Brit. J. Nutr. (1961), **15**, 35, *with 4 plates*

Nutrition of the cat

4.* Calcium and iodine deficiency on a meat diet

By PATRICIA P. SCOTT and J. P. GREAVES

Department of Physiology, Royal Free Hospital School of Medicine, London, W.C. 1

and M. G. SCOTT

Histology Division, Royal Veterinary College, London, N.W. 1

(*Received* 5 *April* 1960—*Revised* 8 *August* 1960)

From time to time during the past century reference has been made to the effects of meat diets on various animal species. The earliest papers refer to lions maintained on carcass meat in the collection of the Zoological Society of London. Crisp (1864) observed enlarged thyroids in lion cubs born at the zoo, and Bland Sutton (1888) described skeletal changes referred to as 'rickets' in cubs and young lions. Of an 8-week-old cub Bland Sutton wrote: 'instead of playing with its companions it preferred to remain quiet...; when attempting to walk it advanced a few paces, then staggered... the hindquarters rolled over...convulsions sometimes occurred'. This cub died at 12 weeks: its skull was found to be softened and much thickened. Bland Sutton noticed that cubs of 6 months or more suffered a less severe form of the disease, often surviving a year or two, the only constant sign being a slow progressive paraplegia. Some cubs, to which he gave supplements of bone dust and cod-liver oil, made a good recovery, and were alive and active without any signs of paralysis 2 years later. In spite of this observation, some 25 years later Marine (1914) wrote: 'In zoological gardens where carnivores are held and bred in captivity and the diet is for the most part beef, goitre, rickets and osteomalacic states are quite common.'

Baumann (1896) observed that dogs fed on flesh diets frequently had enlarged thyroids of low iodine content. Watson (1904) found that fowls fed on raw lean meat and water died, in 3–16 months, with terminal paralytic signs; their thyroids were ten times the normal weight, though histologically normal apart from occasional hyperaemia. The parathyroids were also enlarged, but of normal structure. Watson (1906) reported marked thyroid hyperplasia in suckling rats whose mothers had been fed on meat, compared with the normal thyroids of those whose mothers received a mixed diet.

Heitzmann (1873) noticed that rickets developed in cats fed on milk, boiled meat, white bread, boiled potatoes and fat. He was interested in lactic acid as a factor in the aetiology of rickets, but the diet he used was certainly deficient in calcium and probably also in vitamin D. The cats showed swelling and distortion of the long-bone epiphyses after 4–5 weeks on the diet; rickets was confirmed microscopically. After 4–5 months the long bones were soft '...elastic, like a fish', and at post-mortem the

* Paper No. 3: *Brit. J. Nutr.* (1960), **14**, 361.

'compact layers' of the long bones were reduced, the scapulas were soft and elastic and the bone marrow was hyperaemic.

Telfer (1924) found osteoporosis and 'rachitic' changes in the bones of dogs fed on lean meat with bread and butter—a diet deficient in Ca but with an adequate phosphorus content; normal skeletal development occurred on the same diet supplemented with calcium lactate. Mellanby (1921) distinguished between the osteoporosis produced by Ca starvation and 'true rickets', but Korenchevsky (1922), giving many examples of animals fed on predominantly flesh diets, concludes that the essential difference between 'rickets from calcium starvation' and other forms of rickets is one of aetiology rather than of morphology or chemical composition of the skeleton.

Since cats are frequently fed on meat or meat offals, which they like, it was necessary to examine the effects of this type of diet more fully, particularly because Pottenger & Simonsen (1939) reported that raw meat supported normal growth and reproduction in cats in contrast to cooked meat which was inadequate in both respects. Beef or sheep hearts were chosen for the experiments to be described because the fresh frozen supplies available were cheap, reasonably constant in composition and similar in most respects to carcass meat.

EXPERIMENTAL

Animal management. Fifty-eight weaned kittens, aged 10–14 weeks at the beginning of the experiments, were used; nine were obtained from domestic sources and the remainder were bred, reared and maintained in the laboratory by the methods previously described (Dickinson & Scott, 1956*a*; Greaves & Scott, 1960). Litter-mate kittens were used to facilitate comparisons within each experiment. Two to four kittens were maintained in each cage, unless they suffered from paralysis or infections, when they were housed singly. Diets were given *ad lib.* with tap water for drinking, containing 100 mg calcium/l. The kittens were exercised daily and their appearance and behaviour noted; they were weighed three times weekly.

Diets. In Expts 1–3 the diet consisted of raw minced beef or sheep heart, imported from Australia; its mean composition is given in Table 1. For two animals, the minced heart was boiled with a little water for half an hour in an uncovered pan and offered, after cooling, with the fluid in which it was boiled. Details of various supplements used in Expts 2 and 3 are given in Tables 3 and 4. In Expt 4, a purified diet was used (Table 2) in which the salt mixture was adjusted to produce levels of calcium and phosphorus, and a Ca:P ratio, similar to those of the heart diet. The stock diet given to control animals is described by Dickinson & Scott (1956*a*).

Techniques. During the experiments the kittens were filmed at intervals, to record changes in gait and behaviour; radiological examinations were made of the fore-limbs and vertebral column. In Expts 1 and 2 blood was withdrawn from the antecubital vein. Haemoglobin concentrations were determined by means of a M.R.C. Grey Wedge Photometer; serum calcium was determined by the method of Baron & Bell (1957).

At autopsy the condition of the viscera was assessed, with particular reference to the colour of organs, the amount of blood present and the distribution of fat. Liver,

Table 1. *Composition of beef heart*

Constituent	Per 100 g fresh material: Watt *et al.* (1950) (lean sample)	Per 100 g fresh material: Spector (1956)	Per 100 g dry weight*	Remarks
Calories (kcal)	108	—	440	Adequate
Water (g)	77·6	70–77	—	—
Protein (g)	16·9	16·5	66	Very high
Carbohydrate (g)	0·7	—	2·8	Low
Fat (g)	3·7	3·1–19·5	16	Adequate to high
Ash (g)	1·1	0·92	4	Adequate
Minerals				
Ca (mg)	9	10	40	Very low
P (mg)	203	160–235	800	Rather high
Ratio, Ca:P	—	—	≏0·05†	Extremely low
Na (mg)	—	80–135	400	Rather high
K (mg)	—	255–355	1200	Rather high
Mg (mg)	—	110–125	450	High
Fe (mg)	4·6	4·2–6·2	20	Adequate
Mn (mg)	—	0·03	0·12	Rather low
Cu (mg)	—	0·76	3	High
I (μg)	—	—	10–80‡	Low
Vitamins				
Thiamine (mg)	0·58	—	2·3	High
Riboflavin (mg)	0·89	—	3·5	High
Nicotinic acid (mg)	7·8	—	31	High
Calcium pantothenate (mg)	—	—	5·6–12·2§	Adequate to high
Pyridoxine (mg)	0·29‖	—	1·2	Adequate
Inositol (g)	—	—	1·60¶	Very high
Choline (g)	0·17‖	—	0·68	High
Vitamin A (i.u.)	30	—	0**	Very low
Vitamin D (i.u.)	—	—	?	Probably low
Vitamin C (mg)	6	—	24	Not required

* Approximate, calculated; 75 % moisture is assumed unless otherwise stated.
† Range 0·04–0·07.
‡ Estimated for us by the Chilean Iodine Educational Bureau, London; low value, English sample; high value, Australian sample.
§ Waisman *et al.* (1942).
‖ McIntire *et al.* (1944).
¶ Woolley (1941).
** Estimated for us by Drs T. Moore and I. M. Sharman, Dunn Nutritional Laboratory, Cambridge.

Table 2. *Expt* 4. *Composition of low-calcium purified diet**

Constituent	Amount
Vitamin-free Casein (Genatosan Ltd) (g)	40·0
Lard (g)	20·0
Sucrose (g)	26·5
Arachis oil (ml)	5·0
Salt mixture III† (g)	4·0
Ground sugar-beet residue (g)	3·0
Nutricon tablets (Bob Martin Ltd) (dried yeast with added liver)	3
Choline chloride (mg)	300
Vitamin A (i.u., thrice weekly)	4000

* Total P content, 200 mg/100 g; Ca:P ratio 0·04 (approximately).
† Provided 8 mg Ca/100 g diet (dry).

kidneys, spleen, thymus, heart, biceps-femoris muscles, thyroids, adrenals, pituitary, gonads and accessory organs were weighed. For histological examination, the thyroids were fixed in Susa, sectioned at 5 μ and stained with haematoxylin and Biebrich scarlet. The skull and scapula were examined for hyperaemia and deformity, and the hardness of the bones of the pelvis and cranium was judged by the ease with which they could be cut. One femur, and sometimes the vertebral column also, was cleaned, dried and examined radiologically. The head of the other femur was decalcified with 1% (v/v), nitric acid after fixation in a dichromate–formalin–acetic-acid mixture followed by Orth's fluid and then by 10% formalin (4% formaldehyde) (R. J. C. Stewart, personal communication). The distal ends of the radius and ulna of the same side were treated similarly. Sections were cut of some parietal bones and the heads of some humeri were decalcified with sequestrol NA 2 (Geigy Co., Manchester) and stained with haematoxylin and eosin (H. A. Sissons, personal communication).

