The serum vitamin-B₁₂ concentrations of both patients were very low, but neither suffered from Addisonian pernicious anaemia. Both had been taking a very inadequate diet, and one had recently suffered from

Vitamin-B₁₂ deficiency was not the sole cause of the megaloblastic anaemia in the one patient in whom serial observations were made.

We wish to thank Dr. J. E. Bradley for the 56Co; Dr. E. Lester Smith, F.R.S., of the Research Division of Glaxo Laboratories, for the labelled vitamin B₁₂; Dr. J. O. Terry for permission to investigate Case 1; Dr. G. E. R. Bibbings and Dr. J. W. B. Parsons for much helpful information about the two patients; Miss Barbara Anderson for help with the radioactive measurements, and Mrs. Helen Berriman for the microbiological assays.

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KNOCK-KNEE IN CHILDREN

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To learn more of the natural history of knock-knee over 1,000 examinations were made on unselected normal children from infant welfare clinics and from a school in North-west London. It was considered that a greater understanding of the natural history would simplify the management of children with knock-knee and avoid unnecessary treatment. The methods used were simple, and were applicable in any clinic.

Two groups of children were studied. Those with any defect or disease which might affect their lower limbsfor example, spastics—were excluded.

Material

From Three Infant Welfare Clinics.—Any child who was old enough to walk unaided was seen, and all children were invited to reattend in six months for remeasurement. Studies were made of 451 children aged 1 to 4 years inclusive. Of these, 245 were seen once, 146 on two occasions, and 60 on three occasions, making a total of 717 examinations. Thirty-nine examinations were also made on children aged 5 years and over. The results of two or three examinations on the same child have been used, provided that the child was in a different age group on each occasion. Return visits appear to have been made by a representative sample of the children, as the incidence of knock-knee found at the first examinations is similar to that of the whole series.

Likewise, the proportion of children immunized and receiving vitamin supplements is similar at the first examination and in the complete series.

From an L.C.C. Junior Modern and Infant School.—318 children, aged 5 to 11 years inclusive, were examined. All children in certain classes were seen, provided that their parents had given written permission for examination. These children were not re-examined, and no history was available, as the parents were not present.

History and Examination

In infant welfare clinics, where the child's mother was usually present, the following history was obtained: birth weight; age at which the child first walked unaided; details of diet, including the duration of breast-feeding and whether the child had vitamin supplements; illness as judged by the number of days the child had spent in bed since it started to walk; any habitual sleeping or sitting posture noticed by the mother; whether the mother had ever noticed anything wrong with the child's legs, feet, or back; if she had, details including any treatment received were noted.

In both the infant welfare clinics and the school the following facts were recorded.

Age in Months.

Weight.—Children in school wore vest and pants only, as did the majority of children in infant welfare clinics. If they were weighed naked or in any other clothes the weight was adjusted accordingly. The actual weights were used in calculations on children under 5 years old, but not enough children were seen for this to be satisfactory in the school age groups. For this reason the indices of Sutcliffe and Canham (1950) were used when calculating average heights and weights of children aged 5 years and over. (These indices are corrected for age and sex, and have a standard deviation of 15. The indices range from 65 to 135, with 100 representing the mean. Children in this series are rather heavier, after allowing for weight of vest and pants, and taller than Sutcliffe and Canham's subjects. However, it is reasonable to use these indices to compare different groups within this series.)

Height.—This was measured with the children standing barefoot against a vertical tape or rule. The actual heights were used in calculations on children under 5 years, and the indices of Sutcliffe and Canham for older children.

Knock-knee.—This was measured as the child lay or sat with the length of its legs supported on a couch. The legs were held with the patellae facing vertically upwards, the feet dorsiflexed to a right angle, and the inner surfaces of the knees just touching; the distance between the medial malleoli was then measured. In clinical work the amount of knock-knee recorded is usually less than this, as some pressure is applied to approximate the ankles. Four grades of knock-knee were used: Intermalleolar distance of less than 1 in. (2.5 cm.); 1 in. (2.5 cm.) but less than 2 in. (5 cm.); 2 in. (5 cm.) but less than 3 in. (7.5 cm.); and 3 in. (7.5 cm.) and over.

