While, therefore, the outlook for the diabetic mother has enormously improved, there has been no corresponding improvement regarding the influence of diabetes upon the pregnancy, for the foetal mortality still remains tragically high. Abortion is very common in diabetics, and intra-uterine death in the later weeks adds to the toll; while not infrequently its undue size causes the death during delivery of many a foetus which has survived until term, and yet others die shortly after birth. In Williams's pre-insulin series of cases the foetal mortality, including abortions, was 41 per cent. In 136 pregnancies collected by Skipper the foetal mortality was 45 per cent., and in the thirty-seven pregnancies which he himself observed it was 40.5 per cent. In our twenty pregnancies in the Royal Maternity Hospital in Edinburgh the foetal mortality was 35 per cent.

Priscilla White, writing from Joslin's special clinic in Boston, gives an interesting series of figures. In cases in the pre-insulin era the stillbirth and abortion rate was 44 per cent. After the introduction of insulin there was a reduction in the foetal mortality to 34 per cent., while in cases under the direct and careful observation of the clinic it amounted only to 23 per cent. "Stillbirths and the macerated foetus of the giant type," she writes, "are nearly as characteristic of diabetic pregnancies which are allowed to come to term as they were in the pre-insulin era." Her solution of the problem is the delivery by Caesarean section of "the fully developed but chronologically premature infant." Whether we agree with that view or not, her figures, and those others that I have quoted, are an eloquent plea for the careful ante-natal supervision of such patients by a physician well versed in the management of diabetes, and a clear proof that all such cases must be treated on strictly individual lines and not by any mere routine. For treatment to be fully successful it seems to me that co-operation between the obstetrician and the physician is a *sine qua non*.

Conclusion

I have chosen these three or four diseases to illustrate my thesis that their association with pregnancy can be understood only in the light of the physiological strain of pregnancy. Other examples might equally well have been chosen. I was tempted, for instance, to refer to the temporary benefit in phthisis brought about by the physiological ascent of the diaphragm, compressing the lung and closing up cavities; and to the disastrous relapses which follow the abrupt and ruthless removal of this factor when the uterine tumour suddenly subsides after labour. I was tempted also to refer to kidney diseases, in which the physiological strain is so subtle and so uniform that, as Gibberd has succinctly expressed it, "pregnancy is the best test of kidney function." But these are large subjects, and to have indulged myself would have been to put a wholly unwarrantable tax upon the kindly patience with which you have listened to me.

If I have succeeded in interesting you in my main thesis you will find additional interest in working out its application in these and in other conditions at your leisure.

The London hospitals have received during the past year a present of over 5,000 gramophone records by the courtesy of the B.B.C. and the record manufacturing companies. These records, which have been used for broadcast purposes, are delivered to the hospitals free by the Gramophone Company in accordance with a schedule drawn up by King Edward's Hospital Fund for London in collaboration with the B.B.C.

CALCIUM AND PHOSPHORUS DEFICIENCIES IN A POOR HUMAN DIETARY

BY

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(WITH SPECIAL PLATE)

Dietary surveys and experiments on the feeding of milk and other supplements to children and adults suggest that the diets of various classes of the population both in this and in other countries may be deficient for the maintenance of health. These observations in groups of human beings have led to experiments in which rats were fed on diets similar to those in common use among people whose nutritional state was being studied. One of the best-known of these experiments is that of McCarrison (1926–7), in which a striking parallelism was shown between the health and physique of rats and the health and physique of different tribes in India whose diets were fed to different groups of rats.

In an experiment of this type Orr, Thomson, and Garry (1935) maintained a large colony of rats for two and a quarter years on a diet which approximated the average diet eaten by a working-class community in Scotland as ascertained by dietary survey (Davidson *et al.*, 1933). Another colony received the survey diet with the addition of green food and unlimited milk. Four generations of animals were reared. The rats on the human dietary supplemented with green food and milk were quite normal, and in all respects were equally as healthy as rats kept on the Rowett Institute stock diet (Thomson, 1936). On the other hand, with a similar environment and heredity, the animals fed on the survey diet alone showed a slightly impaired reproductive capacity, a considerably increased death rate, a retarded rate of growth, a lowered haemoglobin content of the blood, and a clinically poorer condition. It was thus shown that the addition of green food and milk converted a deficient human diet into one that was adequate, though Orr and his co-workers were unable to state which factor or factors in this diet were responsible for the benefits obtained.