Expt 1 (*preliminary observations*). *Signs developing in young cats receiving raw heart.* Litter-mate kittens A_1 and A_2 were fed on raw heart from 12 weeks of age and A_3 was given stock diet. After 8 weeks A_1 and A_2 ceased to gain weight and showed an abnormal gait with weakness of the hind-legs. They were returned to the stock diet for 2 and 1 weeks, respectively, when the signs disappeared and growth was resumed. They were then given the heart diet for a second period and used in Expt 2.

Litter-mate kittens A_4, A_5, A_6 and A_7 were fed on raw heart for 24, 26, 29 and 33 weeks respectively to enable Dr C. B. B. Downman (Royal Free Hospital School of Medicine, London) to measure conduction in nerve and contraction of skeletal muscle under terminal anaesthesia. Serum Ca was estimated and observations were made on the bones and thyroids of these animals.

Expt 2. *Effects of various supplements on the signs observed in Expt* 1. Fourteen kittens of mean age 14 weeks were fed on raw heart for upwards of 8 weeks, until they showed the signs observed in Expt 1. The effects of various supplements listed in Table 3 were then determined. At the end of the experiment litter-mates, fed on stock diet throughout, were killed at the same time.

Expt 3. *Effects of adding calcium, vitamin A or iodine to raw or cooked heart from the beginning of the experiment.* When kittens were about 10 weeks old they were fed on raw or cooked heart with the supplements shown in Table 4. The kittens were arranged in groups so that as far as possible litter-mates received different supplements. Single animals of similar ages from other litters were used to replace losses due to infections. Kittens receiving supplementary I were kept in a separate room. With the exception of two, they were killed after the number of weeks shown in Table 4; kittens C_4 (raw heart) and C_7 (raw heart and calcium gluconate) remained on their respective diets, but a supplement of 50 μg I daily was added during a further 6 weeks.

At the end of this experiment the uptake of ^{131}I by the thyroids of kittens C_6 and C_{10} was measured for us by Professor G. W. Harris (Department of Neuroendocrinology, Institute of Psychiatry, London). The thyroids and parathyroids were removed under Nembutal (Abbots Laboratories Ltd, London) anaesthesia from three other kittens (C_{21}, C_{24}, C_{25}) 2 weeks before they were given raw heart diets. Parathormone (Eli Lilly and Co. Ltd, Basingstoke) and calcium gluconate were administered by injection

during the week after the operation to overcome tetany, but were then discontinued, as the kittens adjusted themselves. No remnant of thyroid or parathyroid was found at post-mortem or when the region adjacent to the trachea was examined histologically.

Expt 4. *Ca deficiency on a purified diet.* Three litter-mate kittens (D_1–D_3) aged 8 weeks were fed on the purified diet shown in Table 2 for 7–9 weeks. Six control kittens (D_4–D_9) were given an identical diet but with the addition of salt mixture IV (Greaves, 1959) giving a Ca:P ratio of 1·0; three of the kittens received this diet for more than 20 weeks.

RESULTS

General condition. The appearance of kittens receiving supplemented or unsupplemented heart was exceptionally good, even when they were partly paralysed. Their fur was thick, lustrous and well groomed, their eyes clear and shining, their ears and mucous membranes in excellent condition. No external evidence of vitamin A deficiency was apparent in a kitten, C_{22}, maintained on raw heart and calcium carbonate for more than 7 months.

Mortality. In the earlier stages of the work recorded here five out of twenty-five kittens died, mainly from enteritis, usually in the first 3 weeks; thereafter the surviving kittens apparently adapted themselves to the high-protein régime. Later, the use of antibiotics by mouth reduced losses. Kittens that failed to survive long enough to develop signs of dietary deficiency (7 weeks) have been omitted from the description below.

Growth. Throughout all the experiments male kittens tended to make greater weight gains than female. Weight gains on raw or cooked heart exceeded those on the stock diet at first, but gains were reduced with the onset of behavioural changes and lameness; the gains ceased in those kittens maintained for more than 8 or 9 weeks on raw heart alone. When calcium gluconate or carbonate was added to raw heart, growth was excellent and continuous to adult weight. Failure of kittens to grow on raw heart alone did not appear to be due to loss of appetite since they did not lose weight and the food consumed by a group, or by individuals kept on their own because they were paralysed, did not fall. Addition of vitamin A, vitamin D or copper salts did not improve growth or mitigate adverse signs (Tables 3 and 4) but a slight increase in weight was obtained on giving Befortiss B-Complex (Vitamins Ltd, London), to kittens getting cooked heart, although not in those getting raw heart (Table 3). No other differences were observed between kittens fed on raw heart and those fed on cooked heart. The thyroparathyroidectomized kitten C_{21} failed to grow on raw heart alone, but the similarly prepared kittens C_{24} and C_{25} on a diet of raw heart supplemented with Ca made weight gains that were reasonable but not so great as those of the comparable animals C_{22} and C_{23} with intact thyroid and parathyroid glands.

Behaviour. Kittens given raw or cooked heart, or the purified diet low in Ca, showed characteristic behavioural changes after 3–11 (mean 7) weeks on the diets. They became nervous, bewildered, static, hypersensitive to noise and cowered in corners, resenting handling and biting viciously. Respiration was rapid and shallow, about 60/min at rest against a normal of 25–30/min. Three kittens showing behavioural

changes had convulsive attacks. Additional I (50 μg daily, Table 4) delayed the onset of skeletal dystrophy; less severe signs appeared 11–14 weeks from the beginning of the experiment, and the kittens remained friendly and easy to handle. Supplementing the raw heart with calcium carbonate to give a Ca:P ratio of 0·5 (Table 4, kittens C_{15} and C_{16}) also delayed the appearance of signs but did not prevent their ultimate development. Kittens remained lively both on the raw heart and purified diets when

Table 3. *Expts* 1 *and* 2. *Effects of various supplements on signs produced in kittens by a heart diet*

Kitten no.	Supplement	Period of administration	Effect on weight gain and behaviour
A_1, A_2, B_1, B_2	Thiamine (1 mg, IP)	Once	None
A_2	Vitamin B12 (100 μg, IM)	Twice	None
B_1	$CuSO_4$, 250 p.p.m. in drinking water	15 days	None
B_1	Ca gluconate solution containing 22·5 mg Ca (SC)	Daily for 18 days	Slight improvement
B_2		Daily for 77 days	Marked improvement in locomotion and temper
B_3, B_4, B_5, B_6*	Ca lactate, 1·5 g/100 g heart, mixed in food	10 days	None, food refused; B_5 died
B_3, B_4, B_6*	Ca gluconate, 2·25 g/100 g heart, mixed in food	77 days	Marked improvement in behaviour, activity and bone density
B_3	Vitamin D_2 emulsion, 200 i.u. by mouth along with Ca gluconate	21 days	No improvement over B_4
B_3, B_4, B_6*	Befortiss B-Complex†, 1 ml (SC) along with Ca gluconate	Daily for 3 days (repeated twice)	Weight gain by B_6; little change in B_3 and B_4
B_8–B_{10}	$CaCO_3$, 0·5 g/100 g heart, mixed in food	30 days	Complete recovery
B_{11}–B_{13}	As for B_8–B_{10} with iodine, 50 μg/cat day	30 days	Complete recovery

IP, intraperitoneal injection; IM intramuscular injection; SC, subcutaneous injection.
* Given cooked heart.
† Contains 10 mg thiamine, 1 mg riboflavin, 1 mg pyridoxine, 40 mg nicotinamide.

the calcium-gluconate or calcium-carbonate supplement given was sufficient to raise the Ca:P ratio to 1·0, and they remained easy to handle and advanced to the front of their cages to claim attention. During exercise these kittens galloped, chased and jumped with tremendous zest for short periods before suddenly stretching themselves, panting, on the floor.

Kittens on the unsupplemented stock or control purified diets took their exercise at a slower pace over a longer period and then retired to their sleeping boxes where they curled up and went to sleep. Kittens given additional I throughout were less nervous and more easily handled than those without the supplements, even when suffering from a marked Ca deficiency. One kitten (C_4) kept on raw heart for 9 weeks showed a marked improvement in behaviour when given additional I.

