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Severe undernutrition in growing and adult animals

1. Production and general effects

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Undernutrition has been under investigation by scientific methods for well over 100 years and there is a very large body of literature bearing upon it. It has been reviewed from various aspects, notably by Morgulis (1923), Jackson (1925) and Keys, Brožek, Henschel, Mickelsen & Taylor (1950). The second world war led to the effects of moderate and severe undernutrition in man being studied from numerous angles by Lamy, Lamotte & Lamotte-Barillon (1946*a–f*), Hottinger, Gsell, Uehlinger, Salzmann & Labhart (1948), a group of workers from the Medical Research Council (Medical Research Council, 1951), and by Helweg-Larsen, Hoffmeyer, Kieler, Thaysen, Thaysen, Thygesen & Wulff (1952). The present experiments concern the immediate and delayed effects of prolonged undernutrition in growing animals. Aron (1911) was responsible for some excellent pioneer work along these lines on puppies, and it was followed by much more systematized experiments on rats by Osborne & Mendel (1914, 1915), McCay, Crowell & Maynard (1935) and Jackson (1937). The interest of these workers and the significance of their results have centred upon the effects of the severe and extended undernutrition upon the ultimate size of the animals and upon their total life span. Some results have also been obtained with a bearing upon the gain of weight per unit of food consumed by the animals when they were allowed to eat their fill. No work of this kind seems to have been done on pigs or poultry and these are the animals which have been used for the current work. Interest in farm animals has been confined mostly to the production of optimum diets for market purposes, but some important studies have been made of how the shape and quality of carcasses can be modified by feeding at a high or a low plane of nutrition throughout the growth period (Moulton, Trowbridge & Haigh, 1921, 1922*a*,*b*). Experiments on pigs were carried out by McMeekan (1940*a–c*, 1941) in which the planes of nutrition were reversed after a certain length of time, and Hammond (1952) has been responsible for much of this and other good work of a similar nature. The results of all these and other authors will be quoted as they bear upon specific observations which have been made in the current investigations. Almost no work seems to have been done on the functional effects of severe undernutrition, and the experiments presented here were planned to make good this deficiency, but so much work of an anatomical and structural nature has had to be done first that the more physiological studies have had to be postponed, and are only now being taken in hand.

METHODS AND RESULTS

Animals and methods

The animals used have been Rhode Island Red cockerels and cross-bred pigs. The former are cheaper and provide results more quickly than the latter, but the information obtained from them can only be applied with caution to mammals, for in some respects the results for the two species have not been the same. This divergence has increased the scope and interest of the investigation as a whole.

Poultry. The cockerels were obtained from a local hatchery as day-old chicks and reared for a few days in the usual way on a commercial food designed for birds under about 8 weeks of age. By laboratory analysis, this diet had the composition given in Table 1. It seemed quite satisfactory in all the earlier work, but possibly contained only the marginal amounts of manganese and choline necessary for satisfactory growth,

Table 1. *Composition per 100 g of the standard rations for pigs and poultry*

	Meal mixture	Pig 'pellets'	Chick 'crumbs'
Protein (g)	14	23	19
Fat (g)	3	9	4
Carbohydrate (approx.) (g)	65	55	61
Calcium (mg)	730	1790	1620
Phosphorus (mg)	840	119	87
Sodium (mg)	—	252	199
Potassium (mg)	—	757	761
Magnesium (mg)	—	142	205
Iron (mg)	—	32	17
Chloride (mg)	—	330	390

for some of the birds in two experimental groups developed perosis or 'slipped tendon' when they were being rehabilitated. The day-old birds were placed in an army trailer, which had been purchased as surplus stock. It was warmed electrically and the temperature control was set at 27°, but owing to the large surface of the trailer this temperature was not strictly maintained on very cold nights or hot sunny days. When the birds had reached a weight between 90 and 100 g they were separated into two groups. Those to be well nourished were given as much water and food as they cared to take, and no change was made in the composition of the latter for the whole of their lives. They were moved to an unwarmed brick building with a ceiling, which had once been a stable, when they were ready for the change. There they were confined in wire enclosures provided with metal shelters at one end.

The birds to be undernourished were kept communally in a wooden box. In addition to the general warmth of the trailer they were provided with a source of radiant heat over their heads. This additional heat could be switched on or off without reference to the thermostatic control, but it was in fact only dispensed with during warm days. The birds always had access to water, and they were fed individually twice a day in another box fitted with small partitions so that a number could be fed at once. They were given the same food as the birds being well nourished but in amounts which permitted no gain in weight or only a trifling one. For a bird of

150 g, 8–10 g of food/day was about the right amount. A well-nourished rapidly growing bird of this weight took about 60 g/day.

All the birds were weighed once a week. When mature or semi-mature birds which had so far been fully fed were to be undernourished their food was restricted till they were losing weight at the rate desired. After a time they were moved from the old stable into the warm trailer, and kept there till they were ready for the experiment planned for them.

When birds that had weighed between 150 and 190 g when they were 6 months old were to be allowed to grow as fast as possible, they were fed three times a day to the capacity of their crops as judged by palpation. After about 2 weeks of this regime they were given food *ad lib.*, and by that time had already almost doubled their weight.

Pigs. The pigs were bred on the laboratory farm and were originally a cross between a Large White boar and an Essex sow, but the subsequent generations of sows were nearly always mated with Large White boars so that the characteristics of this breed predominated in the experimental animals.

The animals to be well nourished were provided with 'creep' feeding about half way through lactation, and weaned at the usual time. The diet in the creep and throughout their experimental lives consisted of wheat offals 1, barley meal 5, maize meal 2 and fish meal 1, parts. It had the organic composition, by laboratory analysis, given in Table 1 and was supplemented with a little cod-liver oil. The animals were fed three times a day at 8 a.m., 2 p.m. and 8 p.m. and given as much food as they chose to eat. They were housed in wooden huts 7 by 6 ft with wooden floors about 5 in. above the ground opening into small concrete enclosures 7 by 10 ft open to the air and sun. One, two or three pigs could be, and sometimes were, kept in each of these.