An analysis of the diet showed that it was very deficient in calcium and phosphorus, and the addition of green food and milk greatly increased the content of these elements. The hypothesis that this deficiency might be a major factor in the difference in health and physique of the two groups of rats was strengthened by the fact that numerous experiments with large animals have demonstrated that calcium and phosphorus lack is a common cause of deficiency disease, retardation of growth, and low viability in young at birth (Osborne and Mendel, 1918; Elliot, Crichton, and Orr, 1922; Elliot and Crichton, 1926). Orr (1930) has reviewed the influence of mineral salts in stock feeding, showing the benefits of adding calcium and phosphorus in various forms to the rations of pigs, cattle, and poultry. Similar deficiencies may occur in human diets. A survey made of 607 diets in Scotland in 1926-7 (Orr and Clark, 1930) showed that as family income fell the diet became poorer in calcium. In 205 of the families the intake was less than 0.3 gramme per head per day. In a feeding experiment with the children of these families it

was found that a considerable increase in growth and a definite improvement in health followed the supplementary feeding of either whole milk or separated milk in quantities of from 3/4 pint for younger children to 1¼ pints for older children. As the separated milk, without the fat or the fat-soluble vitamins contained in the fat, had practically the same result as the whole milk, it was thought that the great increase in the calcium and phosphorus intake due to the milk might be an important, and possibly the most important, factor in producing the improvement in growth and health, and that the remarkable results obtained earlier by Corry Mann (1926) in children from the increased consumption of milk might be due largely to the same factors.

In view of the obvious importance of calcium and phosphorus it was decided that these elements should be the first to be tested in the experiments now being developed at the Rowett Research Institute in the investigation of specific dietary deficiencies.

The Experiments

The Diets.—Three groups of rats were fed on different diets. Group 1 was given the survey diet described by Orr *et al.* (Diet 1), whilst Group 2 received the survey diet in which were incorporated the same amounts of milk and green food as were used in the earlier experiment (Diet 2). Diet 3, fed to Group 3 rats, was constructed by the addition of salts of calcium and phosphorus to Diet 1 in such amounts that its calcium and phosphorus contents were the same as those of Diet 2.

Analyses for calcium and phosphorus were carried out daily for a fortnight on samples of Diets 1 and 2, excluding the Sunday diets, which for each group consisted of bread and water only. Average figures for the whole series of analyses are given in Table I.

TABLE I.—*Analysis of Diets 1 and 2 (Averages for Twelve Samples of Each Diet)*

	% Ca	% P	Ca/P
Diet 1	0.121	0.249	0.50
Diet 2	0.284	0.338	0.84
Difference	0.163	0.089	

Diet 3 was constructed by adding the following amounts of salts to Diet 1 per 100 grammes wet weight: calcium lactate (B.P.), 0.324 gramme; Na_2HPO_4 (analytical reagent), 0.105 gramme.

The accuracy of this addition and the efficacy of mixing the added salts with the rest of the diet were checked by the analysis of samples of Diets 1 and 3 taken on the same day. The results are given in Table II, the figures for the recovery of the added calcium and phosphorus being in good agreement with the amounts actually added.

TABLE II.—*Analysis of Diets 1 and 3*

	% Ca	% P
Diet 1	0.099	0.253
Diet 3	0.278	0.340
Difference	0.179	0.087

The animals used were Lister Institute hooded rats, bred at the Rowett Institute for several generations before the start of the experiment. They were bred from stock, the experiment beginning at weaning. Three groups of 21-day-old rats, each containing twenty-four males and twenty-four females, were used. In each group twelve males and twelve females were kept for breeding, and four males and four females were killed for examination at 40, at 70, and at 100 days of age. In almost every case each male rat in Group 1 had a female litter mate in the same group; in addition these two rats had a male and a female litter mate in both Groups 2 and 3. It was thus possible to compare litter mates of the same age and both sexes in different groups.