Posture and gait. Kittens on heart alone showed progressive weakness, inco-

ordination and paresis, which began in the hind-legs. Their playful habits disappeared entirely. At first they preferred to sit rather than stand, later to lie rather than to sit, and finally were unable to stand at all. Their backs became sunken and the whole foot (tarsus and metatarsus) was placed on the ground instead of the phalanges (Pl. 1 *a*).

Table 4. *Expt* 3. *Diets given to kittens, and some results*

Kitten No.	Kitten Litter	Kitten Sex	Diet	Supplement*	Length of experiment (weeks)	Mean daily weight gain (g)	Behavioural signs	Degree of osteoporosis (shown by X-ray)†	Thyroid, histological hyperplasia†
C_1	(*a*)	♀	Raw heart	None	8	13·7	+	3	3
C_2	(*b*)	♂			8	14·7	+Fr	4	4
C_4	(*c*)	♂			9	18·7	+	—	—
C_6	(*c*)	♂			9	9·3	+Fr	4	2
C_{17}	(*e*)	♀			15	11·1	0	3	0
C_3		♀	Raw heart	Vitamin A	8	15·3	+Fr	3	3
C_5	(*c*)	♀			9	10·7	+	3	1
C_7	(*a*)	♂	Raw heart	Ca gluconate	12	12·6	0	—	—
C_9	(*g*)	♀			12	10·9	0	0	1
C_{11}	(*d*)	♀			11	15·3	0	0	2
C_{22}	(*f*)	♀		$CaCO_{3(a)}$	15	11·3	0	—	—
C_8	(*b*)	♀		Ca gluconate, vitamin A	12	7·4	0	0	4
C_{10}	(*d*)	♀		Ca gluconate, vitamin A	11	14·6	0	0	3
C_{23}	(*f*)	♂		$CaCO_{3(a)}$, vitamin A	15	13·6	0	—	—
C_{14}	(*g*)	♂	Cooked heart	Ca gluconate	12	16·2	0	0	2
C_{13}	(*b*)	♀		Ca gluconate, vitamin A	12	12·4	0	0	2
C_{15}		♂	Raw heart	$CaCO_{3(b)}$	12	17·9	+	1	2
C_{16}		♂		$CaCO_{3(b)}$	12	19·3	+	2	3
C_{18}		♀		I	11	11·4	+	1	1
C_{19}	(*e*)	♀			15	10·3	+	2	0
C_{20}		♀			15	8·1	+	3	1
C_{26}	(*b*)	♀	Stock		8	9·7	0	0	0
C_{27}	(*g*)	♀			8	6·0	0	0	0
C_{28}		♂			6	12·3	0	0	0
C_{29}		♂			7	14·4	0	0	0
C_{30}		♂			5	8·7	0	0	0
C_4	(*c*)	♂	Raw heart	I	6‡	4·7	—	3	1
C_7	(*a*)	♂		Ca gluconate, I	5‡	28·1	—	0	0

Fr, Fracture occurred.

* Amount given: vitamin A, 5000 i.u. three times weekly; Ca gluconate, 2·25 g/100 g wet diet; $CaCO_{3(a)}$, 0·50 g/100 g wet diet; $CaCO_{3(b)}$, 0·25 g/100 g wet diet; I, 50 μg/day.

† Arbitrary scale, 0–4.

‡ Immediately after experimental period shown for these kittens higher in the table.

A limping gait was characteristic. Fractures of the fore- or hind-limbs appeared in kittens A_2, A_4–A_7, C_2, C_3 and C_6 and three of them developed a paresis of the hind-limbs following the onset of behavioural signs; paresis and fractures were precipitated by jumping or by convulsions. Even the severest signs were subject to spontaneous partial, or in some instances complete, remissions. Similar signs were noted in kittens given supplements of I or insufficient amounts of Ca (Table 3), but the postural changes developed more slowly and were less severe. Posture and

gait were rapidly improved by giving calcium gluconate or carbonate (Table 3) or I. Prostrate kittens B_8–B_{13}, C_4 and C_7, were able to stand and walk within a week of supplementation, but limping due to fractures and paresis only diminished slowly, and recovery was usually incomplete in the relatively short experimental periods.

Skeletal changes. Radiological examination of the skeleton during life and at autopsy showed rarefaction of the bones in all the kittens receiving raw heart, except in those receiving a supplement of calcium gluconate or calcium carbonate sufficient to produce a dietary Ca:P ratio of 1·0 (Pls. 1*g*, 2*a*). Similar rarefaction was found in the skeletons of kittens on the low-Ca purified diet, but not in those of their controls. Ca loss was most apparent from the bodies of the vertebras and especially those of the lumbo-sacral region which curved ventrally and tended to collapse in severe deficiency (Pl. 2*a*). Losses were also found from the sternum, ribs, scapulas and pelvis. Radiological comparison of femurs (Pl. 1*g*) showed reduction in the width of cortical bone, increased volume of the marrow cavity and a marked reduction in the bony trabeculae of the proximal and distal ends of the bones compared with those from kittens receiving adequate supplementary Ca or the stock diet. At autopsy the bones of the kittens on heart alone, particularly the fronto-parietals, scapulas and pelves were dark red (Pl. 1*b*). These bones were so softened that they could be cut with scissors whereas bone forceps were required for those of the kittens receiving adequate Ca. Even the bones from kittens (C_{15} and C_{16}) receiving the reduced Ca supplement were distinctly harder than those of kittens receiving heart alone or heart supplemented with I. The long bones were straight and not misshapen unless fractured (Pl. 1*f*, *g*), although the scapulas were deformed (Pl. 1*d*) and the weight-bearing areas of the long bones slightly expanded. Histological examination showed the bony trabeculae separating the inner and outer tables of the parietal skull bones to be reduced in number, with the spaces created filled with blood vessels and marrow tissue. The width and density of cortical bone were reduced in the femur, radius and ulna; dilated blood vessels, fibroblasts and other connective-tissue cells filled the enlarged Haversian canals. Osteoclasts were numerous and active at sites normally occupied by osteoblasts (Pl. 3*c*). The epiphysial cartilage was regular and of normal width. Cartilage cells were undergoing normal hypertrophy before replacement by bone, but the bony trabeculae were poorly developed at the metaphysis (Pl. 3*a*); in the shaft the haematopoietic marrow was grossly expanded compared with that of kittens given supplements of Ca or fed on the stock diet. Osteoid tissue was not formed in the kittens fed on heart alone; such limited bone as was present was of normal structure. The condition was similar to osteitis fibrosa or osteoporosis rather than to rickets or osteomalacia. Bony changes did not occur in the thyro-parathyroidectomized kitten C_{21} which failed to grow. Pl. 3*b*, *d* shows the normal structure of the femur of a kitten C_{13} fed on cooked heart supplemented with Ca and vitamin A.

Nervous system and muscle. Kittens that became paralysed in the hind-limbs were examined for neurological and myopathic disturbances with the help of Dr C. B. B. Downman of the Royal Free Hospital School of Medicine, London, and Dr Marion Smith of the Institute of Neurology, London. The onset of paralysis was sudden, the

kittens showing some spontaneous improvement in subsequent weeks. The tone of the muscles of the hind-limbs was weak, and no placing reaction could be elicited. Pinching between the toes caused sluggish withdrawal of the hind-leg on either side, and the crossed extensor reflex was very pronounced. Both hind-limbs were extended on pinching the scrotum. These abnormal reflexes can be elicited in a spinal-cat preparation and indicated damage to the central rather than the peripheral nervous system. Investigation of the spinal cord by Marchi's technique showed typical compression lesions at the site of collapse of the vertebral bodies observed radiologically. Ascending tracts had degenerated cephalad and descending tracts caudad to the lesion. Ca-deficient kittens that were not paralysed did not show histologically demonstrable changes in the spinal cord, but at autopsy it was observed that their brains had a much less firm consistency than those of kittens receiving supplementary calcium or stock diet. Muscular wasting, shown by loss of weight of the biceps femoris compared with controls, or unequal weights of muscles from either side, was observed only in partly paralysed kittens. Histological examination of wasted muscles showed no gross myopathy; reduction in diameter of muscle fibres and the occurrence of scattered regions infiltrated with plasma cells were secondary to lesions in the nervous system due to collapse of vertebras. Although the heart appeared dilated at autopsy in some of the severely affected kittens, the weights of the organ were not different from those of controls. Urination and defaecation were apparently normal, but in partly paralysed cats the bladder was observed to be distended at autopsy.