In the first experiments pigs to be undernourished were removed from the sow and creep for a progressively longer time each day towards the end of lactation, and weaned on to the diet just described in very restricted amounts, so that their weights remained almost or quite stationary for long periods of time. This procedure stabilized the weights at 7–15 kg. In more recent experiments the piglets have been undernourished from a much earlier age and they have been weaned at 7–14 days on to a commercial pelleted food with the composition, by laboratory analysis, shown in Table 1. This procedure made it possible to stabilize their weights at 4–5 kg. After some weeks they were gradually changed to a diet consisting of equal quantities of the pellets and the standard dietary mixture described above made up in water, and each received about 45 g/day with a little cod-liver oil. All the undernourished piglets were fed individually three times a day at 8 a.m., 2 p.m. and 6 p.m. or later.

The larger undernourished animals were housed in a wooden hut similar to the ones used for the well-nourished pigs. It was provided with two doors and two small external runs 1 × 1·5 m in size. It was fitted with a partition and a false roof about 1 m from the floor, which could be removed for cleaning purposes. Heating elements were installed in this roof but there was no thermostatic control. The smaller undernourished piglets have been kept in insulated boxes 1 × 1 × 0·5 m raised about 0·5 m from the ground, with thermostatically controlled heating and a small run with a wire roof 1 × 1 m which could be opened or closed to them by an insulated door. These pens were kept in an unwarmed brick building and the temperature inside them maintained at about 24°. All the accommodation for the undernourished pigs was cleaned out every day.

When they were to be allowed to grow as fast as possible the amount of food given at each meal was increased steadily and the meal mixture without pellets was usually being given *ad lib.* in 2–2½ weeks. By this time the animal had already gained as much as 4 or 5 kg.

Rearing difficulties. Parasites and infectious epidemics have not been troublesome in the experiments on the cockerels, but worms have been a source of trouble in the work on piglets and undoubtedly caused some deaths. All the pigs on the farm probably carry a few round-worms, and most of the piglets become infected within a few days of birth, but all this passes unnoticed in rapidly growing and healthy animals. When the growth of the pigs was prevented by undernutrition, it did not prevent the growth of their parasites, and the intestines of some of these small animals were found after death to be filled with mature and fully grown worms. The effects attributable to worms appeared mainly to be great abdominal distension and sometimes nausea and a distaste for food. In the undernourished animals the last was rapidly fatal. One pig which died suddenly was found to have one end of a large worm in the bile duct. The trouble has been largely overcome by early weaning and by giving Coopane (piperazine adipate, Cooper & McDougall Ltd) tablets in twice the recommended dosage for 1 week and repeating this course of treatment in 2 or 3 weeks' time so long as the animals remained undernourished. Gastro-intestinal infections have not so far been a serious cause of trouble. One of them, however, carried off four out of a group of eight animals at an early stage of their period of deprivation, but the other four survived and two of them were among the most satisfactory in the undernourished series. When they had been undernourished for from 10 to 12 months, weighed about 5 kg and appeared to be in good shape, four of the animals developed an extensive *prolapsus ani* which could be replaced temporarily and appeared to cause the animals no pain. The animals were killed without attempting any surgical treatment and only one had any round-worms in its gut. The general state of the hair and skin made the undernourished pigs want to scratch, which led to the loss of several from superficial abrasions followed by infections of various parts of the body, e.g. the cornea. The wastage has largely been prevented by lining all the walls of the pens and runs with smooth sheet aluminium and by rubbing the skins with Lanette Wax Cream which has seemed to make the skin less harsh and irritable.

Cold has been the cause of most of the fatalities. It was not realized at first how very susceptible undernourished animals are to a fall in temperature and, although precautions were taken, they were not sufficient to prevent further losses. Pigs which succumbed to cold were generally found in the morning lying near an opening, not up against the source of heat or huddled up with the others which might have kept them warmer (Mount, 1959). They may have been driven to lie there because they were the weakest, but sometimes these animals were housed alone. The cockerels too were found as a rule outside the circle of radiant heat. They were usually not dead and, like the pigs, could sometimes be revived by warming them up and then giving them additional food (Rogers, 1919; Morgulis, 1923).

Pigs kept for a long time at a steady weight sometimes became very much weaker without warning and even unable to walk. They retained their appetites, and a little extra food for a few days restored them. This happened several times to a boar pig which weighed 13·5 kg when he was 2 years old and ultimately grew into a large animal.

Treatment after death. When the animals were killed or died without warning or illness they were brought to the laboratory where they were dissected, the organs weighed and parts of the tissues removed for chemical examination. If animals had been ill for a short time or had died from worms, their bones, skulls and beaks or teeth were taken but not the soft tissues. The results of the more detailed and chemical examinations of the liver, skeletal and cardiac muscle, skin and bones will be reported in subsequent communications. Generally speaking, each result was appraised by comparing it with the appropriate ones made (*a*) on an animal of the same size (but much younger), and (*b*) on an animal of the same age (but much larger). Both comparisons were helpful even though it meant using more animals.