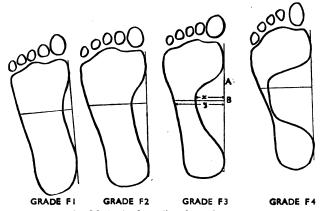


Fig. 1.—Method of grading footprints (see text).

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Postural Deformities of the Feet.—Many children appear to have flat feet. In infants this is normal; the flat appearance, as is well known, is due to a fat pad which obliterates the arch. Some children show a flatness which persists, and sometimes, with or without this pes planus, there is an eversion of the foot—pes valgus. This might be associated with the deformity of the knees and even be a causative or aggravating factor. These abnormalities of the foot are difficult to measure exactly, and the valgus element in particular cannot be accurately assessed. Footprints were taken by smearing the feet with petroleum jelly and then letting the child walk over photographic paper. This gave a measure of the flatness of the arch but did not indicate how much of it was due to eversion of the foot. The footprints were measured as in Fig. 1. A line (A) was drawn along the medial border of the foot and a perpendicular (B) drawn from this line through the highest point of the arch. The ratio of the height of the arch (x) to the width of the foot (y) along this line was used to grade the footprint into one of four groups:

Where, upon measurement, the right and left footprints fell into more than one of the above grades, that grade representing the grosser degree of flatfoot was used.

Valgus Feet.—Eversion of the feet was assessed by watching the child walk and stand. Valgus feet were recorded as such only if the valgus was pronounced enough to be visible when the child was observed from behind. The grades used were "moderate" and "severe." Minor amounts of valgus were ignored.

Results

The incidence of knock-knee at different ages is shown in Fig. 2. Children under 5 years of age were placed in half-yearly age groups. Schoolchildren were divided into three age groups: 5 and 6 years; 7, 8, and 9 years; and those of 10 and 11 years. The incidence of knock-knee increases until 3 to 3½ years of age; it then declines. Between 3 and 3½ years of age only 26% of children had less than 1 in. (2.5 cm.) of knock-knee, 52% had between 1 and 2 in. (2.5 and 5 cm.), while 22% had a knock-knee of 2 in. (5 cm.)

There was no sex difference in the incidence of knock-knee in children under 5 years of age. In schoolchildren, although the incidence of knock-knee of 3 in. (7.5 cm.) or more was the same in both sexes, lesser amounts of knock-knee were more common amongst the girls.

Where the knock-knee angle remains constant the intermalleolar distance must increase as the leg grows. The length of the tibia is about 7 in. (17.5 cm.) at 3 years and

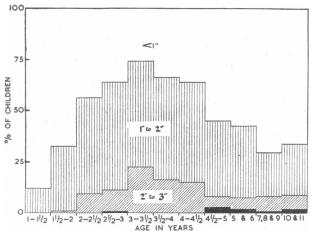


Fig. 2.—Incidence of knock-knee at different ages. Black areas indicate knock-knee of over 3 in. (7.5 cm.).

about 10 in. (25 cm.) at 7 years. Thus a knock-knee of 2 in. (5 cm.) at 3 years will have become 3 in. (7.5 cm.) at 7 years if the angle remains constant (Fig. 3). Consequently, if the angle between the legs is used to measure knock-knee

instead of the intermalleolar distance, the incidence of knockknee at different ages will show a much more dramatic peak at 3 to 4 years. The curves in Fig. 4 were obtained by using the average length of the tibia at different ages to convert the intermalleolar distances into degrees of genu valgum. At 3 years of age 22% of children were found to

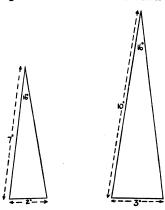


Fig. 3.—Relationship between intermalleolar distance and leg length. Left at 3 years. Right, at 7 years.

have a knock-knee of 2 in. (5 cm.) or more (which corresponds to about 16 degrees), but by 7 years of age only 1 or 2% of children had knock-knee of 3 in. (7.5 cm.) or 16 degrees. Lesser amounts of knock-knee show a similar trend.