The management of the animals was sufficiently like that described by Orr *et al.* to merit but little discussion. The amount of food fed was regulated so that a small quantity was left every day, but the actual food consumption was not measured. Tap-water was given *ad lib.* The rats were weighed at the beginning of the experiment and thereafter twice weekly. The animals killed for examination were radiographed prior to dissection of the upper and lower incisors and the femora, tibiae, and fibulae of both legs. The upper incisors and the bones of the right leg were used for histological examination, while the lower incisors and the bones of the left leg were reserved for chemical analysis. The remaining rats of each group were used for breeding, standard methods being employed.

The experiment is being carried out over three generations, the results reported in this paper dealing almost entirely with the first generation. Data relating to all the generations will be published in full at a later date.

Results

(*a*) *The Rate of Growth.*—The accompanying chart shows the rate of growth of the male rats in the first generation. It will be seen that the growth rates of

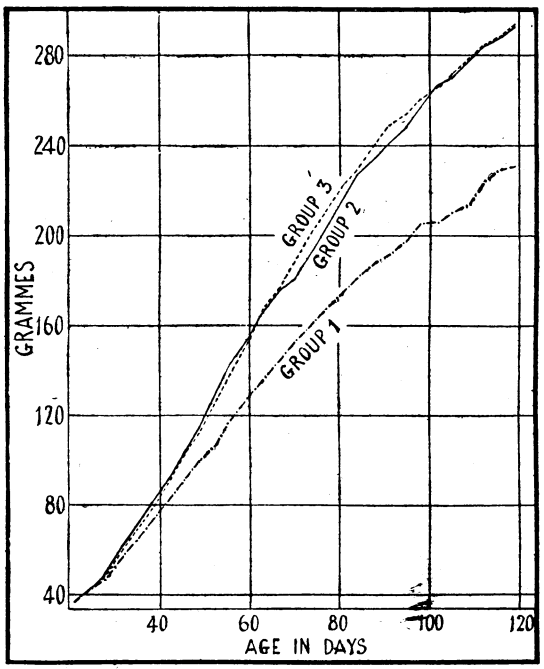

Chart showing the average growth curve of the first generation males, from 21 to 119 days old.

Groups 2 and 3 are identical, and are much superior to that of Group 1. Exactly similar results were obtained with the females, though, as is always the case, the weights were lower than those of the males. The growth curves of the second generation have also been obtained, and it has been found that in this case the Group 3 rats do not grow as fast as those in Group 2, but are still

much better than those in Group 1. The general condition of the rats on Diet 1 was poor; these rats had not the sleek appearance of their litter mates in Groups 2 and 3, who were always in good condition.

(*b*) *X-Ray Photographs.*—In all cases the films showed a striking difference in the degree of calcification of the rats in Groups 1 and 2; very little difference could be seen between Groups 2 and 3. Figs. 1, 2, and 3 (Special Plate), reproducing *x*-ray photographs of litter mates in the three groups, demonstrate this fact.

(*c*) *Histological Examination of the Teeth.*—This examination was used to demonstrate the relative values of the three diets, in the same way as was done by Mullick and Irving (1937) in assaying the nutritional value of Indian diets. Schour and his co-worker (Schour and Ham, 1934) and many others have pointed out that the width of predentin in the rodent incisor tooth offers a very delicate test for the degree of calcification, being wider when calcification is impaired. Longitudinal sections of decalcified upper incisor teeth were cut, stained with haematoxylin and eosin, and the predentin width in the apical part of the tooth measured. The normal value for this width is from 16 to 20 μ. The average results obtained from the first generation are given in Table III.

TABLE III.—*Width of Predentin (μ) in Longitudinal Section in Upper Incisors (Average Results from the First Generation)*

Age in Days	Sex	Groups		
		1	2	3
40	M	29	25	22
	F	31	20	21
70	M	41	23	19
	F	34	22	19
100	M	38	20	21
	F	25	20	21

These results show quite clearly that calcification is deficient in the rats of Group 1 but is normal in those of Groups 2 and 3. In addition it is possible that calcification is most impaired in Group 1 at 70 days, improving after this time. Photomicrographs of teeth from litter mates are reproduced in Figs. 4, 5, and 6. The section of the tooth from the Group 1 rat shows vascular inclusions in the predentin; these were quite commonly found in teeth from Group 1 rats at 70 and 100 days of age, but were always absent in the teeth of rats in the other two groups. The histological examination of the bones failed to reveal any differences which could be compared quantitatively. Results from this examination have not been included in this paper.