Table 5. *Mean values with their standard errors for organ weights and haemoglobin concentration of kittens of similar age, 25–30 weeks, fed on supplemented or unsupplemented heart or on stock diet*

Diet	No. of kittens	Hb concentration (g/100 ml)	Kidneys (mg/100 g body-weight)	Thyroids and parathyroids (mg/100 g body-weight)	Adrenals (mg/100 g body-weight)
Raw heart only	9	12·87 ± 0·23	920 ± 77	17·61 ± 0·99	15·70 ± 0·37
Raw heart + Ca	10	13·09 ± 0·43	658 ± 19	11·32 ± 1·51	14·36 ± 0·23
Raw heart + I	4	12·53	811	10·49	13·96
Raw heart + Ca + I	2	11·4	526	8·52	12·60
Stock diet	7	9·79 ± 0·51	719 ± 63	12·68 ± 1·19	12·92 ± 0·81

Thyroids and parathyroids. The thyroids of kittens and cats fed solely on heart were dark red, owing to hyperaemia, in marked contrast to the light-brown colour of thyroids in cats on the stock diet, purified diet, or on heart supplemented with 100 μg I daily. The hyperaemic thyroids were enlarged and abnormally heavy (Table 5) weighing (with the parathyroids) up to 20 mg/100 g body-weight. The degree of enlargement depended on the length of time for which the kittens were fed on the diet, which provided between 5 and 40 μg I daily. The glands of control kittens on the stock diet (providing 200–300 μg I daily) weighed about 12 mg/100 g body-weight (Table 5). Those of adults on the same diet weighed about 10 mg/100 g. Histologically, the normal thyroids contained abundant colloid in follicles of various sizes, showing all stages of secretion, rest and reabsorption. Kittens 18 weeks old after 8 weeks on a diet

of heart alone had thyroid follicles containing small amounts of colloid only, with well-marked absorption vacuoles and high cuboidal epithelium (Pl. 4*d*). The changes were progressive (Pl. 4*a*, *b*, *c*); after 29 weeks on the diet little colloid remained, the follicular epithelium was columnar, often multi-layered and in some parts thrown into folds. Blood vessels were distended with erythrocytes. After 33 weeks on the diet colloid had entirely disappeared, and the follicles were atrophic with signs of fibrosis.

The parathyroid glands of all kittens fed on heart were enlarged, but were otherwise similar to those of kittens fed on the stock diet.

Hyperplasia of the thyroid but to a less extent ($P = 0{\cdot}005$) occurred in cats fed on heart supplemented throughout with 0·5 g calcium carbonate/100 g wet diet. Although the gland was hyperaemic and most of the follicles were small, the epithelium remained cuboidal, and a considerable quantity of colloid was present even after 40 weeks on the diet (Pl. 4*e*). A terminal experiment, under anaesthesia, showed that a kitten (C_6, fed on raw heart) given ^{131}I intravenously concentrated, in 1 h, 2·5 times as much ^{131}I per g thyroid tissue as its pair-mate (C_{10}) which had received raw heart supplemented with calcium gluconate at the rate of 2·5 g/100 g wet diet.

The thyroids of kittens receiving a supplement of 100μg I (as KI) daily were normal in weight and structure, but 50μg I daily did not altogether prevent hyperplasia.

The thyroids of kittens reared on the purified diet with a Ca:P ratio of 1·0 and providing 50μg I daily were slightly hyperplastic compared with those of controls, but hyperplasia was far more advanced in the thyroids of kittens on the low-Ca purified diet, though it provided the same amount of I.

Blood and viscera. All animals that received the raw-heart diet, whether supplemented or not, had a haemoglobin concentration and packed-cell volume significantly greater ($P = 0{\cdot}001$) than control animals of the same age and weight maintained on the stock diet. Hyperaemia of organs, especially liver and spleen, was a notable feature of all animals fed on raw heart with or without supplements.

Serum-Ca concentrations were determined several times in the first and second experiment and were always within the normal range, 10–12 mg/100 ml serum (Stewart & Percival, 1927; Burns, 1933), except for one severely deficient kitten which was unable to stand and was found to have 6·9 mg Ca/100 ml serum.

Examination of several organs suggested a general increase in the amount of lymphoid tissue. The kidneys seemed relatively heavier in kittens fed on heart than in those on the stock diet, though the difference was not statistically significant; supplementing raw heart with Ca, however, significantly reduced the kidneys' weight ($P = 0{\cdot}005$) (Table 5) to a level similar to that for normal animals (Latimer, 1939*a*). Thymus and spleen were generally enlarged, although in kittens with fractures the thymus was reduced or absent and the adrenals were enlarged, possibly because of 'stress'.

Recovery. Supplementation of the raw-heart diet with calcium gluconate or calcium carbonate (to bring the Ca:P ratio of the diet to 1·0), after the appearance of the behavioural signs, produced a rapid improvement in posture and gait: the kittens were able to walk within a week and weight gains were resumed. Radiological improvement in the bones took much longer; moreover, if fractures with compression of the cord had occurred, function improvement of paralysis was very limited.

Reproduction. Male kittens reared on raw heart alone failed to reach sexual maturity. The seminiferous tubules of the testes remained inactive, although the Leydig cells were abundant and the epididymis showed signs of secretory activity. Normal development of the testes occurred in kittens reared on raw heart with an adequate supplement of calcium carbonate, and sexual maturity was reached at an earlier age (28 weeks) than in controls fed on the stock diet (36–40 weeks).

Female kittens reared on raw heart alone did not show signs of oestrous behaviour but those fed on heart supplemented with Ca became pregnant at an early age. Pregnancies were usually successful and the kittens reared were apparently normal except that their thyroids were hyperaemic and hyperplastic. Female cats that were reared on the stock diet and then fed on raw heart alone from the time of conception generally aborted. However, if adequate supplements of Ca and I were given with the raw heart normal litters were reared (Scott, Greaves & Scott, 1960).

DISCUSSION

Albright, Bauer, Ropes & Aub (1929) suggested that the 'well known deleterious effect of a meat diet may be due to its high phosphorus content' and observed that Ca metabolism is inseparably linked with P metabolism since, in human beings in balance experiments, the ingestion of phosphoric acid or acid phosphate provoked marked decalcification (Bauer, Albright & Aub, 1929). This observation explains why adequate bone formation only occurred in the kittens fed on raw heart (with a Ca:P ratio of about 0·05) when the Ca:P ratio was adjusted to 1·0 by the addition of Ca salts. When the ratio was raised to only 0·5, which provided about 0·4% Ca in the diet on a dry-weight basis, the amount of Ca was found to be inadequate. On the other hand, no evidence of osteoporosis was seen in kittens fed on purified diets that provided 0·43% Ca (dry basis) at a Ca:P ratio of just over 1·0. Gershoff, Legg, O'Connor & Hegsted (1957) produced true rickets in kittens fed on vitamin D-deficient diets containing 1% Ca, with 1% P, and 2% Ca with 0·65% P. They found that the kittens did not eat the 3:1 ratio diet as readily as the 1:1 diet; the death rate was higher and the weight gain less on the high-ratio diet, but rickets was more severe on the low-ratio diet, probably because of more rapid growth. However, when the Ca:P ratio of a mixed diet was maintained at 1·3:1, Dickinson & Scott (1956*b*) found that kittens were able to tolerate large amounts of Ca (up to 5·6% dry weight) and P (up to 4·3%) in the diet without ill effect, food intake simply being increased to compensate for the reduced calorie value of the diet. Care should therefore be taken when supplementing meat diets with Ca to keep the Ca:P ratio near to 1·0.

Marine (1915) found that rats fed on liver, with bread and water, showed some reduction in colloid and an increase in the size of the thyroid cells. Burget (1917) and later Remington (1937) and Hou (1940) extended these observations. They found that rats maintained on high-protein diets containing liver showed hyperplasia of the thyroid with reduced iodine content, and Marine (1922) in a review stated that 'liver, particularly pig's liver, was the most potent of a great variety of meats in causing thyroid hyperplasia in dogs and cats...'.

The degree of hyperplasia, passing on to atrophy, of the thyroids in the kittens described here was correlated with the length of time they were fed on the heart diet and indicated a state of I deficiency which could be overcome by adding fairly large amounts of I to the diet. Marine & Lenhart (1909*a*) showed that hyperplasia occurred more frequently in young than in older animals, and was correlated with increased size and reduced I content of the gland. But it seems that the dietary I requirement may be raised on high-protein diets, such as the heart diet used for our kittens. In rats, McRoberts (1958) obtained evidence that the protein level of the diet influenced the size, the amount of I present in, and the degree of histological hyperplasia of the thyroid gland. Hypertrophy was more pronounced in rats that received 30% casein and 0·1 p.p.m. I than in those receiving 20% casein with the same amount of I. In order to prevent hyperplasia of the thyroid gland on the 30% casein diet, 0·4 p.p.m. I were necessary. Verzhikovskaya (1957) obtained results similar to those obtained with our kittens with rats fed for 3 months exclusively on meat: the thyroids weighed 16·6 mg/100 g body-weight, compared with the weight of 8·2 mg/100 g body-weight shown by controls, closely similar to the normal proportional thyroid weight of the adult cat (Latimer, 1939*b*). Further, she found that the rate of uptake of ^{131}I by the thyroids of the meat-fed rats was twice that of the controls, reaching a maximum in the experimental rats in 6–12 h against 24 h in the controls. Conversely, Klimek, Hrstka & Bucko (1957) found that increasing the starch content and lowering the amount of casein in a diet reduced accumulation by the thyroid of ^{131}I fivefold compared with that in rats fed on other diets; the radioactivity of the urine was approximately equal in all groups.

