4 ⁵ ₁₂	4 ¹⁰ ₁₂	8 ⁶ ₁₂	2.	9 ³ ₁₂	9 ⁸ ₁₂	9 ¹¹ ₁₂	2.	10 ⁶ ₁₂	10 ¹¹ ₁₂	11.	11 ⁶ ₁₂
Family Relationships	7	8&24	35		34	23&27		1	2&24	17&25		33			32
Cranial base angle	flat	VV flat	V flat	8	4	12	12	flat	VV flat	12	12	SI flat	12	flat	flat
HORIZONTAL DEVELOPMENT Ant.Cr.base	<<4	<<<4	<4	<4	4	4	8	<4	4	8	8	4	12	4	8
Naso. maxilla	<4	<4	4	4	8	8	8	8	4	8	8	8	12	12	8
Mandible	4	4	4	4	4	12	12	12	12	12	12	12	16	12	12
VERTICAL DEVELOPMENT															
Posterior cranial base	4	<<4	4	12	4	12	12	8	<4	12	12	8	8	8	12
Nasal	4	4	4	8	4	8	12	8	<8	<8	12	8	12	12	8
Body of Maxilla	4	4	4	8	8	8	12	8	8	12	12	12	Ad.	12	8
Alveolar Process of Maxilla	4	12	4	12	8	12	12	16	12	12	16	12	Ad.	Ad.	12
Ramus of the mandible	4	4	<4	4	8	8	12	12	8	12	16	8	12	16	16
Body of the mandible	4	4	4	8	8	8	12	12	8	12	12	12	12	Ad.	16

TABLE 7

	14	15	16	17		18		19	20	21	22		23	24
	Gregory U.	Alan A.	Marion S.	1. Robert N.	2.	1. Lynette U.	2.	Robyn B.	Laurence U.	Yolanda C.	Merryn E.	2.	Leonie M.	Mrs. Backhouse
Age at examination	11 ⁹ / ₁₂	13 ⁶ / ₁₂	13 ⁶ / ₁₂	13 ¹⁰ / ₁₂		13 ¹⁰ / ₁₂		14	16 ⁷ / ₁₂	18	19 ² / ₁₂		18	
Family Relationships	18 20 & 31	30	29	9 & 25		14 20 31		28	14 18 & 31		26		6 & 27	28
Cranial base angle	flat	flat	V flat	flat	flat	12	16	Poor x-ray flat	flat	Bad x-ray SI flat	flat	flat	12	flat
HORIZONTAL DEVELOPMENT														
Ant.Cr. base	8	8	8	12	Ad.	8	16	4	12	8	Ad.	Ad.	16	8
Naso. maxilla	8	12	12	12	12	8	12	8	12	16	Ad.	Ad.	12	8
Mandible	8	Ad.	> Ad.	16	Ad.	12	12	12	16	Ad.	Ad.	Ad.	16	Ad.
VERTICAL DEVELOPMENT														
Posterior cranial base	8	12	12	12	?	12	?	?N	16	?12	Ad.	Ad.	12	8
Nasal	8	12	12	16	16	8	8	8	12	Ad.	8	8	12	12
Body of Maxilla	8	16	Ad.	Ad.	Ad.	8	12	12	8	Ad.	Ad.	Ad.	Ad.	12
Alveolar Process of Maxilla	12	16	Ad.	16	Ad.	12	Ad.	16	Ad.	Ad.	12	12	16	16
Ramus of the Mandible	8	16	4	16	Ad.	12	16	16	Ad.	16	Ad.	16	16	16
Body of the mandible	12	12	Ant.Ad. Post 4 Gen 16	16	Ad.	12	16	12	Ad.	Ad.	16	12	16	? 4