There were 7 girls and 21 boys with bow-legs. Except in children under 2 years old, the distance between the knees was so small—usually less than $\frac{1}{2}$ in. (1.3 cm.), and always less than 1 in. (2.5 cm.)—that it is not likely to be important clinically.

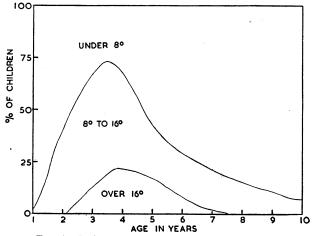


Fig. 4.—Incidence of knock-knee according to age.

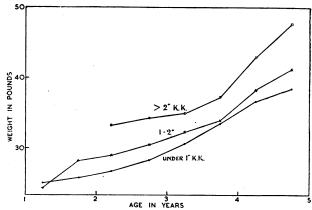


Fig. 5.—Relationship between weight and knock-knee in girls.

TABLE I.—Number of Children in Each Age Group with Knock-knee: Grade and Mean Heights and Weights

Age in Months	Knock- knee (in.)	Boys					Girls				
		No. in Group	Mean Age	Mean Weight (lb.)	Standard Deviation of Weight	Mean Height (in.)	No. in Group	Mean Age	Mean Weight (lb.)	Standard Deviation of Weight	Mean Height (in.)
12–17	<1 1-2 2-3	20 5 0	14·5 14·6	25·138 26·825		30·825 31·1	22 2	15·5 17	25·134* 24·313	3-135	30·714 31
18–23	<1 1-2 2-3	30 13 0	20·1 21·2	27·28* 27·721	3·005 2·587	32·714 33·192	32 19 1	20·7 21·2 23	25·994† 27·932 25·875	2·446 2·946	32·452 33·197 32·5
24–29	<1 1-2 2-3	29 31 5	26·3 26·6 26·4	28·987* 30·752* 32·71	2·904 3·246 2·12	34·733 34·984 35·5	18 21 5	26·3 26·4 27·4	26·563 29·065 33·35	2·789 3·27 1·755	33·972 34·488 35·95
30–35	<1 1-2 2-3 3+	24 36 7 1	32·2 32·6 32·9 32	31·039 32·21 35·071 36·5	2·982 3·378 2·432	36·062 36·618 37·25 37·25	17 25 5 0	32·8 32·8 32·4	28·268 30·479 34·3	3·116 2·378 3·903	35·5 36·11 36·9
36–41	<1 1-2 2-3	8 23 12	37·8 38·4 38·6	33·875* 34·179 36·613*	2·902 3·111 4·304	38·812 38·043 38·136*	17 27 9	38·3 37·9 38	30·672* 32·255 35·194	3·115 2·766 4·535	37·235 37·193 38·306
42-47	< 1 1-2 2-3	15 30 6	43·7 44·6 44·5	34·955* 36·597* 39·468	3·102 3·984 3·136	39·516 39·4 39·875	17 18 10	44·2 44·3 45·4	33·246 33·774 37·35	3 644 2·522 3·739	38·766 38·556 39·386
48–53	<1 1-2 2-3	15 20 7	50·2 50·6 49·9	36·375 38·878 42·268	3.638 5.088 2.662	40·316 40·8 41·536	11 15 5	49·2 50·1 50·2	36·67 38·229 42·95	3·008 4·572 6·123	40·5 40·116 41·5
54-59	<1 1-2 2-3 3+	19 12 3 1	56·3 57·4 55·7 59	40·053 41·125 43·021 54	4·510 4·577 5·710	42·539 42·354 42·25 45	14 16 2 1	56 55·6 56 57	38·529 41·352 47·75 62·5	3·309 3·739	41·696 42·062 43·125 45

^{*} In each of these groups one observation was not obtained. † In this group two observations were not obtained. Five girls and nine boys with bow-legs are not included.