(*d*) *Chemical Analyses.*—These are limited to the ash contents of the femur, tibia, and fibula combined, and of the lower incisors. The results are given in Table IV. The percentage of ash in the bones of Group 1 rats is in every case much lower than the corresponding figures for the animals in Groups 2 and 3. The differences between Groups 2 and 3 are not significant. The lowered calcification of the bones of Group 1 rats and the similarity in the calcification of Group 2 and Group 3 animals are more truly expressed when the ash contents (in absolute amounts) of the bones of Groups 2 and 3 are stated as percentages of those of the Group 1 rats. Despite this similarity it cannot, however, be concluded that calcium and phosphorus in inorganic form are equally as available as those elements in milk and green food, since there are no figures for the total calcium and phosphorus contents of the animals. The relative availability can only be decided by balance experiments.

TABLE IV.—*Weight and Composition of Dry Extracted Bones and Teeth (Average of Four Rats)*

			BONES				TEETH			
Age	Sex	Group	Wt. of Bone	Wt. of Bone Ash	Ash expressed as % Group 1	Ash % of Bone	Wt. of Tooth	Wt. of Tooth Ash	Ash expressed as % of Group 1	Ash % of Tooth
days			gramme	gramme			gramme	gramme		
40	M	1	0.1484	0.0532	100	36.06	0.0510	0.0362	100	70.88
		2	0.2005	0.0860	163	42.94	0.0529	0.0389	107	72.70
		3	0.1953	0.0832	157	43.60	0.0546	0.0398	110	73.09
	F	1	0.1463	0.0567	100	38.58	0.0504	0.0366	100	72.63
		2	0.1869	0.0836	147	44.79	0.0534	0.0393	107	73.64
		3	0.1528	0.0705	124	43.82	0.0519	0.0384	105	74.01
70	M	1	0.2924	0.1317	100	44.88	0.0856	0.0657	100	77.16
		2	0.4392	0.2458	187	55.56	0.1027	0.0790	120	76.94
		3	0.4086	0.2292	174	56.10	0.1000	0.0783	119	78.40
	F	1	0.2232	0.1054	100	46.50	0.0766	0.0596	100	77.53
		2	0.3438	0.1919	182	56.03	0.0910	0.0723	121	79.50
		3	0.3481	0.2034	193	58.42	0.0927	0.0749	125	78.98
100	M	1	0.4075	0.2122	100	51.78	0.1164	0.0878	100	75.44
		2	0.6002	0.3642	172	60.41	0.1362	0.1061	121	77.93
		3	0.6603	0.4142	194	62.70	0.1459	0.1142	130	78.20
	F	1	0.2769	0.1442	100	52.06	0.1043	0.0790	100	75.77
		2	0.4653	0.2895	202	61.88	0.1308	0.1025	130	78.63
		3	0.4897	0.3075	213	62.75	0.1302	0.1020	129	78.65

The tooth-ash figures show much slighter differences between the three groups. This result is in marked contrast to the histological findings, which follow the bone-ash figures closely. This lack of correspondence between the histological and chemical data with teeth has often been noted by us and by other workers, and shows that the histological examination is a much more sensitive test of normal tooth calcification than is chemical analysis.

(*e*) *The Reproductive Performance of the Rats of the First Generation.*—This is shown in Table V.

The figures show that the rats from Group 1 mated less readily, producing smaller litters with a low weaning weight; the reproductive performances of rats from Groups 2 and 3 were considerably better.