TABLE 7

	Mrs. Nicholson 25	Mrs. Emmerson 26	Mrs. Myatt 27	Mr. Barlow 28	Mrs. Sheppard 29	Mrs. A. Ashton 30	Mrs. Ulph 31	Mrs. Green 32	Mrs. Masterton 33	Mrs. G. Ashton 34	Mrs. Mullens 35
Age at examination											
Family Relationships	9&17	22	6&23	19	16	15	14, 18 20	13	10	5	3
Cranial base angle	bad x-ray	bad x-ray	12	flat	Ad.	Ad.	flat	Ad.	Ad.	16	Poor x-ray flat
HORIZONTAL DEVELOPMENT											
Ant. Cr. base	? 4	?16 Ad.	16	4	16	12	8	12	16	16	8
Naso. maxilla	8	16	12	12	Ad.	<12	12	12	16	12	8
Mandible	12	12	12	12	16	Ad.	12	12	Ad.	12	12
VERTICAL DEVELOPMENT											
Posterior cranial base	?	Ad.	16	Ad.	16	Ad.	12	12	?12	12	?16
Nasal	16	12	12	> 8	12	12	12	12	12	12	12
Body of Maxilla	16	12	12	Ad.	Ad.	> Ad.	Ad.	16	16	12	12
Alveolar Process of Maxilla	Ad.	16	16	Ad.	16	> Ad.	Ad.	Ad.	Ad.	12	Ad.
Ramus of the Mandible	Ad.	16	16	Ad.	16	16	Ad.	16	Ad.	16	16
Body of the mandible	12	8	4	< 8	12	16	16	12	Ad.	12	16

CEPHALOMETRIC EVALUATION

TABLE 8

No.	PATIENT	GONIAL ANGLE	S - Go % Na - Me			ANS - Me % Na - Me		
			-1SD	M 65% ± 4%	+1SD	-1SD	M 54% ± 2%	+1SD
1	Peter H		60%					61%
2	Rodney B	144	48					61
3	Debra M.	137	56					60
4	David C.	132		62				62
5	Grahame A.	131		63				60
6	Nerida M. 11/65	127		67				57
	8/68	126		68				58
7	Stephen H.	121		67				59
8	Gail B.	116	49				56	
9	Gail N. 1/66	130		66			56	
	8/68	121		62			56	
10	Cheryl M	122		63				58
11	Graham S	123		62				58
12	Christine D.	120		66				60
13	Cheryl G.	128		65				60
14	Gregory U.	136	59				56	
15.	Alan A.	131		62				57
16	Marion S.*	125*	55*					59*
17	Robert N. 1/66	131		64			55	
	8/68	135		62				62
18	Lynette U. 2/66	132		68				62
	7/68	130		69				60
19	Robyn B.	121		69				58

CEPHALOMETRIC EVALUATION

TABLE 8

No.	PATIENT	GONIAL ANGLE	$\frac{S - Go}{Na - Me} \%$			$\frac{ANS - Me}{Na - Me} \%$		
			-1SD	M 65% $\pm$ 4%	+1SD	-1SD	M 54% $\pm$ 2%	+1SD
20	Laurence U.	132		65				62
21	Yolanda C.	119		63				58
22	Merryn E. 1/66 7/68	120 122			76 78		56	59
23	Leonie M.	124		68				59
24	Mrs. Backhouse	130		66				67
25	Mrs. Nicholson	132		66			54	
26	Mrs. Emmerson	126		69			55	
27	Mrs. Myott	134		64			53	
28	Mr. Barlow	135			77		56	
29	Mrs. Sheppard	130		64			55	
30	Mrs. Ashton (Alan)	135		66				63
31	Mrs. Ulph	132		68				58
32	Mrs. Green	120		69				58
33	Mrs. Masterton	121		65				60
34	Mrs. Ashton (Graham)	122			70		54	
35	Mrs. Mullens	128	60					60

CEPHALOMETRIC EVALUATION

TABLE 8

No.	PATIENT	Y Axis to F.H.			Y Axis to S.N.			SNA			SNB			
		-ISD CL. III	M 60°4' ± 3°4'	+ISD CL. II	-ISD CL. III	M 66° ± 3°	+ISD CL. II	-ISD	M 81° ± 3°	+ISD	ANB	-ISD	M 78° ± 3°	+ISD
1	Peter H.		57				72			85	10		75	
2	Rodney B.			66			86	75			12	63		
3	Debra M.	56					73	75			6	69		
4	David C.			68			73		79		7	72		
5	Graham A.	53				68			79		4		75	
6	Nerida M. 11/65 8/68		61	68		65 65				86 86	5 4		81	82
7	Stephen H.	56				68			81		2		79	
8	Gail B.		57				77	68			1	67		
9	Gail N. 1/66			65		69			80		4		76	
	8/68			66		67			79		2		77	
10	Cheryl M.		64			69				85	7		78	
11	Graham S.	Portion not located				67			80		3		77	
12	Christine D.		61				72		84		5		79	
13	Cheryl G.		60				77		82		2		80	
14	Gregory U.			67			70		80		4		76	
15	Alan A.		56			68			80		1		79	
16	Marion S.*			70*		69*			82*		1		81*	
17	Robert N. 1/66 8/68			65 73			74 75	75	80		6 1	74 74		
18	Lynette U. 2/66 7/88		59	67		64 65			81	85	1 -2			84 83
19	Robyn B.		62			68			81		3		78	