The precise relation between thyroid activity and the skeletal changes in Ca deficiency and imbalance is not understood. Marine & Lenhart (1909*a*) remarked that 'rickets... and osteomalacia are practically always associated with anatomical changes in the thyroid'. Mellanby & Mellanby (1921) noticed that dogs used in their dietary experiments on rickets showed hyperplasia of the thyroid, which was more marked when the fat (especially butterfat) intake was raised, but was not apparent when cod-liver oil was the only fat included in the diet. Murray (1923) found thyroid hyperplasia in all of forty-three puppies on Ca-free diets that produced 'rickets from calcium starvation'; the hyperplastic thyroid vesicles contained colloid, but diets high in Ca, producing 'true rickets', were associated with thyroids whose vesicles were empty of colloid. Luce (1923), however, found that Ca-deficient diets consistently produced hyperplastic parathyroid glands in rats, but not accompanied by corresponding changes in the thyroid, even on diets containing 0·04% Ca. On the other hand, high-Ca, rachitogenic diets were shown by Thompson (1932) to produce diffuse thyroid hyperplasia in rats, which was prevented by small additions of KI; she concluded (Thompson, 1933) that goitre, caused primarily by I deficiency, was exacerbated in rats by excess Ca. In marked contrast, for kittens on the heart diet additional Ca proved to have a 'thyroid-sparing' effect. Mellanby (1922–3) added dried thyroid to 'border-line' rachitogenic diets and found that it increased the severity of the condition in young puppies, in spite of a reduced growth rate.

There is considerable clinical evidence in man of a relationship between the action

of thyroid hormones and the normal development of bone (Anonymous, 1958). Aub, Bauer, Heath & Ropes (1929) found that patients with exophthalmic goitre and hyperfunctioning thyroid adenomata had a urinary Ca excretion markedly above normal and not dependent on the elevated metabolic rate alone. They found that the ingestion of thyroid gland by normal individuals increased the elimination of Ca. In patients suffering from myxoedema, Ca and P excretion was markedly diminished to levels below those found in normal individuals, although their serum Ca and P values were essentially normal; quantitative evidence suggested that most of the excess Ca excreted originated from tertiary calcium phosphate in the bones. Thyrotoxicosis produces rapid bone growth in children, with accelerated skeletal development, but in adults it leads to osteoporosis and may eventually result in fractures (Aub *et al.* 1929; Bartels & Haggart, 1938; Robertson, 1949; Anonymous, 1958). Krane, Brownell, Stanbury & Corrigan (1956), on the basis of observations on human beings receiving ^{45}Ca, suggested that both bone formation and destruction proceed at increased rates in thyrotoxicosis. The experiments described here support the view that the thyroid gland is hyperactive in the kittens on the heart diet; it is possible that the hyperactivity of the thyroid may be consequent on a raised output of thyrotrophic hormone by the anterior pituitary on high-protein diets. The existence of pituitary stimulation is also suggested by the rapid growth and early attainment of sexual maturity seen in some of the kittens reared on heart supplemented with Ca.

Except in severely affected kittens, some of which had convulsions, the enlarged parathyroids were able to compensate for the low Ca intake on the heart diet, maintaining serum Ca at normal levels (Stewart & Percival, 1927) by withdrawing Ca from the skeleton, but Albright *et al.* (1929) maintained that the principal function of the parathyroid hormone is to lower the concentration of P in blood by increasing its urinary excretion. Thus parathyroid hormone appeared to differ from thyroxine, which brought about a simultaneous increase in urinary output of both P and Ca. The softening of brain tissue of the heart-fed kittens may be explained by the finding of Hess, Gross, Weinstock & Berliner (1932) that in rickets the total Ca in the blood of rats was normal but that the Ca content of the brain was markedly diminished, whether the diets were high or low in Ca.

Many workers have shown the importance of vitamins A and D for normal bone growth, yet in spite of the known lack of vitamin A in the heart diet, and the suspected shortage of vitamin D, overt signs of deficiency were not apparent, although the vitamin A content of the liver and kidneys was reduced (Moore, Sharman, Scott & Greaves, unpublished results). Moreover, additional supplies of vitamins A and D made no apparent difference to the kittens, whether they were receiving heart alone or supplemented with Ca. Coplan & Sampson (1935) found that deficiency of vitamin A produced hypertrophy of the thyroid gland in female rats, and an increase in pituitary thyrotrophin with consequent increased thyroid activity has been reported by Schulze & Hundhausen (1939). These findings suggest that interpretation of the thyroid changes seen in the kittens may be further complicated by the low vitamin A content of the heart diets, though under the conditions of these experiments no difference was found between the glands of kittens that received supplementary vitamin A and of

those that did not. Owing to the methods of weaning (Dickinson & Scott, 1956*a*) reserves of fat-soluble vitamins were probably high in the experimental kittens at 10 weeks of age, so that it was not surprising that deficiencies did not appear within the relatively short time of most of the experiments reported here. A pair of kittens maintained throughout the growing period on heart supplemented with calcium carbonate were in excellent condition and produced a good litter of kittens after 8 months on the diet, but signs of vitamin A deficiency in the form of skin and eye lesions appeared in their offspring when they were 4 months old.

Examination of the limited information available about the composition of heart (Table 1) suggests that it is a particularly rich source of B vitamins. This view is supported by the lack of response to attempts to improve the kittens' condition by administration of Befortiss B-Complex and individual B vitamins in Expt 2, except when cooked heart was used. (The method of cooking was designed to encourage maximal destruction of heat-labile constituents subject to oxidative processes.) A notable feature of kittens on the heart diet was their superficially excellent appearance, and da Silva (Scott, da Silva & Lloyd-Jacob, 1957) commented that cats maintained for 3 months exclusively on lean beef muscle had an extremely good appearance and especially soft fur, but he made no mention of any skeletal abnormalities.

Many brief reports have appeared during the past 10 years about '*osteogenesis imperfecta*', a disease attributed to a variety of causes in cats, particularly Siamese, and dogs (Skeggs & Theobald, 1957; Holmes & Price, 1957; Coop, 1958). The signs described are similar in all respects to those we have observed in kittens fed on unsupplemented raw or cooked heart. We had the opportunity of carrying out an autopsy on a clinical case, a 20-week-old Siamese with a history of lameness after jumping (Henderson & Keywood, 1959), which showed fractures similar to, and histological changes in bone and thyroid gland identical with, those of our kittens. This animal had an excellent coat and healthy, though hyperaemic, viscera; it had been fed on meat with a little milk. Material from similarly affected kittens has been received from Salisbury, Rhodesia, through the kindness of Dr E. V. Cock and Mrs Phyllis Robinson: in this region incidence of the condition seems to be high. Lions in the London Zoological Society's collection also suffer from a similar condition apparently caused by failure to consume the bones supplied with their ration of meat (Fiennes & Graham-Jones, 1960). The daily administration of $4\frac{1}{2}$ oz calcium borogluconate to a dystrophic lioness brought about a marked improvement in her condition.

It is apparent that, properly supplemented, cooked or raw heart muscle with its associated fat forms an excellent diet for domestic cats, giving a maximal growth rate, a thick lustrous coat and shining eyes. Appetite is maintained on this single food for months which increases the danger from both unsupplemented heart and carcass meat because the cat remains contented, grows well and is in apparently good health until a crisis due to Ca deficiency occurs. By this time the degree of osteoporosis is so severe that repair of the skeleton is a slow process.

SUMMARY

1. Experiments are described in which kittens were fed on raw or cooked heart exclusively, or variously supplemented with calcium gluconate or carbonate, KI, $CuSO_4$ and vitamins A, D and those of the B complex.

2. The heart contained small or negligible quantities of calcium, iodine and vitamin A and had a very low Ca:P ratio of about 0·05.

3. Ten-week-old kittens fed on a diet of heart alone developed, after an average of 7 weeks, characteristic signs, which included nervousness, ataxia and finally paralysis of the hind-limbs.

4. X-ray examination of affected kittens revealed marked osteoporosis (osteitis fibrosa) which was confirmed histologically; rachitic changes did not occur. Paresis was due to pressure following collapse of vertebras and other bony structures.

5. Raw heart was shown to contain adequate amounts of copper and of vitamins of the B complex, but some destruction of the vitamins occurred on cooking the heart.