TABLE V.—*Reproductive Performance of First Generation Rats*

	Group		
	1	2	3
Average time between introduction of male and birth of litter (days)	48	34	26
Average number born per litter..	8.7	9.7	10.0
Average weight at birth (grammes)	5.30	5.36	5.48
Average weight at weaning (21 days) (grammes)	24.3	32.0	29.3

Discussion

The results quoted show clearly that, using rats *bred from stock*, the improvement in a poor human diet induced by milk and green food supplements can be largely reproduced by the addition of equivalent amounts of calcium and phosphorus salts. This result is in agreement with the work of Sherman and Campbell (1935), who found that the improvement in the nutritional quality of a diet caused by adding dried milk was also obtained by using an equivalent amount of $CaCO_3$. In a recent paper Coward *et al.* (1938) have shown that the addition of calcium and phosphorus salts to a poor human diet fed to rats increased the ash content of the bones. These results are of great interest in confirming our findings, but it is unfortunate that the diets chosen do not approximate

more closely to those actually consumed by man as shown by dietary surveys. Further, we cannot agree, for the reasons given above, that these authors are justified in stating that the calcium in milk is no more available to the animal than is the calcium in inorganic salts. This can only be decided by balance experiments; and indeed the literature on this subject states quite clearly that milk calcium is the more readily available (Givens and Mendel, 1917; McClugage and Mendel, 1918).

Conclusions

It has previously been shown that the nutritional value of a poor human dietary can be greatly improved by the addition of milk and green food supplements. The experiments here reported demonstrate that in rats *bred from stock* this improvement is due largely to the calcium and phosphorus contained in the supplements. This conclusion is of particular interest at the present time, when much stress is being laid on mineral metabolism, and it is being realized that a deficiency of calcium in particular is likely to occur in human diets. An increased consumption of milk, as now widely practised in America, is the most efficient means of ensuring an adequacy in this respect.

We wish to express our indebtedness to Sir John Orr, F.R.S., for his interest and criticism.

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L. Löfgen (*Finska LäkSällsk. Handl.*, December, 1937, p. 937) has searched for a patent foramen ovale among the 785 bodies examined post mortem at the Medico-Legal Institute in Helsingfors during 1935, 1936, and 1937. No child under 10 was included in this study, and there were only 170 women. In as many as 120 cases (15.3 per cent.) a patent foramen ovale was found. The smallest only just admitted a fine sound, the largest was over 1 cm. in diameter. In most cases the diameter was from 2 to 5 mm. Comparing his findings with those of other observers the author notes how widely they have differed, partly, no doubt, because of the differences in the ages of the persons examined. Those—and they are in the majority—who have included children of all ages in their studies must necessarily find a comparatively high proportion of cases, for the anatomical closure of a patent foramen ovale may occur long after birth. A patent foramen does not seem to influence growth, for the average height of the adults examined by the author was normal, and he is of the opinion that a patent foramen gives rise to no anatomical changes such as hypertrophy or dilatation of the heart. With regard to the diagnosis during life, he considers this impossible as the condition so seldom gives rise to clinical manifestations when unaccompanied by other heart lesions. The author discusses briefly the association of a patent foramen with paradoxical or crossed embolism.

FRACTURE OF THE NECK OF THE FEMUR

BY

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(WITH SPECIAL PLATE)

The treatment of fractures of the neck of the femur by the insertion of the Smith-Petersen nail is now so firmly established that attention is focused more on refinements of the technique of insertion than on comparisons with other methods. As Hey Groves has said, the Smith-Petersen nail has completely dominated the situation. There are certainly several other fractures which have more pressing claims to Kellogg Speed's title of "the unsolved fracture."

A Simplification of the Smith-Petersen Method

A year ago I published an account of a method of inserting the nail. It was not claimed that this was exactly original, but I suggested that it was probably the most simple procedure yet recorded. I have since further simplified this considerably, and I now feel that anyone with a moderate degree of operating skill—equivalent to that possessed by any competent house-surgeon—can place a Smith-Petersen nail correctly at the first attempt by this method, which has the additional advantage that it demands a minimum of team-work and instruments. It does not take long: the average duration of the operation in each of the last dozen cases has been slightly more than half an hour, and this comprises the total time spent by the patient in the theatre.