Effects of undernutrition

Appearance and behaviour

Pigs. By the time a pig had been undernourished for some months it had changed greatly in appearance. It had usually lost most of its hair, and it was noticed that the black parts of the skin in one litter which was the result of a cross back to an Essex boar lost their hair first. When hair grew again, as it did (Jackson, 1932), it was fine but subsequently became coarser if it was not abraded. In the later stages of undernutrition the pigs sometimes had long coarse hair, not unlike that of a mature pig, and a general appearance of age, so that they looked like 'little old animals'. A photograph of one such pig has been published (McCance & Widdowson, 1955). The skin of the back and legs, but not of the abdomen, was usually crusted over with what appeared to be dry keratinous material and if the piglets succeeded in finding a surface on which they could rub themselves they scratched unceasingly. Sections of the skin (Pl. 1 *a*, *b*) showed considerable hyperkeratosis. Some of the shed epithlium was not completely keratinized and contained degenerate nuclei (parakeratosis), and a number of the follicles contained plugs of keratinized cells. There was also an increase in the prickle cell layer (acanthosis) and prolongation of the rete pegs with a moderate number of cells in mitosis. A few dyskeratotic cells were also to be seen. The corium was oedematous, particularly in its upper third, and contained some plasma cells, histiocytes and occasional polymorphs. The black parts of the skin lost some of their pigment. One group of eight piglets was kept very warm and survived without loss for some months. They always lay very close together, and their skins were usually moist and slimy when their cage was opened, although pigs are thought not to sweat (Robinson & Lee, 1941). Their skins did not become crusted to the usual extent.

The appearance of the skins gave the undernourished pigs a very abnormal appearance, which became progressively more so until they were allowed unlimited food. The lesions then gradually cleared up over a period of some months, and the skins of pigs that were allowed to mature after a year or two of undernutrition appeared to be normal. Slight para- and hyper-keratosis with acanthosis and inflammatory changes were still visible microscopically.

The superficial crusting and appearance of hyperkeratosis was reminiscent of the changes induced in human skin by a deficiency of calories (McCance & Barrett, 1951). Since hyperkeratosis and other skin lesions have been attributed to vitamin A deficiency the livers of twelve pigs, which had been treated in various ways, were submitted to the Dunn Nutritional Laboratory for vitamin A analysis and the results are given in Table 2. The livers of normal pigs on the diets described contained 65–130 i.u. vitamin A/g, whereas those of the undernourished pigs usually contained considerably more (100–800 i.u./g). The livers of two pigs, which were being given unlimited food and growing rapidly after a long period of undernutrition, contained low normal amounts of the vitamin. The changes in the skins are being further investigated, in particular the possibility that they are due to a deficiency of zinc in the ration (Lodge & Lucas, 1959).

Table 2. *Concentration of vitamin A in the livers of well-nourished, undernourished and rehabilitated pigs*

Treatment	Age (months)	Weight at death (kg)	Vitamin A (i.u./g)	Vitamin A (i.u./liver)
Normal	0·8	5·1	120	21700
Normal	1·1	8·0	130	39000
Normal	2·0	20·9	65	51400
Normal	14	209	70	165000
Undernourished	15	12·7	370	140000
Undernourished	9	6·7	620	87500
Undernourished	11	5·7	800	188000
Undernourished	13	8·0	146	40700
Undernourished	10	5·0	760	61600
Undernourished	10	3·6	87	10600
Undernourished then rehabilitated	23	209	60	200000
Undernourished then rehabilitated	17	55	40	51800

The undernourished animals did not as a rule carry themselves on their toes as pigs normally do. Some stood and walked 'on their heels' and even with their toes raised off the ground. In spite of the general standstill of growth, keratin continued to be formed and their nails became very long (Pl. 2*a*). Their voices changed from the usual grunt to something more like a croak. For a month or two they became excited at feeding time and sometimes they sucked vigorously at the tail and even the penis of another animal till it became quite swollen, but they never showed any signs of cannibalism and when there was nothing to disturb them they lay quietly as a rule in the darkness of their insulated cage and did not display the activity which is such a feature of undernourished rats. One or two animals became oedematous, and collections of fluid were found under the skin, but the others never showed signs of pitting oedema.

Poultry. The cockerels lost most of the feathers from their body and became almost naked, but they developed a few weak wing feathers and some longer ones on the thigh (Pl. 2*b*). They went on forming keratin, for their claws continued to grow. Their skins never became crusted like those of the pigs. There was probably some slight hyperkeratosis in the undernourished birds, but no other changes like those seen in the pigs. This was partly due, perhaps, to the structure of fowl skin: dense collagen in the papillary layer of the corium lying upon a panniculus of muscle. More extensive observations upon the histological changes in the skin of the undernourished birds are being made. Their beaks increased in size, which gave the heads of the birds the appearance shown in Pl. 2*b*. Sometimes the upper half of the beak grew longer than the lower half and curled down beyond it in front. If the animals were then given unlimited food, sooner or later the overhang disappeared and this was certainly due sometimes to its breaking off.

The birds were never at rest. They appeared to spend all their time pecking at the empty food trays and flooring. This activity was partly due to the fact that the lamp which provided the birds with additional warmth was luminous. When it was replaced by an infrared lamp they seemed to keep much more quiet.

Oedema has only been noted in one bird, and in this one both feet became very swollen. No cause other than undernutrition was discovered but there may have been one.

Weight and size of organs (pigs)

The liver, heart, kidneys, spleen, stomach, small intestine, brain, adrenals, thyroid, testes and pancreas were weighed in undernourished animals and in well-nourished animals killed for the purpose when they were the same weight. One or two of the hearts were slightly enlarged, but, except for the spleen, the brain and the adrenal glands, the results for other organs were similar when expressed as a percentage of the body-weight (Aron, 1911; Jackson, 1925; Keys *et al.* 1950). The spleens of four undernourished animals were all below 0·1% of the body-weight and averaged 0·077%. The spleens in four paired controls of the same size averaged 0·27% of the body-weight. The brains of the undernourished animals were larger than those of well-nourished animals of the same body-weight. The adrenal glands were larger in the undernourished animals than in the paired controls and the two glands together averaged 0·052% of the body-weight in seven animals against 0·019% in five healthy paired controls. Hypertrophy of these glands has been recorded in starvation and undernutrition in man, but not consistently so (Keys *et al.* 1950).

Erythrocytes and haemoglobin (pigs)

Cell counts and haemoglobin determinations were made on the blood removed from seven undernourished animals and from various controls of the same size and of the same age. Table 3 shows that there were fewer erythrocytes in the circulating blood than in animals of the same age, but that there was more circulating haemoglobin than in healthy animals of the same size who are, as is well known, often anaemic. The white blood cells require no comment.