6. The thyroids of heart-fed kittens were hyperplastic and significantly heavier than those of controls supplemented with calcium. Kidneys were also heavier and haemoglobin concentrations higher in heart-fed kittens.

7. Supplementation of the heart with sufficient calcium, as gluconate or carbonate, to give a Ca:P ratio of 1·0, entirely prevented the occurrence of signs referable to the skeleton, and thyroids were less hyperplastic even after 8 months on the diet. Supplementation to give a Ca:P ratio of 0·5 was insufficient to prevent signs of deficiency.

8. Supplementation with 50μg I daily prevented gross enlargement of the thyroid, and 100μg daily completely prevented hyperplastic changes.

9. Supplementation with vitamins A and D made no apparent difference to kittens, but some evidence was obtained that the offspring of cats that had not received these supplements would show signs of vitamin A deficiency.

10. Identical behavioural, skeletal and thyroid changes were observed in kittens given a low-Ca, high-protein purified diet, but not in controls receiving a similar diet with a Ca:P ratio of 1·0.

11. The growth and general appearance of the kittens on the heart diet supplemented with Ca were extremely good, and these animals were capable of satisfactory reproduction.

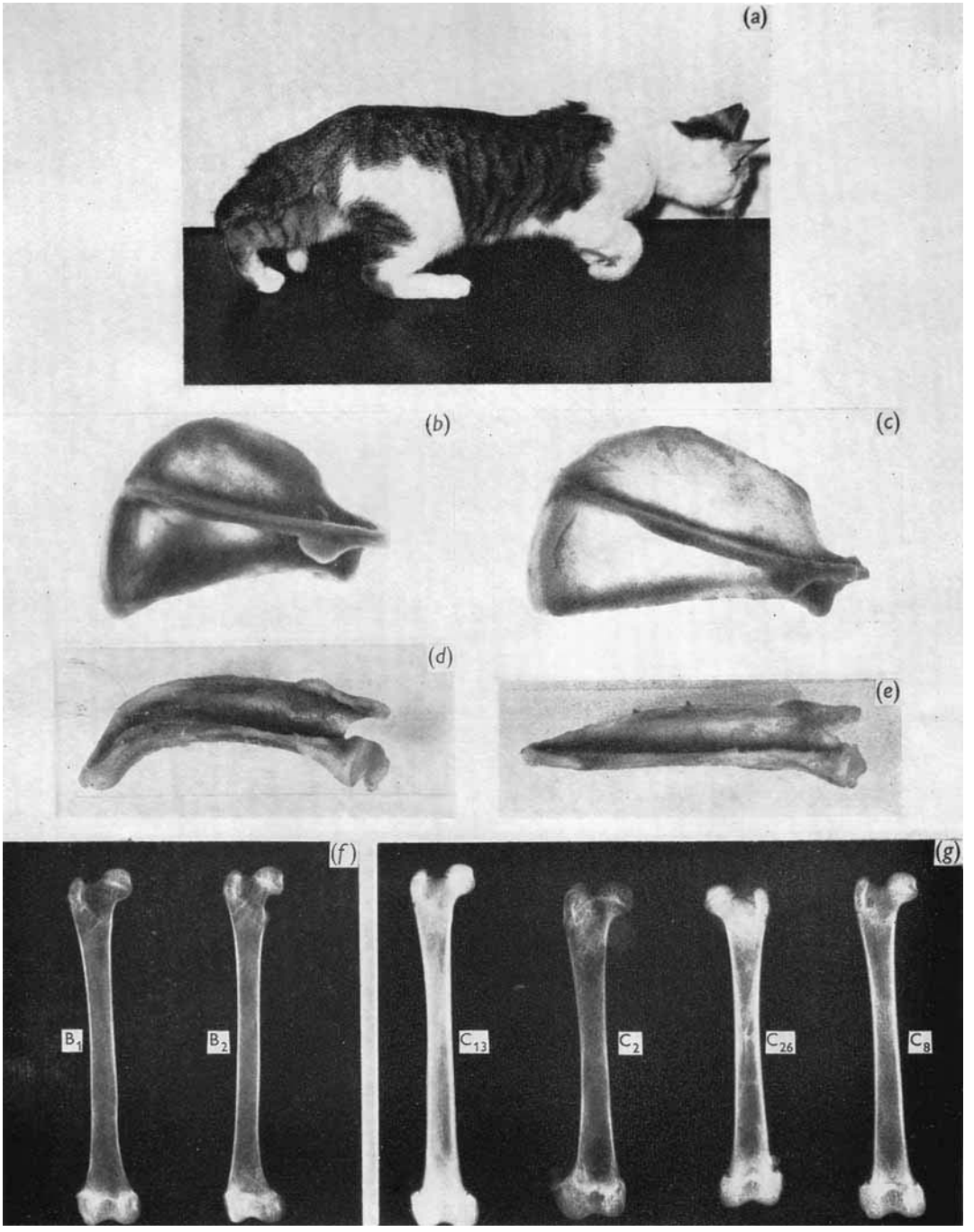
12. The results are discussed in relation to a large literature on flesh diets and to recent observations on clinically occurring similar conditions in cats and lions.

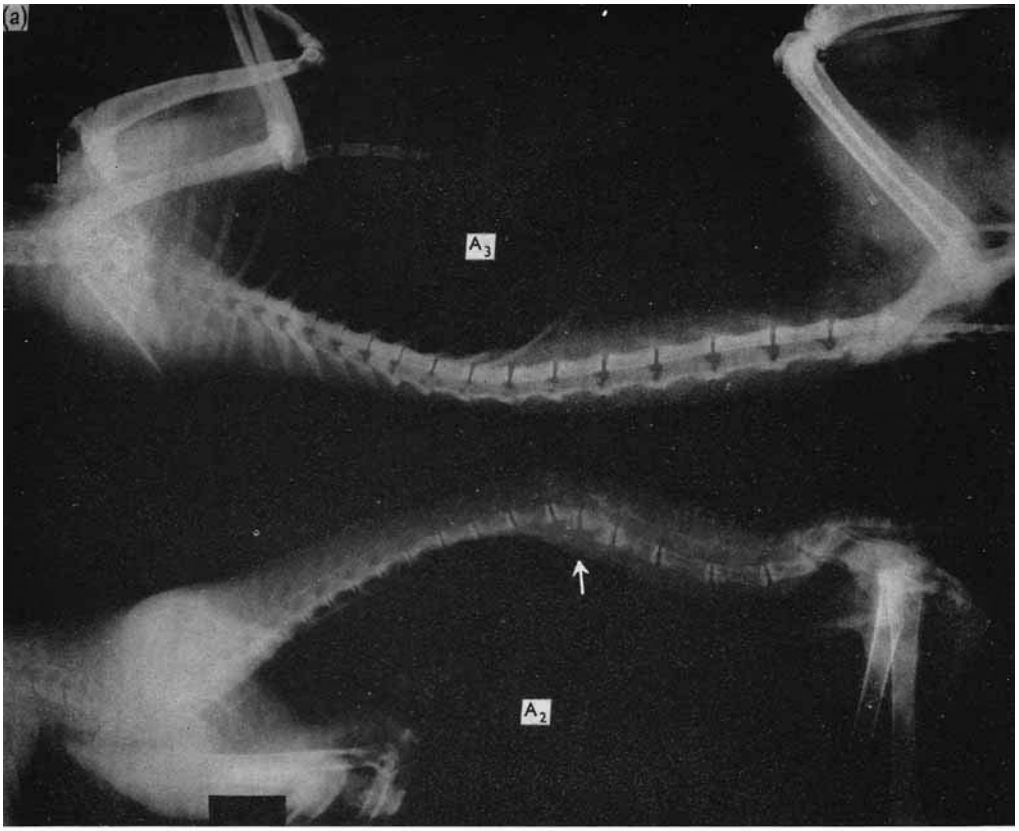
13. Evidence is presented to suggest that the high-protein nature of the diet, the deficiency of Ca and of vitamin A, as well as the low I content were all implicated in the thyroid changes observed.

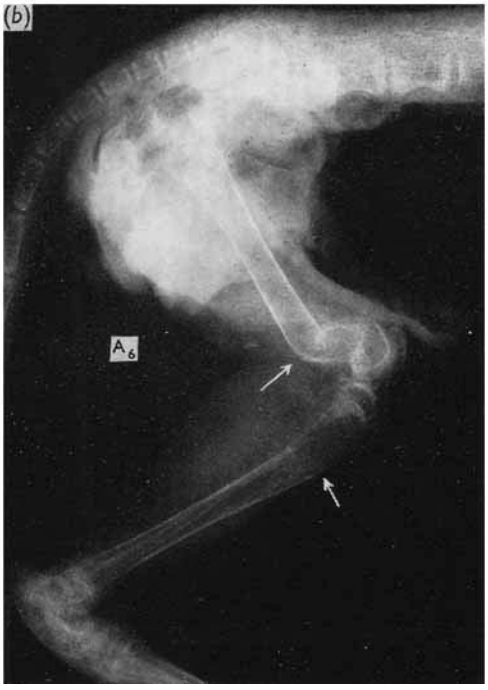
We thank Petfoods Ltd, Melton Mowbray, Leicestershire, for grants towards the cost of these investigations, Mr C. Fowler for assistance with the radiography and Miss A. Elkins and Mr A. Holland, who cared for the animals.