TECHNIQUE

The first step is to attach the patient's feet to the foot-pieces of an orthopaedic table by plaster-of-Paris. Reduction is performed by the Whitman manœuvre; other variations, such as those of Tavernier, Leadbetter, etc., are reserved for difficult fractures. Traction is exerted by hand only: it is difficult to assess the amount of traction which occurs when a screw-axis is used. When the necessary amount has been obtained by hand it is secured by one turn of the screw. The skin having been protected with sterile towels, four Michel clips are applied to the skin over the fracture. The first of these is placed over the middle point of a line joining the symphysis pubis and anterior superior iliac spine. The second is situated half an inch medial to this, on the line joining it and the opposite anterior superior iliac spine. The third one is placed anterior to the lateral margin of the great trochanter, approximately one and a half inches from its superior margin. The fourth is put in position midway between the first and third. A calibrated guide is then introduced directly anterior to the neck of the femur along the line of these clips until it abuts against either the head of the femur or the acetabulum. A fifth Michel clip is applied one and a half inches posterior to the point of entry of the guide.

Antero-posterior and lateral skiagrams are now taken (Plate, Figs. 1 and 2). The antero-posterior direction is ascertained from either the position of the guide or that of the clips, and the lateral direction from the position of the guide. The point of entry of the guide in the bone is determined by taking a point somewhere between the guide and the fifth Michel clip. In the last twenty cases more than 75 per cent. have been parallel to the guide or deviating only very slightly. The calibrations of the guide are counted and 0.5 cm. subtracted to allow for the fact that the guide is in front of the neck and therefore nearer the *x*-ray tube; it may also be necessary to allow for impaction. A half-inch incision is now made between the point of entry of the guide and the posterior Michel clip. The cortical bone is drilled with a quarter-inch

WILLIAM E. GAUNT, JAMES T. IRVING, AND WILLIAM THOMSON: CALCIUM AND PHOSPHORUS DEFICIENCIES IN A POOR HUMAN DIETARY

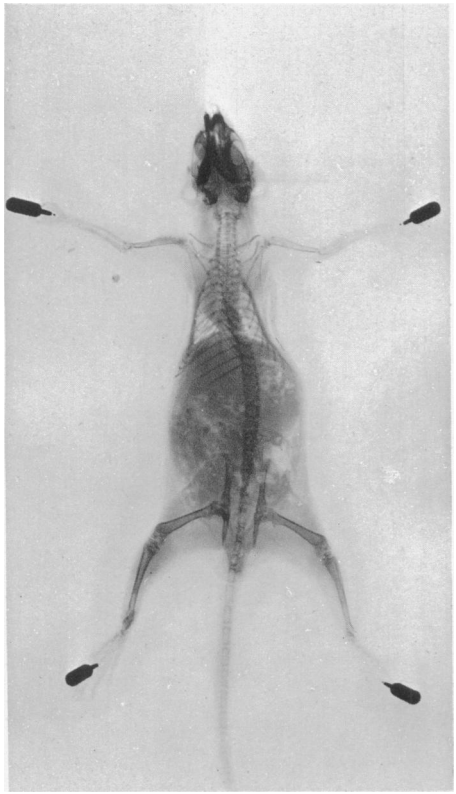

FIG. 1, Group 1.

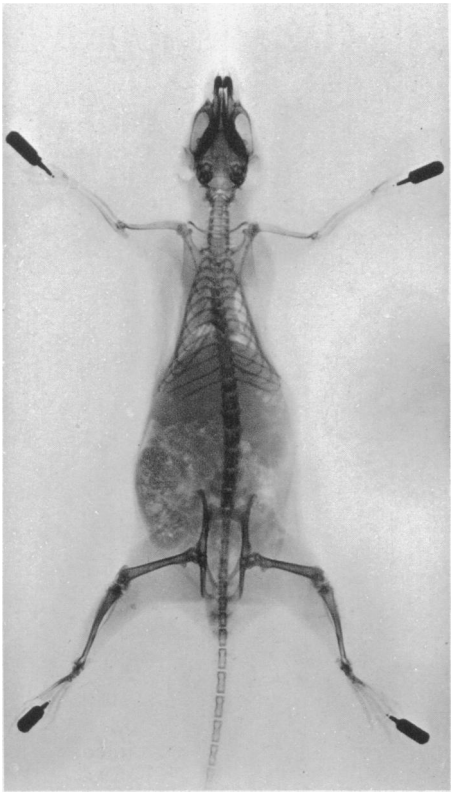

FIG. 2, Group 2.