Serum urea (pigs)

No formal tests of renal function have so far been carried out, but from time to time determinations of the concentration of urea and creatinine have been made in the serum of undernourished pigs. These figures for creatinine have ranged from 1·2 to 1·8 mg/100 ml and for urea from 34 to 60 mg/100 ml. They may be regarded as normal but the small amount of food provided for these piglets meant a small intake of water, and it was often difficult to induce the piglets to take more. The slightest diarrhoea or refusal of food has on occasion raised the concentration of urea in the serum to 90 or 100 mg/100 ml. The concentrations of urea in the urine at such times have ranged from 3·51 to 4·23% and there is no reason to think that the kidneys of these animals have ever been functionally abnormal, and with recovery and rehydration the serum concentrations have returned to the normal range. The concentrations measured in the serum of rehabilitated and of a few normal pigs of 10–20 kg have also been found to lie between 33 and 50 mg/100 ml.

Table 3. *Effect of undernutrition on the erythrocytes, white cells, haemoglobin and haematocrit of pigs*

Description	Erythrocytes ($10^{-6}/mm^3$)	White cells ($10^{-3}/mm^3$)	Haemoglobin (g/100 ml)	Haematocrit (g)	Mean red cell diameter (μ)	Mean red cell volume (μ^3)
Undernourished: mean	5·68 (7)	7·7 (3)	10·2 (7)	27·5 (4)	6·3 (6)	61·0 (4)
range	3·38–8·47	5·3–9·0	6·4–12·2	24·0–32·0	5·6–7·2	50·5–71·0
Well-nourished animals of same weight: mean	5·75 (1)	9·0 (5)	7·4 (5)	29·9 (5)	5·8 (5)	78·2 (1)
range	—	7·0–12·0	5·0–10·2	22·0–45·0	5·7–6·0	—
Well-nourished animals of same age: mean	9·97 (4)	12·0 (1)	15·4 (4)	49·4 (4)	5·7 (1)	47·4 (3)
range	8·13–10·85	—	13·4–16·9	45·4–54·5	—	43·9–51·6

Figures in parentheses are the numbers of animals investigated.

Bones

Aron (1911) noted that bones continued to grow in young undernourished dogs even if their weight was almost stationary. This observation has been confirmed in other animals (Thompson & Mendel, 1917–18; Jackson, 1925). The present experiments have brought out this aspect of undernutrition again, and also the changes which may take place in the proportions of the skeleton. The femur and humerus have been removed for the examination of their chemistry and structure and reports will be made upon them later.

The proportions of the individual bones and bony structures in undernourished animals may differ considerably from those in animals of the same weight. Thus the femur of the cockerels became too long for its thickness and in most undernourished pigs the thickness:length ratio of the humeri changed in the opposite direction. The changes in the pig bone may have been due to age (McMeekan, 1940*a*). The growth of some parts of the skull was not interfered with to the same extent as that of others. The molars of the pigs continued to appear although there was no room for them in the jaw, and X-ray photographs showed them to be impacted. Diagrams of such a skull were given by McCance & Widdowson (1955), and more impressive ones have since been examined. The skulls of pigs and cockerels have been preserved for further examination. The fourth, fifth, sixth, seventh and eighth thoracic vertebrae, and the sixth right rib were removed from the pigs and measured. During undernutrition the vertebrae increased in length in a head–tail direction, but their diameter from front to back did not change consistently and neither did the lengths of the spinous processes. During undernutrition the ribs continued to grow in 'length' (Hammond, 1932), but some resorption of the edges of the bone must have gone on at the same time, for the ribs at death were 'thinner' than in animals of the same weight which had suffered no nutritional setback. The shape of the bow, i.e. the 'length':'spring' ratio (Hammond, 1932) did not change, so the undernourished animals had a larger thoracic cage.

Rehabilitation

In general, as already stated, the administration of unlimited food abolished the abnormal appearance and characteristics of the animals whose growth had been held up even for long periods, but some new effects were observed. Once the animals had begun to eat freely they gained weight very rapidly, but not as a rule quite so rapidly as the controls. Curves similar to those given by McCance & Widdowson (1955) for the gains in weight of cockerels after prolonged undernutrition have been obtained several times. Fig. 1 shows the growth curves of two female litter-mate pigs, one of which had been held at a weight below 7 kg for over a year. Fig. 2 shows the growth curves of two female pigs and of a male litter-mate held at a weight of about 14 kg for nearly 2 years. Similar, intensely rapid, growth has been observed by Ferry (1913), Thompson & Mendel (1917–18) and Jackson (1937) in mice and rats and by Morgulis (1923) in salamanders. Most previous workers on rehabilitation (Aron, 1911; Jackson, 1925, 1937; Clarke & Smith, 1938) came to the conclusion that animals undernourished for long periods never attained the full size of their litter-mates which had been allowed to grow freely from birth. Fábry & Hrůza (1956) and Hrůza & Fábry (1957), however, found that the administration of growth hormone allowed them to do so. The present experiments were not planned to study the final size of animals that had been undernourished, but it was found that some birds which were rehabilitated for 27 weeks ceased to gain weight after a further 20 weeks. At this time they averaged 2·7 kg. Brood-mates reared normally for the whole of their lives did not cease to gain weight until they had reached about 4 kg.