REFERENCES

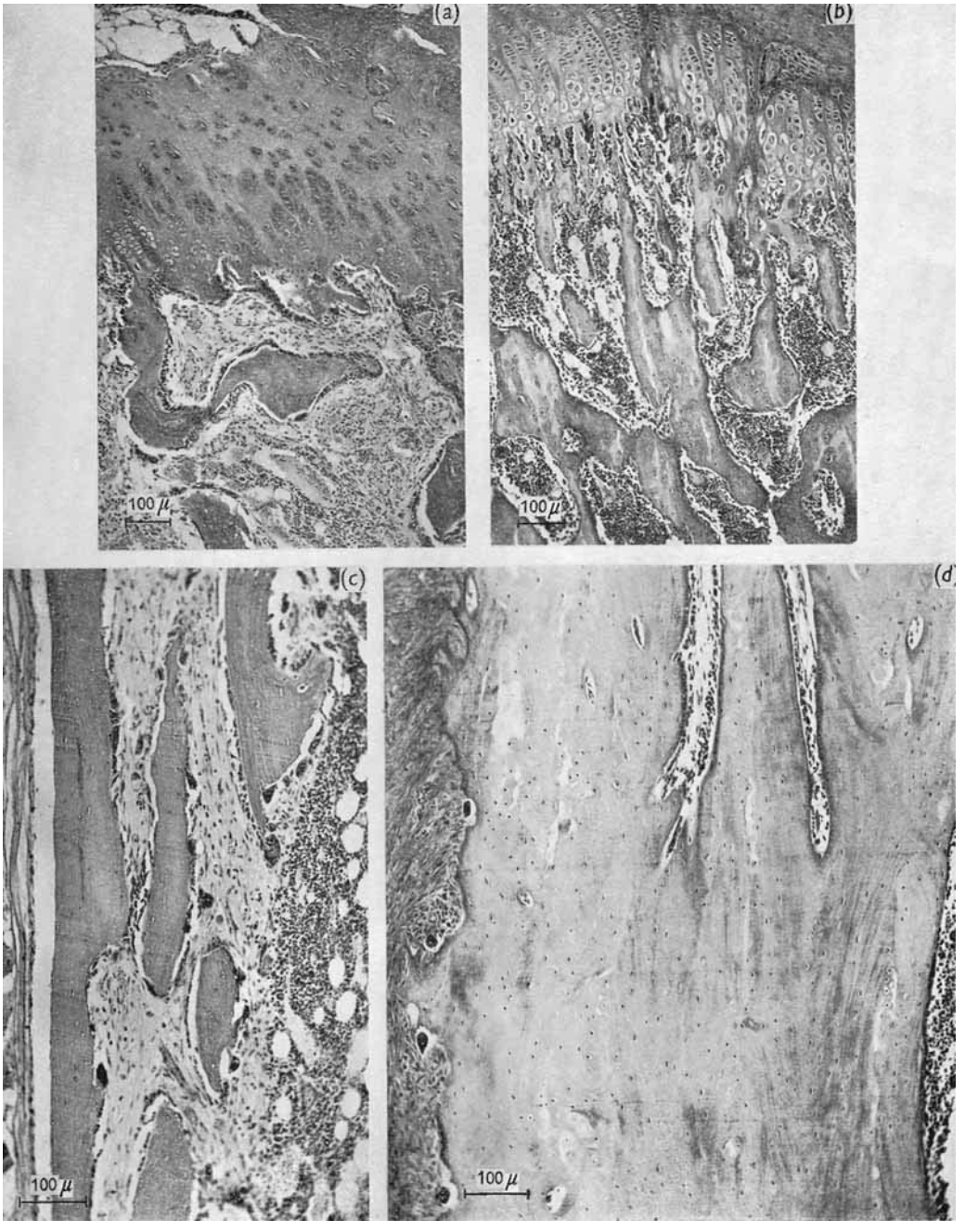
Albright, F., Bauer, W., Ropes, M. & Aub, J. C. (1929). *J. clin. Invest.* **7**, 139.
Anonymous (1958). *Brit. med. J.* i, 567.
Aub, J. C., Bauer, W., Heath, C. & Ropes, M. (1929). *J. clin. Invest.* **7**, 97.
Baron, D. N. & Bell, J. L. (1957). *Clin. chim. Acta*, **2**, 327.
Bartels, E. C. & Haggart, G. E. (1938). *New Engl. J. Med.* **219**, 373.
Bauer, W., Albright, F. & Aub, J. C. (1929). *J. clin. Invest.* **7**, 75.
Baumann, E. (1896). *Munch. med. Wschr.* **43**, 309.
Bland Sutton, J. (1888). *J. comp. Med. Surg.* **10**, 1.
Burget, G. E. (1917). *Amer. J. Physiol.* **44**, 492.
Burns, C. M. (1933). *Biochem. J.* **27**, 22*P*.
Coop, M. C. (1958). *J. Amer. vet. med. Ass.* **132**, 299.
Coplan, H. M. & Sampson, M. M. (1935). *J. Nutr.* **9**, 469.
Crisp, E. (1864). *Trans. path. Soc. Lond.* **15**, 260.
Dickinson, C. D. & Scott, P. P. (1956*a*). *Brit. J. Nutr.* **10**, 304.
Dickinson, C. D. & Scott, P. P. (1956*b*). *Vet. Rec.* **68**, 858.
Fiennes, R. N. T-W. & Graham-Jones, O. (1960). *Proc. Zool. Soc.* **133**, 573.
Gershoff, S. N., Legg, M. A., O'Connor, F. J. & Hegsted, D. M. (1957). *J. Nutr.* **63**, 79.
Greaves, J. P. (1959). The nutrition of the cat: protein requirements and other studies. Ph.D. Thesis, University of London.
Greaves, J. P. & Scott, P. P. (1960). *Brit. J. Nutr.* **14**, 361.
Heitzmann, C. (1873). *Wien. med. Pr.* **14**, 1035.
Henderson, G. L. B. & Keywood, E. K. (1959). *Vet. Rec.* **71**, 317.
Hess, A. F., Gross, J., Weinstock, M. & Berliner, F. S. (1932). *J. biol. Chem.* **98**, 625.
Holmes, J. R. & Price, C. H. G. (1957). *Vet. Rec.* **69**, 1047.
Hou, H. C. (1940). *Proc. Soc. exp. Biol., N.Y.*, **43**, 753.
Klimek, M., Hrstka, V. & Bucko, A. (1957). *Čsl. Gastroenterol. Výživa*, **11**, 325.
Korenchevsky, V. (1922). *Spec. Rep. Ser. med. Res. Coun., Lond.*, no. 71.
Krane, S. M., Brownell, G. L., Stanbury, J. B. & Corrigan, H. (1956). *J. clin. Invest.* **35**, 874.
Latimer, H. B. (1939*a*). *Growth*, **3**, 89.
Latimer, H. B. (1939*b*). *Growth*, **3**, 435.
Luce, E. M. (1923). *J. Path. Bact.* **26**, 200.
McIntire, J. M., Schweigert, B. S. & Elvehjem, C. A. (1944). *J. Nutr.* **28**, 219.
McRoberts, M. R. (1958). The effects of certain dietary factors upon iodine utilization. M.Sc. Thesis, Purdue University.
Marine, M. D. (1914). *J. exp. Med.* **19**, 70.
Marine, M. D. (1915). *J. exp. Med.* **21**, 452.
Marine, M. D. (1922). *Physiol. Rev.* **2**, 521.
Marine, M. D. & Lenhart, C. H. (1909*a*). *Arch. intern. Med.* **4**, 253.
Marine, M. D. & Lenhart, C. H. (1909*b*). *Arch. intern. Med.* **4**, 440.
Mellanby, E. (1921). *Spec. Rep. Ser. med. Res. Coun., Lond.*, no. 61.
Mellanby, E. (1922–3). *J. Physiol.* **57**, ii.
Mellanby, E. & Mellanby, M. (1921). *J. Physiol.* **55**, vii.
Murray, I. (1923). *Brit. J. exp. Path.* **4**, 335.
Pottenger, F. M. & Simonsen, D. G. (1939). *J. Lab. clin. Med.* **25**, 238.
Remington, R. E. (1937). *J. Nutr.* **13**, 223.
Riser, W. H. & Schnelle, G. B. (1956). *J. Amer. vet. med. Ass.* **128**, 609.
Robertson, J. D. (1949). *Ann. R. Coll. Surg. Engl.* **4**, 3.
Schulze, E. & Hundhausen, G. (1939). *Arch. exp. Path. Pharmak.* **192**, 43.
Scott, P. P., da Silva, A. C. & Lloyd-Jacob, M. A. (1957). In *U.F.A.W. Handbook on the Care and Management of Laboratory Animals*, 2nd ed., p. 491. [A. N. Worden and W. Lane-Petter, editors.] London: UFAW.
Scott, P. P., Greaves, J. P. & Scott, M. G. (1960). *J. Reprod. Fertil.* **1**, 130.
Skeggs, J. W. & Theobald, J. A. (1957). *J. Amer. vet. med. Ass.* **130**, 450.
Spector, W. S. (ed.) (1956). *Handbook of Biological Data.* London: W. B. Saunders Co.
Stewart, C. P. & Percival, G. H. (1927). *Biochem. J.* **21**, 301.
Telfer, S. V. (1924). *Quart. J. Med.* **17**, 245.
Thompson, J. (1932). *J. Nutr.* **5**, 359.
Thompson, J. (1933). *Arch. Path.* **16**, 211.
Verzhikovskaya, N. V. (1957). *Vrach. Dyelo.* no. 10, p. 1067.
Waisman, H. A., Henderson, L. M., McIntire, J. M. & Elvehjem, C. A. (1942). *J. Nutr.* **23**, 239.



