THESIS SUBMITTED FOR THE

DEGREE OF

M A G I S T E R C H I R U R G I A E

IN THE UNIVERSITY

OF CAPE TOWN

BY

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M.B., CH.B.

1947.

THE EFFECT OF VASODILATATION

AS OBTAINED BY

LUMBAR SYMPATHECTOMY

ON THE GROWTH OF BONES

IN NORMAL YOUNG ANIMALS.

CONTENTS.

1. INTRODUCTION.

The effect of changes in the circulation of blood on the metabolism of bone in general is well known to surgeons. The bones adjacent to an acute inflammatory process may share in the regional hyperaemia and undergo considerable osteoporosis. One of the most notable examples of this process has been observed in the upper cervical vertebrae in association with acute inflammatory lesions of the pharynx and of the glands in the neck which may lead to osteoporosis of such a degree as to produce spontaneous fracture of a vertebra. Conversely, with a diminution in blood supply, we see osteosclerosis. For instance in Syphilis of bone, although temporary decalcification may result at the onset of the disease when the bloodflow is increased, later, with the development of end-arteritis obliterans, as the vascularity of the bone diminishes, sclerosis of the bone regularly takes place. While in the adult changes in bloodflow manifest themselves mainly in terms of osteoporosis or osteosclerosis, in the young another factor i.e. the effect on the rate of growth is being introduced. It is well known that in cases of congenital arteriovenous fistula (or in acquired arteriovenous fistula during the growth period) there occurs typical lengthening of the regional bones. The same is known to occur in chronic tuberculosis of

bone or .....

bone or from any other cause producing longstanding hyperaemia near the growing ends of young bones before the epiphyses have united.

The basic rate of growth of a limb may be modified by factors which may be classified as :

(1) General, (2) Local.

(1) GENERAL.

The most important general factor is the inherent growth energy of the cells at the epiphyseal line, under the complex influences of hormonal and metabolic activities.

Disturbances of these general factors may lead to such conditions as Dwarfism, Gigantism, Ricketts, Achondroplasia and Dyschondroplasia.

(2) LOCAL.

In addition to the inherent growth energy there are local factors influencing the cells at the epiphyseal line. Apart from trauma and diseases of the epiphyseal cartilage itself, the main local factors involved are: changes in blood supply and interference of the nerve supply. Enhancement of the rate of growth due to changes in the blood supply is seen in cases of vascular tumours,

chronic infections .....

chronic infections, arterior-venous fistulae and sundry other rarer conditions. How far interference of the bloodflow to the epiphyseal cells is responsible for the retarding of growth is not fully understood.

Apart from the examples already mentioned, the problem of the effect of bloodflow per se on the growth of a not fully developed bone, may be of definite practical importance to the surgeon should he be consulted by a young individual in whom for some reason or other the growth of one limb has been retarded, as for instance in Anterior Poliomyelitis.

In this condition there are usually two features very apparent on clinical examination. Firstly, the wasting and shortening of one of the limbs, and secondly its coldness and cyanosis. The first of these factors is due to two major accessory local factors, (1) the lack of normal muscular activity and (2) the interference of circulation.

In practically all conditions where bone growth is retarded or excessive it is difficult to determine the part played by the changes in bloodflow alone, since other factors come into play which are difficult to assess and which cannot be standardized. In arteriovenous fistulae for instance venous stasis may prove a great stimulus to the epiphyseal cells.....

cells. In poliomyelitis the paralysis of muscles and the trophic disturbances vary to such a degree from case to case that it is difficult to determine whether the diminished bloodflow plays any part in the retarding of bone growth.

Lumbar sympathectomy with its resulting vasodilatation, therefore, creates an ideal condition for studying the relationship of increased bloodflow to bone growth. In the normal animal all the other factors stimulating bone growth are equal and we are only concerned with the growth stimulus obtained from increased vascularity following on lumbar sympathectomy.

IT IS THE PURPOSE OF THIS PAPER TO STUDY THE EFFECT OF VASODILATATION CAUSED BY LUMBAR SYMPATHECTOMY ON THE GROWTH OF BONES IN NORMAL YOUNG ANIMALS.

II. A CRITICAL REVIEW OF THE PAPERS RELATED TO THIS INVESTIGATION.

The question whether experimental changes in bloodflow, particularly as effected by sympathectomy, may accelerate the growth of bone has been occupying the minds of research workers ever since Claude Bernard (1867) removed the superior cervical sympathetic ganglion of young cats and rabbits and reported that no increase in growth was obtained.