Proportions of the body. The only dog which Aron (1911) rehabilitated became very fat, but Jackson (1937) did not comment upon this obesity in rats and reported that rehabilitation restored the normal proportions of the body and its organs. The work of Hammond (1952) and McMeekan (1940*a–c*; 1941) led us to expect that rehabilitation of pigs after a prolonged period of undernutrition would lead to the production of very fat animals and that the same would apply to poultry. It has not altogether been so and the reason may have been that McMeekan's male pigs were castrates, but these cockerels and male pigs were not. The fat in the rehabilitated cockerels has not been measured and quantitatively compared with that in the controls, but it has

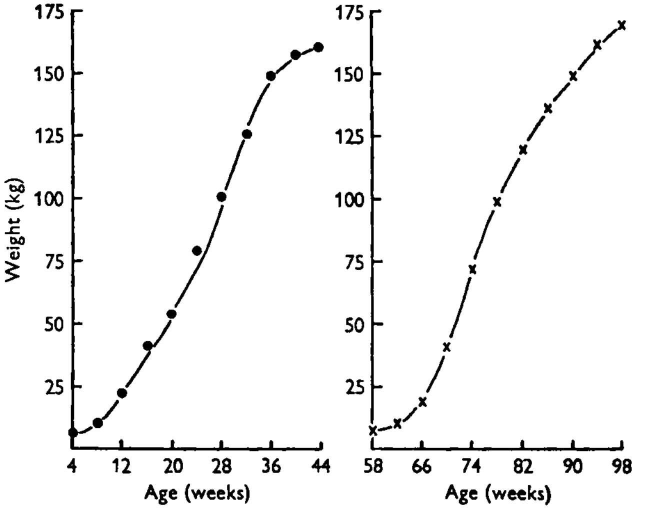

Fig. 1. Comparison of the weight increase of a female pig on full diet from birth (●—●) and of her female litter-mate after being held below 7 kg for a year by restriction of diet (×—×).

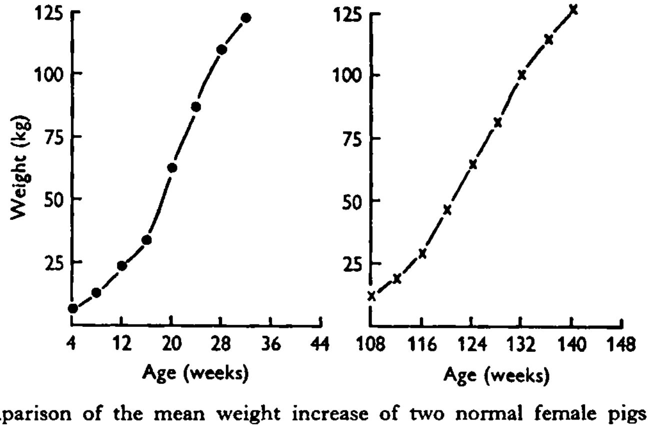

Fig. 2. Comparison of the mean weight increase of two normal female pigs on full diet from birth (●—●) and of a male litter-mate after being held at a weight of about 14 kg for nearly 2 years by restriction of diet (×—×).

not been greatly increased. The fat was carefully measured after death according to Hammond's (1952) technique in two gilts and three boars, and compared with that in animals of the same size (sometimes litter-mates). All the pairs had had unlimited amounts of the same kinds of food during the period of growth. The results are shown in Table 4. The gilt killed at 54·5 kg was inordinately fat, but not so the other animals. Measurements of the specific gravity of the carcasses of the third pair of animals indicated that the normal one contained 43% of fat, the rehabilitated one only 12%.

Shape of the ribs (pigs). McMeekan (1940*c*) reported that a high plane of nutrition following a low one increased the 'spring' of the ribs and made them more bowed, but stated that one of his animals had some curvature of the spine which may have accentuated the findings in that particular specimen. Measurements have been made of the ribs of the rehabilitated animals and the findings for them and for their controls are given in Table 5. The ribs of the animals being rehabilitated were certainly on

Table 4. *Effect of undernutrition and rehabilitation on the body length and fat measurements of pigs, obtained as described by Harrington & Pomeroy* (1954–5)

	Animal			Fat measurements					
							Rump		
Pair no.	Normal (N) or rehabilitated (R)	Body-weight (kg)	Sex	'Body' length* (mm)	Shoulder (mm)	Mid-back (mm)	1 (mm)	2 (mm)	3 (mm)
1	N	50·9	♀	655	32	13	22	12	15
	R	54·5	♀	657	48	30	62	45	51
2	N	200	♀	944	65	35	55	51	51
	R	209	♀	1038	75	46	66	55	72
3	N	20·9	♂	354	25	6·5	12	7	13
	R	18·4	♂	462	16	5·5	6	4·5	4
4	N	36·8	♂	551	34	9·8	19	12	20
	R	36·4	♂	570	24	9	14	12	11
5	N	159	♂	905	64	36	50	39	50
	R	160	♂	993	64	22	48	50	53

* Measured from the symphysis pubis to the top (anterior) end of the sternum.

Table 5. *Effect of rehabilitation on the weight and shape of the sixth right rib of pigs*

Animal			Rib					
Normal (N) or rehabilitated (R)	Body-weight (kg)	Sex	Weight (g)	Circum-ference length (cm)	Greatest thickness* (cm)	'Length' (cm)	'Spring'* (cm)	Ratio 'length': 'spring'
N	50·9	♀	23·3	16·5	1·73	14·2	4·43	3·21
R	54·5	♀	14·4	17·4	1·48	12·7	5·40	2·35
N	200	♀	68·0	25·3	1·82	20·4	6·12	3·33
R	209	♀	66·7	23·8	1·90	19·6	7·16	2·74
N	20·9	♂	8·9	11·6	1·41	9·93	3·16	3·14
R	18·4	♂	6·5	12·4	1·32	8·68	4·09	2·12
N	36·8	♂	15·4	15·3	1·64	12·75	4·18	3·05
R	36·4	♂	14·8	15·5	1·25	12·27	4·37	2·80
N	159	♂	59·7	20·8	1·96	16·2	6·20	2·62
R	160	♂	60·6	22·2	2·17	16·7	6·58	2·54

* See Hammond (1932).

the whole lighter, 'thinner' and longer round the circumference than those of their controls. They were also more bowed as indicated by the 'length' and 'spring' and the ratio of the two.