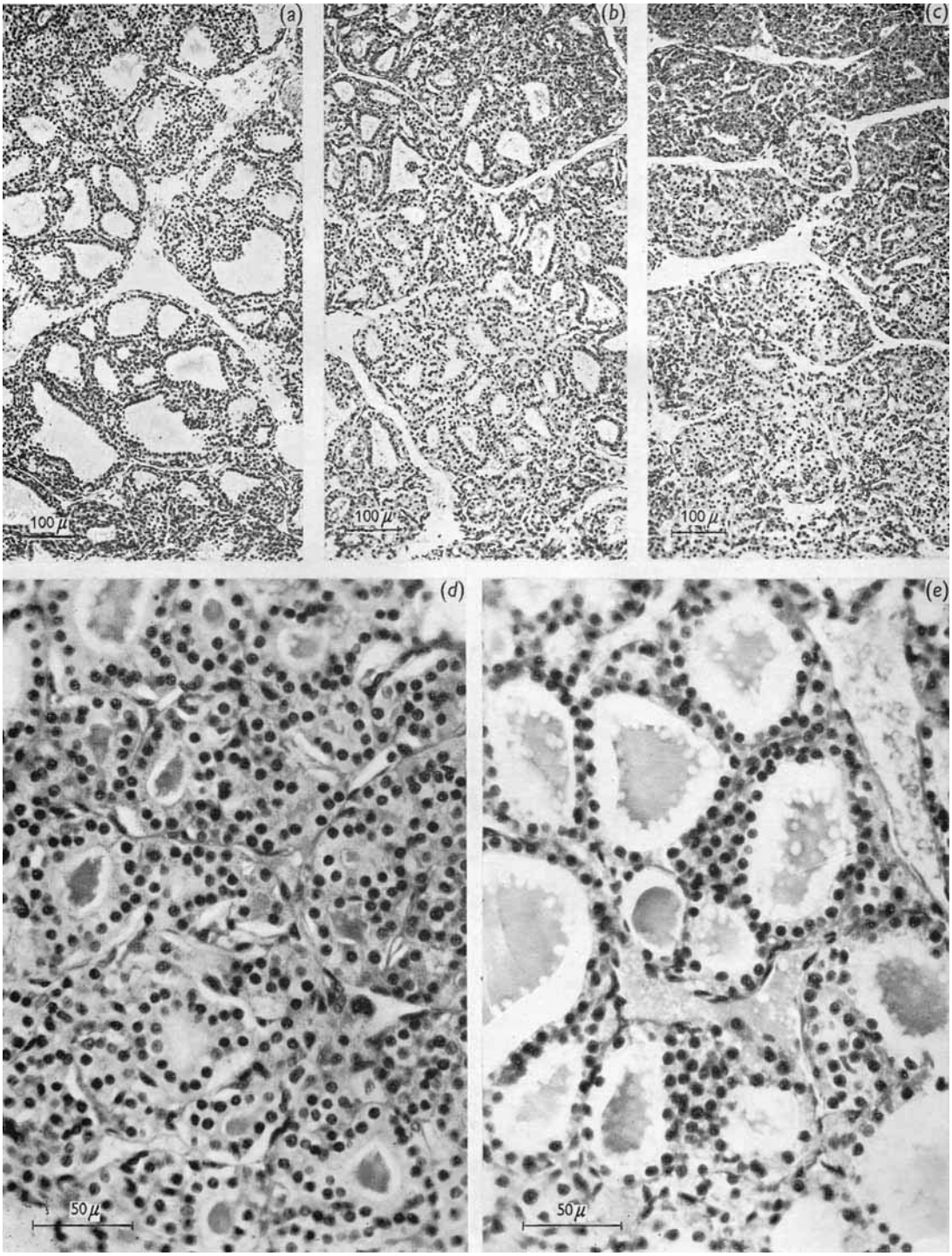




PATRICIA P. SCOTT, J. P. GREAVES AND M. G. SCOTT



PATRICIA P. SCOTT, J. P. GREAVES AND M. G. SCOTT



PATRICIA P. SCOTT, J. P. GREAVES AND M. G. SCOTT

Watson, C. (1904). *J. Physiol.* **31**, v.
Watson, C. (1906). *J. Physiol.* **34**, xxix.
Watt, B. K. & Merrill, A. L. (1950). *Handb. U.S. Dep. Agric.* no. 8.
Woolley, D. W. (1941). *J. biol. Chem.* **140**, 453.

EXPLANATION OF PLATES

Plate 1

(*a*) Kitten showing characteristic defects of posture and gait that result from a diet of raw heart. Note lumbar lordosis and plantigrade position of hind-limb.

(*b*) Lateral view of scapula of kitten (A_2) 7 months old, fed for 24 weeks on heart only, showing hyperaemia (dark areas).

(*c*) Scapula of kitten (A_3) 7 months old, fed on stock diet throughout.

(*d*) Anterior view of scapula shown in (*b*). Note curvature.

(*e*) Anterior view of normal flat scapula shown in (*c*).

(*f*) A radiograph of femurs of litter-mate kittens B_1 and B_2 fed on heart. Note increased formation of trabeculae in B_2, which had received Ca gluconate by injection for 11 weeks (Table 3).

(*g*) Radiograph of femurs of litter-mate kittens from Expt 3 (Table 4). C_2 and C_{26} fed on raw heart and stock diet, respectively, for 8 weeks; C_{13} and C_8 fed on cooked heart and raw heart, respectively, for 12 weeks both supplemented with Ca and vitamin A. Note reduced cortex of C_2 accompanied by an expanded marrow cavity. The bone is not deformed.

Plate 2

(*a*) Radiograph of eviscerated carcasses of kitten A_2 fed for 24 weeks on raw heart and A_3 fed on stock diet, both 7 months old. Note typical collapse of vertebral bodies in lumbar region of A_2 and rarefaction of its limb bones.

(*b*) Radiograph of partly dissected hind-limb of kitten A_6, 10 months old, fed on raw heart for 27 weeks. Note folded pathological fracture of distal metaphysis of femur and line of arrested growth at head of tibia.

Plate 3

Sections from femurs decalcified and stained with haematoxylin and eosin: *a* and *b* at proximal metaphyses and *c* and *d* longitudinal section through shaft: endosteum on right.

a and *c* from femur of kitten shown in Pl. 2*a*, fed on heart alone. *b* and *d* from femur of C_{13} shown in Pl. 1*g* fed on cooked heart supplemented with Ca and vitamin A.

Note reduction in trabeculae and cortical bone with increased fibrous connective tissue and osteoclasts in *a* and *c*. No evidence of rickets in either bone.

Plate 4

Sections of thyroids stained with haematoxylin and eosin.

a, *b* and *c*, litter-mate kittens A_4, A_6 and A_7 fed on raw heart for 24, 27 and 33 weeks, respectively. Note progressive loss of colloid followed by atrophic changes.

(*d*) Thyroid of kitten C_2 fed for 8 weeks on raw heart, showing hyperplasia, columnar epithelium of follicles and loss of colloid.

(*e*) Biopsy specimen from kitten fed on raw heart and Ca throughout for 40 weeks. Note the presence of colloid and cuboidal follicular epithelium.