TABLE II.—Number of Children Aged 5-11 Years in Different Knock-knee Grades, with Mean Indices of Height and Weight

			Boys		Girls			
		No. of Children	Mean Weight Index	Mean Height Index	No. of Children	Mean Weight Index	Mean Height Index	
Bow-legs Grade of	knock-	11	105	115-6	2	83.5	100-5	
knee: <1 in. 1-2 ,, 2-3 ,, 3-4 ,,		108 41 5 4	102·5 113·4 124·4 135	107·8 114·4 125·2 116·3	108 54 21 3	103·7 114 126·8* 135	106·9 111·3 115·3 124·4	

^{*} One observation not obtained.

Relationship Between Knock-knee and Body Weight.—The weight curves of the girls are related to different amounts of knock-knee in Fig. 5. The differences between the weights on the upper and lower curves were statistically significant. The mean weight of children with knock-knee is greater than the mean weight of children without knock-knee (Tables I and II). This was true in both sexes and for all ages, except in the youngest group of girls, where

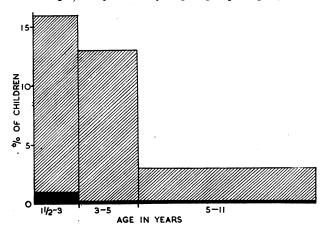


Fig. 6.—Incidence of valgus ankles. Cross-hatching indicates moderate valgus; black areas indicate severe valgus.

there are only two observations in the 1-2 in. (2.5-5 cm.) knock-knee grade.

Relationship Between Knock-knee and Height.—There is a tendency for children with more than 2 in. (5 cm.) of knock-knee to be taller than those of the same age with less than 1 in. (2.5 cm.) of knock-knee. However, amongst a group of heavy children those with knock-knee are not taller than the rest. It is known that heavy children are above average in height, and there is probably no other relationship between height and amount of knock-knee than that due to the increased weight.

Valgus Feet.—The incidence of valgus feet was alike in each knock-knee grade, and no sex difference was found. Valgus feet became less frequent with increasing age (Fig. 6).

Flatfoot.—The footprints showed that the incidence of flatfoot decreased as the age increased. Among children under 18 months, 97% were graded as F1. By 10 or 11 years only 4% of children remained in this grade (Fig. 7). No association was found between knock-knee and flatfoot. The incidence of flatfoot was similar in each knock-knee grade. No constant relationship was found between body weight and flatfoot.

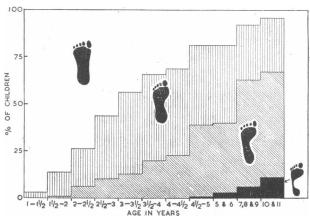


Fig. 7.—Incidence of flatfoot in different age groups.

When comparing the birth weights of children in different knock-knee grades it was found that the mean birth weight was slightly higher in those with increased amounts of knock-knee. There does not seem to be any association between the age at which the child started to walk and the development of knock-knee. No relationship was found between the duration of breast-feeding and the development of knock-knee. The percentage of children taking vitamin supplements was similar for each grade of knock-knee. The number of days spent in bed through illness showed no relationship to the development of knock-knee.

Mothers were usually extremely vague about habitual sleeping or sitting postures. Many children sleep in a prone-kneeling position when young, and this did not seem to be especially common in those children who had knock-knees. Other information about posture was too unreliable or too scanty to be useful.