Vertebrae (pigs). Measurements of the length in a head–tail direction and of the diameter from front to back were made on the thoracic vertebrae of three male and two female pigs, and their controls. In the rehabilitated male animals and the large female animal the vertebrae were longer than in their controls, but in the small female the mean length was the same as that in the control. These findings are in agreement with the length of the carcasses of these animals shown in Table 4, and the inconsistency with the small female was most probably due to the animal's being so fat that it was unduly heavy for its length. The diameter of the vertebrae from the rehabilitated animals did not differ consistently from that of their controls.

Food conversion. Thompson & Mendel (1917–18) found that the amount of food required to promote unit gain of weight during the rehabilitation of their mice was less than it was during normal growth. Figures given by Aron (1911) show that it was not true of his dog, but it was a very fat animal and, therefore, would require more food per unit of weight increment than a lean one. Jackson (1937) found that the food required to maintain constant weight in undernourished rats declined as they grew older and his graphs and figures show that the rats that had been undernourished never raised their intake of food as high as that of the control animals yet they grew for a time as fast or faster. Jackson did not comment upon this himself. It has only been possible to make a few observations of this matter in the poultry and pigs and these are given in Table 6. They do not demonstrate more economical food conversion

Table 6. *Effect of undernutrition upon subsequent rate of growth and food conversion*

	Range of weight investigated		Normal (growing) animals		Animals being rehabilitated	
Animal studied	Initial (kg)	Final (kg)	Time taken to gain weight (days)	Food eaten (kg)/kg gain in weight	Time taken to gain weight (days)	Food eaten (kg)/kg gain in weight
Chicks: batch 1	1·2	2·0	28	7·8	38	7·2
batch 2	0·4	1·0	25	3·5	30	3·5
Pigs: 1	27	46	21	3·7	28	3·8
2	46	92	60	7·2	70	6·8
3	68	114	45	4·0	42	4·4

during rehabilitation, but the numbers are very few and in pigs involve only three animals. The figures show, moreover, that the rates of growth were not quite so rapid after undernutrition as they were during uninterrupted growth.

Sexual appearance and development. It has been shown before (Jackson, 1937) that severe and protracted undernutrition in a growing animal was not incompatible with satisfactory reproduction after rehabilitation. The experiments now being described have added little to this generalization. The cockerels appeared normal when they were allowed to mature and one of them mated with a pullet which had been sent in error, undernourished for 6 months and then rehabilitated. Fertile eggs were laid. The boar pig which was allowed to reach sexual maturity after being held below 14 kg for 2 years was not able to serve gilts on heat because of the weakness of his back legs. He was taken to the Unit for the Physiology of Reproduction in the University of Cambridge where a sample of semen was obtained when he weighed about 130 kg. Its volume was 100 ml and it contained 25 ml of jelly from Cowper glands, and 23·6 million spermatozoa, with normal activity, per ml. It was concluded that his reproductive capacity was normal, and the 'weakness' of his legs was found at death to be due almost certainly to a subacute form of swine erysipelas which had attacked the main joints of both his front and back legs, and must have given rise to considerable pain. Several other well-nourished animals in the herd have been affected in a similar way.

Soon after the first gilt was allowed to have unlimited food and to grow rapidly it was noticed that the vulva was becoming swollen. This swelling became very conspicuous and persisted throughout the whole growth period. It was beginning to subside when the animal was killed at a weight of 209 kg. Thus it was difficult to see when the animal was ready for the boar, and she never became pregnant in spite of several attempts to make her so by normal mating and artificial insemination. After death she was found to have perfectly normal ovaries containing fairly recent corpora lutea, and a normal reproductive tract. The second gilt to be rehabilitated reacted in just the same way and Pl. 3*a* shows the appearance of her vulva when she herself weighed about 23 kg. Pl. 3*b* shows the vulva of an animal of the same size that had never been undernourished. The photography and reproduction were standardized and the pictures are strictly comparable as regards size. This animal was killed at a weight of 54·5 kg. One of her ovaries contained some cystic follicles, but otherwise no abnormalities, macroscopic or microscopic, were found in the internal parts of the reproductive system. Other female animals that have been rehabilitated have also had large vulvae but not such enormous ones as the first two.

It is impossible to say as yet if this enlargement of the vulva is the analogue of the gynaecomastia reported by a number of authors in prisoners of war and other undernourished persons who were being rehabilitated (Keys *et al.* 1950). Preliminary observations suggest that a local accumulation of subcutaneous adipose tissue was a factor, but there was also considerable hyperplasia of the vulval apocrine glands (Pl. 4*a*, *b*); and this, together with the cystic ovaries, indicates that there may have been premature and unbalanced production of follicle-stimulating hormone by the pituitary. Further work is needed to establish the precise cause of the swelling.

DISCUSSION

These experiments were suggested by observations made in the years just after the second world war, and were undertaken to extend our knowledge of undernutrition and its sequelae.

The work has taken a long time owing to inexperience and technical troubles. It has shown among other things that the pig is a valuable experimental animal for the study of undernutrition. It has normally a very rapid rate of growth, which magnifies the effect of growth, yet it has many resemblances to man and it can be weaned very early and studied during what is normally the suckling stages of development. The findings on the bones and teeth, and on the soft tissues and other physiological aspects of this work, will be reported separately.

SUMMARY

1. By reduction of food young pigs were held at weights of 4–14 kg for 1–2 years. Cockerels were held between 100 and 200 g for 6 months.

2. The skins of the pigs became highly abnormal in the absence of a vitamin A deficiency. The cockerels did not develop adult plumage, but the skin remained normal.

3. Normal growth and differentiation of the heads and bodies was prevented and led to changes of many kinds. The teeth, for example, continued to develop and impacted in the undeveloped jaw. The nails and beaks continued to grow.