Bidder (1874) resected 1.5 cm. of the cervical sympathetic trunk in halfgrown rabbits. After one month the sympathectomized ear was warmer and 0.5 cm. longer than the normally innervated ear.

Stirling (Harris & Wright 1931) repeated the above experiment with the same result.

Cohnheim (Harris & Wright 1931) was of the opinion that no growth really takes place above the normal growth after sympathectomy.

The first clinical report comes from Helferich in 1887 who reported two cases in which one limb was lengthened by means of passive hyperaemia.

(a) A girl, sixteen years old, had an increase of 3 cm. in the length of a limb following a chronic ulcer, and the opposite healthy extremity .....

healthy extremity was lengthened 2 cm. by the use of passive hyperaemia.

(b) A boy, ten years old, had shortening of $3\frac{1}{2}$ cm. following a fractured femur, and the leg was lengthened $1\frac{1}{2}$ cm. subsequent to the use of stasis hyperaemia.

Cannon, Newton et al (1929) after complete unilateral sympathectomy, from sellate to pelvic ganglia on two kittens, concluded that after 4 months there was no difference in growth in either soft tissue or bone. They state "..... indeed we have found no evidence that the sympathetic division of the autonomic system plays an important part in the growth and development of the organism".

Bacq Z.M. (1930) after sympathectomizing albino rats, by removal of the ganglia from renal vessels to pelvis, found no increase in bone growth.

Pearse and Morton (1930) fractured both fibulae in dogs and tied the popliteal vein below the saphenous branch on one side, with results demonstrating that bone formation can be stimulated by venous stasis and that union of bone can be accelerated.

Harris R.E. and Wright G. (1931) performed cervical sympathectomies on kittens and rabbits and with well conducted investigations found an .....

found an increase in temperature (1.67 - 2.85°C) that was maintained but no undue growth of the fore limb of the operated side.

Bisgard (1933) who operated on kid goats found that no increase in growth was obtained over a period of 8 months.

Clinically the growth of a young bone has been observed to exceed the normal limits of growth for that particular individual as a result of various pathological states e.g. Arteriovenous fistulae, chronic ulceration in the neighbourhood of growing epiphyses and vascular tumours.

Harris and McDonald (1936) remarked about this phenomenon: "From our observations it seems definite that prolonged increase in blood supply of growing epiphyseal lines can cause them to grow more rapidly than would otherwise be the case. It is reasonable to expect that the increase in blood supply that follows on lumbar sympathectomy would produce a similar effect".

"Our clinical experience during the last five years leads us to believe that, under appropriate circumstances appreciable enhancement of the rate of growth of the leg can be obtained by lumbar sympathectomy".

They describe three cases in children on whom a left lumbar sympathectomy was performed in the treatment of Hirschsprung's disease.

In all .....

In all these cases the left limb showed a demonstrable increase in length as compared to the right limb.

Their clinical experience led Harris and McDonald (1936) to perform left lumbar sympathectomies on kittens, puppies and lambs. They reported that there was no sustained increase in heat and no demonstrable increase in bone growth. On three of the lambs the external iliac vein was ligated in addition to the sympathectomy but it failed to produce a sustained vascular increase and the results were therefore negative. They were forced to conclude " ..... there is not the same vascular response to lumbar sympathectomy in animals as in humans and neither is it sustained".

Moreover they could not verify their results obtained in humans.

White and Smithwick (1944) in their latest book page 225, sum up as follows: "It is a common clinical observation in children that tuberculosis in a joint may cause increased growth of bone at the neigh bouring epiphyses and abnormal lengthening of the extremity. This is due to local hyperaemia. On the other hand the more diffuse hyperaemia of sympathectomy does not cause an increased growth either of bone or soft tissue, at least in normal young animals ....."

"These negative results in normal young animals do not necessarily rule out the possibilities of accelerating growth activity in epiphyses .....

in epiphyses whose blood supply is pathologically reduced viz. in children with residual paralysis after anterior poliomyelitis".

III. SUMMARY OF THE LITERATURE.

The following workers reported that no undue bone growth results from sympathectomy on a n i m a l s :

Claude Bernard 1867, Bidder 1874, Cannon Newton et al 1929, Basq Z.M. 1930, Harris K.E. and Wright G. 1931, Bisgard 1933, Harris R.I. and McDonald 1936. Nowhere in the literature could the author find a report of increased bone growth after sympathectomy on animals.