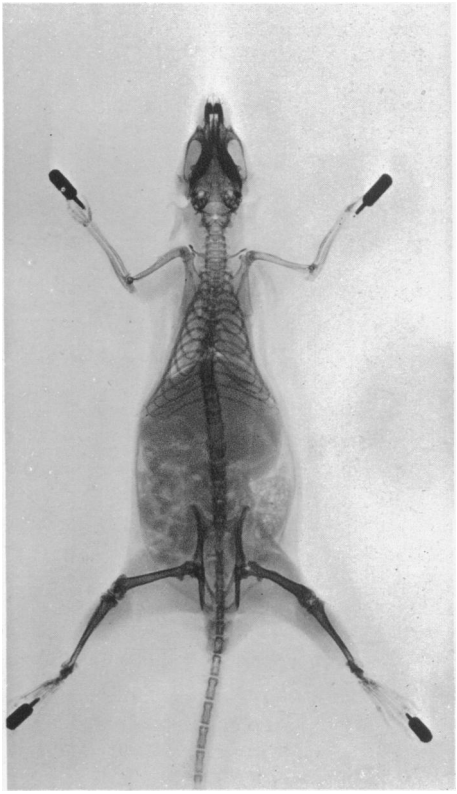

FIG. 3, Group 3.

Seventy-day female litter mates (first generation). Note poor calcification in Group 1, good calcification in Groups 2 and 3.

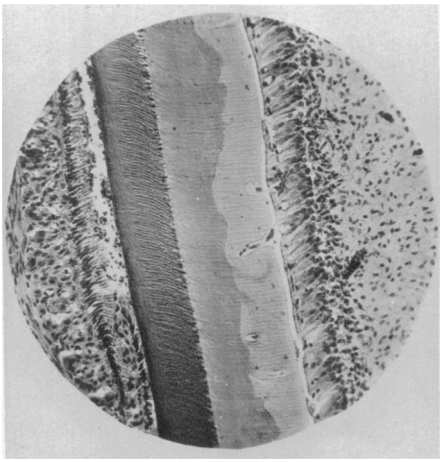

FIG. 4, Group 1.—Tooth ash 77·15 per cent.; bone ash 44·62 per cent.

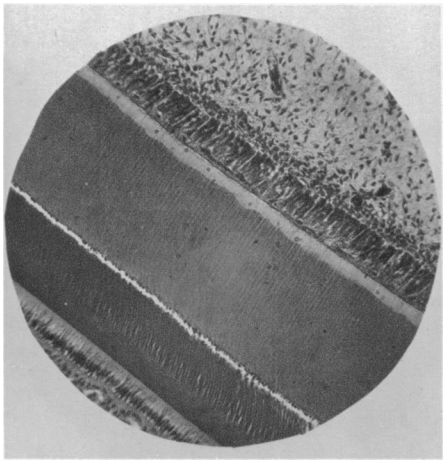

FIG. 5, Group 2.—Tooth ash 78·29 per cent.; bone ash 56·12 per cent.

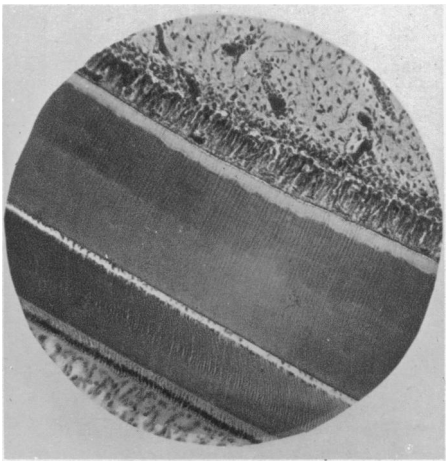

FIG. 6, Group 3.—Tooth ash 77·38 per cent.; bone ash 56·89 per cent.

Longitudinal sections of the apical region of the upper incisor teeth of seventy-day male litter mates (× 100). Note that the predentin is wide in Group 1, narrow in Groups 2 and 3 (17 μ); there are vascular inclusions and an irregular calcification line in Group 1, no inclusions and a regular calcification line in Groups 2 and 3.