4. The adrenals became unduly large for the weight of the body, the spleens unduly small.

5. The pigs were not anaemic.

6. During rehabilitation on unlimited rations: (*a*) food conversion was about normal and the increase of weight very rapid, (*b*) the abnormal appearances gradually disappeared, but (*c*) the vulvae of the female pigs became very swollen long before the animals attained sexual maturity and remained so. An examination of the internal organs at this stage revealed nothing abnormal that could account for the swelling except small cystic follicles in one ovary. The swelling was partly fat, but mainly hyperplasia of the vulval apocrine glands.

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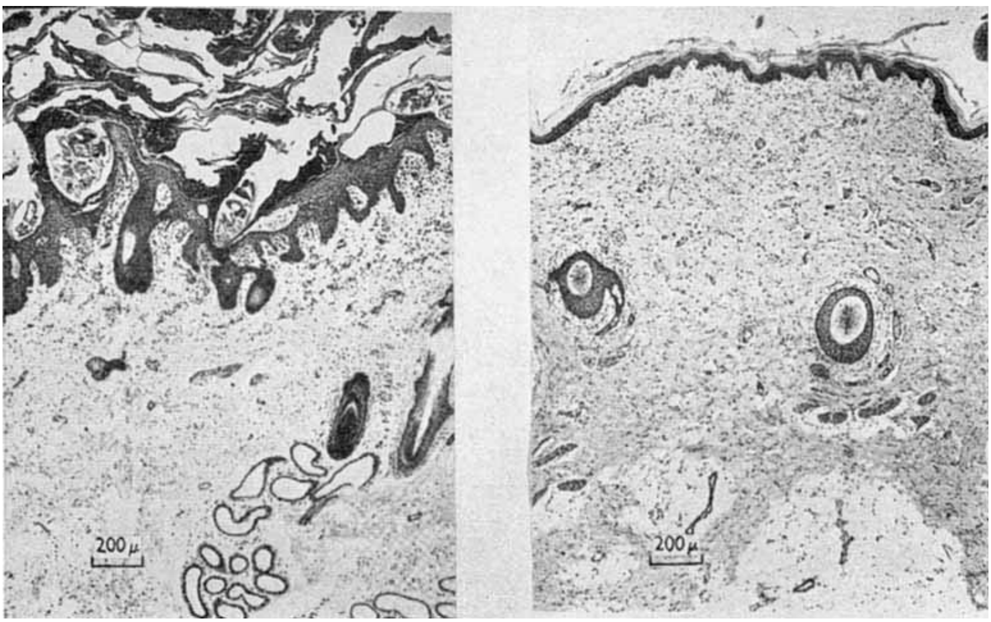
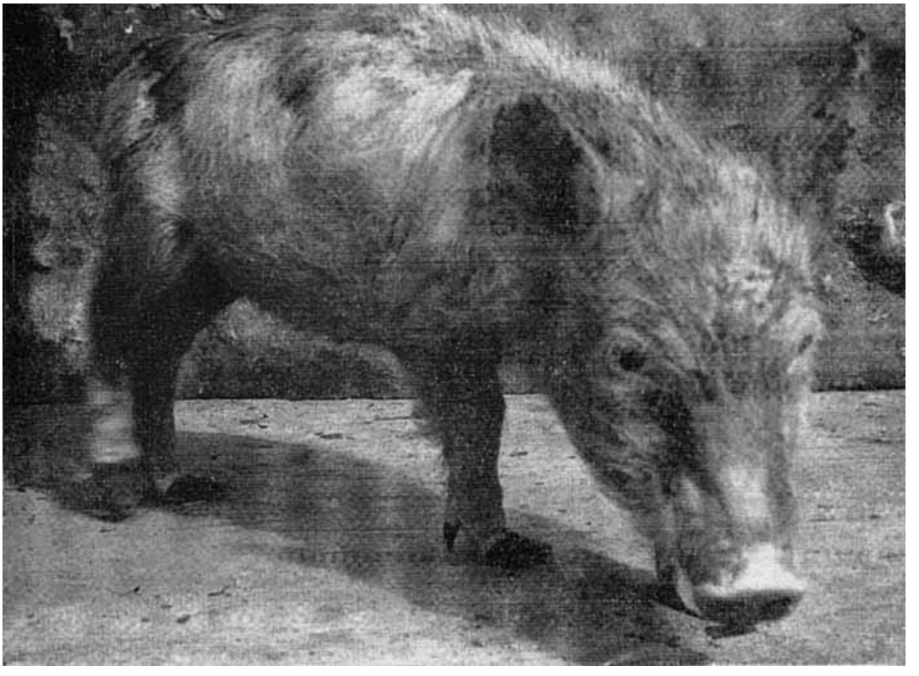


a *b*

R. A. McCANCE



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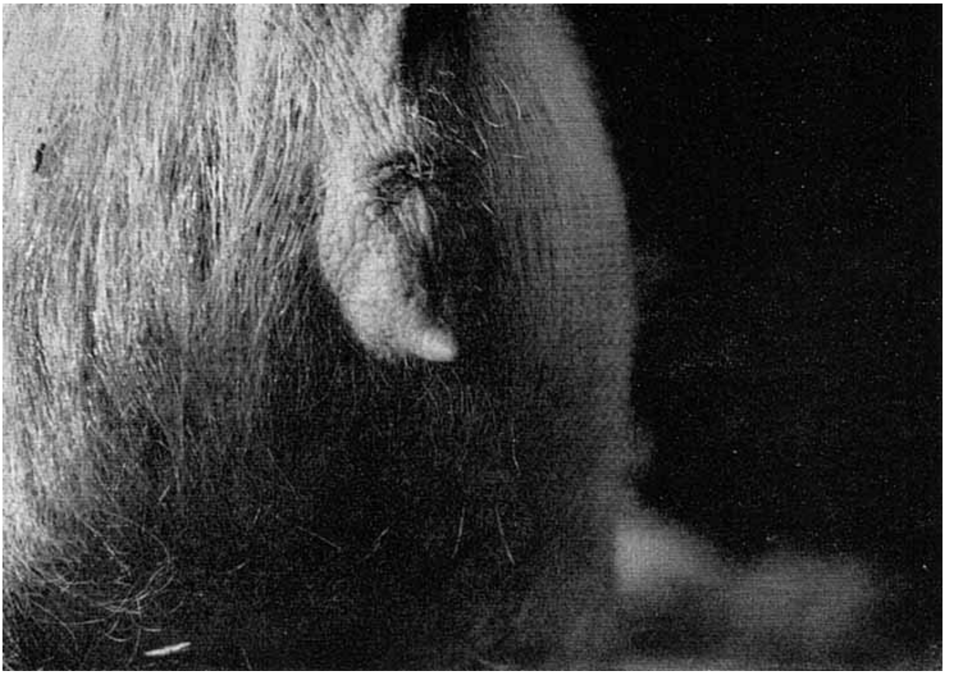