Roughly 1% of children seen in these infant welfare clinics had been advised to wear wedged shoes at some time. About 4% had been taught foot and leg exercises (this figure is high because a physiotherapist was attached to one of the clinics). An additional 2% had attended hospital solely for observation. Only one child was seen who had worn night splints for knock-knees. He was aged 59 months and had 4 in. (10 cm.) of knock-knee. In the past he had worn night splints for six months and had been given exercises at hospital for a similar period. Neither of these treatments had been effective, and he was still under hospital observation.

Conclusions

Knock-knee is commonest among children aged 3 to $3\frac{1}{2}$ years. At this age 22% of children were found to have a knock-knee of 2 in. (5 cm.) or more. Only 1 to 2% of children aged 7 years and over have an equivalent amount of knock-knee.

The mean weight of children with knock-knee is greater than the mean weight of comparable children without knock-knee.

The development of knock-knee is not associated with any of the following factors: valgus feet; flatfoot; age at which the child started to walk; duration of breast feeding; quantity of vitamin supplements taken during the first 18 months; illness as judged by the number of days spent in bed.

Knock-knee is very common among toddlers, but fortunately it usually improves without treatment. Apart from operative procedures, no effective treatment for knock-knee is known.

Knock-knee in children under 7 years of age can probably be safely ignored unless it is excessive or unless an underlying cause, such as epiphysial damage from a fracture or renal rickets, is present.

An underlying cause for knock-knee should be sought if: (1) the knock-knee is excessive—over $3\frac{1}{2}$ in. (9 cm.); (2) the knock-knee is of unequal amount in the two legs; (3) the child is short for its age: this might rarely be due to an epiphysial dysplasia or to an endocrine disorder; (4) there is a family history of severe knock-knee or other bony deformity; this could be due to a metabolic disorder such as Fanconi's syndrome.

Toddlers' knock-knee can be allowed to join the growing group of developmental deviations which seldom need treatment, such as the infant's tight foreskin (Gairdner, 1949) and the baby's umbilical hernia (Woods, 1953).

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ENCEPHALOPATHY DURING SALICYLATE TREATMENT OF ACUTE RHEUMATISM

BY

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Salicylates are still widely used in the treatment of acute rheumatism, often in toxic doses. Some patients have an idiosyncrasy to salicylates and develop anaphylactic or allergic symptoms which are sometimes fatal. Other well-known toxic effects (Gross and Greenberg, 1948; Goodman and Gilman, 1956) include "salicylism" (tinnitus and deafness, nausea and vomiting, sweating and vasodilatation, etc.), haemorrhages due to hypoprothrombinaemia, capillary damage, or thrombocytopenia (Rappoport et al., 1945; Troll and Menten, 1945), and respiratory alkalosis associated with low pCO₂, high pH, and later an elevated bicarbonate level in the plasma (Guest et al., 1945; Rapoport and Guest, 1945; Boyle et al., 1947; Farber et al., 1949; Reid et al., 1950; Singer, 1954).

Salicylates may also produce cerebral excitation (Gross and Greenberg, 1948; Goodman and Gilman, 1956), with delirium, hallucinations, disorientation, restlessness, excitability, and irritability; later there may be depression leading to coma with respiratory failure and cardiovascular collapse, sometimes with terminal asphyxial convulsions. Ryder et al. (1945) describe a fatal case with symptoms partly attributable to a severe respiratory alkalosis, in which necropsy revealed a toxic encephalopathy with nerve-cell degeneration and haemorrhages.

The case reported here was treated with orthodox doses of sodium salicylate and developed an encephalopathy, from which the patient nearly died.

Case Report

A labourer aged 20 was admitted to hospital on February 25, 1954, under Dr. Kenneth Harris. He had had scarlet fever and rheumatic fever at the age of 12. He had not been feeling well for a fortnight, and for the past week had had pain, swelling, and stiffness of both knees and ankles. He was febrile (temperature 101.4° F.: 38.6° C.), and his pulse was dicrotic (100 a minute). He was flushed and looked ill. Both knees and ankles were swollen and