TABLE 8

[illegible]

CEPHALOMETRIC EVALUATION

TABLE 8

No.	PATIENT	FACIAL ANGLE			ANGLE OF CONVEXITY			AB TO FACIAL PLANE		
		-1SD CL.II	M 87° ± 3°	+1SD CL.III	-1SD CL.III	M 0° ± 5°	+1SD CL.II	-1SD CL.III	M 4.1° ± 3°	+1SD CL.II
1	Peter H.		88				+23			-14
2	Rodney B.	83					+27			-17
3	Debra M.		87				+13			-8
4	David C.	77					+13			-8
5	Grahame A.		90				+ 8		-6	
6	Nerida M. 11/65 8/68	81	86			+5	+ 8			-10 -8
7	Stephen H.			93		0			-5	
8	Gail B.		89			0			-2	
9	Gail N. 1/66	82					+ 7			-10
	8/68	80				-2			-4	
10	Cheryl M.	83					+14			-11
11	Graham S.	Porion not located				+4			-6	
12	Christine D.		90				+ 8		-6	
13	Cheryl G.		87			+4			-4.5	
14	Gregory U.	82					+ 6		-4	
15	Alan A.			93		0			-3	
16	Marion S.*			94		0*			-3	
17	Robert N. 1/66 8/68	77	84			0	+11		-3	-12
18	Lynette U. 2/66 7/68	82	89			0 -5		+2	-2	
19	Robyn B.		85			+3			-3	

TABLE 8

[illegible]

DENTAL EVALUATION										TABLE 9				
No.	PATIENT	OCCLUSION CLASS					ARCH FORM*	CROSS BITE	PALATAL CONTOUR	INCISOR RELATIONSHIP		MESIO DISTAL	MUTILATION	CARIES
		NORM	I	II DIV.1	II DIV.2	III				VERTICAL	HORIZONTAL	INCISOR CROWDING		
1	Peter H.			*			N		N	NOT	ERUPTED		NONE	
2	Rodney B.			*						OPEN	×	×	×	
3	Debra M.			*			B		N	0	5 mm.	N	No	G
4	David C.	*					N		N	$\frac{2}{3}$	0	U-S L-C U-S L-N	7 teeth after models	XO soon taken
5	Grahame A.			*			N		N	0	4 mm.		No	
6	Nerida M. 11/65		*				N		N	full in-cisor	0	slight	None	
	8/68													
7	Stephen H. 2/66		*				N		N	$\frac{1}{2}$	2 mm.	L Spacing	Yes Loss of pre-molars	
	7/68													
8.	Gail B 8/65			*			UC	Bilat.		0	4 mm.			
	7/68						LN	Post	H	0	1 mms.	S	Yes	G
9	Gail N. 8/68		*				N	UL 2		$\frac{1}{2}$	0		Yes	
10	Cheryl M.	*					N		N	$\frac{2}{3}$	0		No	
11	Graham S.	*					N		N	$\frac{1}{2}$	3 mm.		U & L L6 lost	
12	Christine D. 5/65						C in Ant.	UR 2 only		5/65 $\frac{1}{3}$		$\frac{1}{1}$ diastema		
	11/65					*	U & L			11/65 0	0			
13	Cheryl G	*					UN LB		N	$\frac{1}{2}$	3 mm.	LS	No	
14	Gregory U.		*				UC LN		H	0	0	C	Yes	
15	Alan A.					*	UN LB	Bilat. Post.	N	0	0	N		
16	Marion S.		*				B Post	Post Cross Bite	F	$\frac{3}{4}$	0	C		

TABLE 9

[illegible]

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