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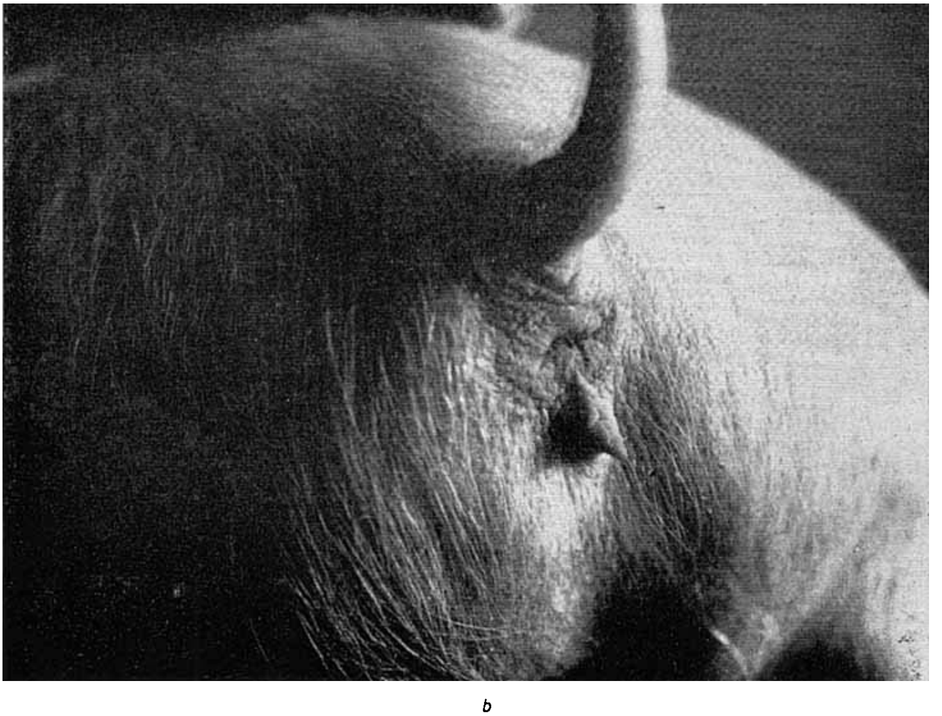

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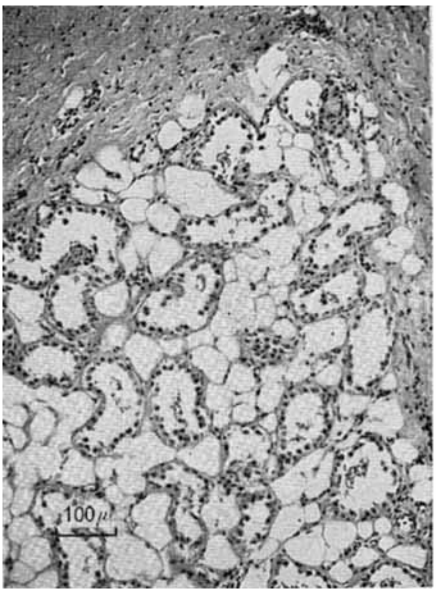

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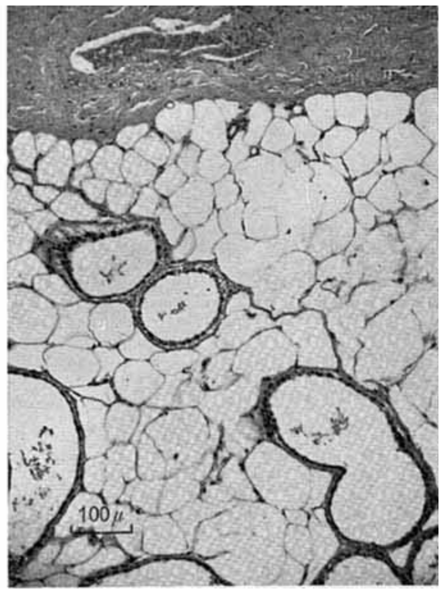

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EXPLANATION OF PLATES

Plate 1

(*a*) Section of the skin of an undernourished pig. Haematoxylin and eosin.
(*b*) Section of the skin of a normal pig of similar size. Haematoxylin and eosin.

Plate 2

(*a*) An undernourished pig, aged 11½ months, weight 5 kg, showing the appearance of the skin and head, the long nails and the stance.
(*b*) An undernourished cockerel, aged 6 months, weight 160 g., showing the feathering and the shape of the head and beak.

Plate 3

(*a*) The vulval region in a female pig, weight 23 kg, undergoing rehabilitation.
(*b*) The vulval region of a normal pig of similar size, photographed and reproduced to be of strictly comparable dimensions.

Plate 4

(*a*) Section of the vulva of the pig being rehabilitated. Haematoxylin and eosin. Note the active appearance and hyperplasia of the apocrine glands.
(*b*) Section of the vulva of the control pig. Haematoxylin and eosin.

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