Favourable results from lumbar ganglionectomy in c h i l d r e n have been reported by Harris (1930), White (1931), Harris and McDonald (1936).

The difference in the results reported on humans and animals is striking and stimulated these investigations of the problem in animals.

In man an increase in circulation is regularly observed following lumbar sympathectomy and it is claimed that this hyperaemia stimulates the cells to further activity resulting in growth increase in young subjects.

In the cases operated on for Hirschsprung's disease, lumbar sympathectomies of healthy left legs are performed, whereas in the usual case lumbar sympathectomy is being performed for vascular disease. Three cases operated on for Hirschsprung's disease are described by Harris and McDonald (1936). All three showed increase in growth of

the leg .....

the leg. Their most favourable results were, however, obtained in children operated on for cold, cyanosed and partially paralysed limbs following anterior poliomyelitis.

All authors experimenting with animals were uniformly unsuccessful to demonstrate increase in growth of bone after sympathectomies. It is of great importance to draw attention to the fact that most investigators failed to demonstrate hyperaemia on the sympathectomized side, although it was particularly anticipated. (Harris and Wright 1931, Bisgard 1933). Only Harris and Wright 1931, could demonstrate a difference in skin temperatures of kittens and rabbits which, however, was minimal amounting to 2.85°C at the most. There is, therefore, no evidence that the operation resulted in an increase in bloodflow. It is obvious that only in cases where a difference in temperature in favour of the sympathectomized side can be demonstrated can we expect an increased degree of growth.

IV. EXPERIMENTAL INVESTIGATIONS.

(a) ANIMAL MATERIAL

The selection of the type of animal for the purpose of this investigation was a matter of no small concern.

Rats, guinea pigs, rabbits and cats were examined post mortem and lumbar sympathetic trunks and ganglia carefully observed in all the animals.

In order to demonstrate changes in the rate of growth it is imperative that the animals should be young to have a long period of growth ahead. The extremities should be big to enable macroscopic changes in length to be measured after operation and during the growth period. For this reason the smaller laboratory animals are unsuitable.

The rat and guinea pig during the period of growth are very small and the sympathetic chain too small for practical purposes of operation. Nevertheless, the adult guinea pig has a well developed sympathetic system and the ganglia are even larger than those of the adult rabbit.

Kittens would be suitable for the experiment for the same reason as the guinea pig viz. they have a well developed sympathetic

system and .....

system and large ganglia. In view of the fact that the rabbit has the biggest paws and for practical reasons for keeping and feeding, the rabbit was decided upon. In the rabbit the sympathetic chain is not well developed. Only with great care and with the aid of a dissecting microscope is it possible to perform satisfactory operations on young rabbits.

A few kittens were operated on but because of bad facilities for keeping the animals all were destroyed by a monkey and, as no similar material was available at the time, these investigations had to be abandoned.

A young monkey, provided by the courtesy of Prof. Goetz, was operated on under general anaesthesia and by a retro-peritoneal approach the left upper three lumbar ganglia were removed. Although immediately after the operation difference in skin temperature of up to 3°C could be demonstrated in favour of the left foot, no marked temperature difference could be demonstrated after 14 days. Therefore no growth discrepancy is expected and this experiment will not be discussed in detail. The period of growth is also too long to be investigated for the purpose of this thesis.

Fifteen young rabbits, with body weights ranging from 230 Gm. - 630 Gm. were each subjected to a LEFT LUMBAR SYMPATHECTOMY.

A left .....

A left lumbar sympathectomy is easier to perform for the right handed operator. More so when no assistants are available.

There were three litters and every rabbit was labelled with a metal tag bearing its number.

RABBITS NOS. 2, 6, 15, 16, 17 and 20 were from one litter.

RABBITS NOS. 4, 7, 11, 12, 13 and 14 from another.

RABBITS NOS. 8, 9 and 10 were from a third litter.

(b) ANATOMY AND PHYSIOLOGY.

In order to develop the operative technique in survival experiments numerous dissections were performed on adult rabbits to demonstrate the ganglia and the sympathetic trunks. Two new born rabbits were dissected but with the naked eye the trunk and ganglia could not be demonstrated beyond reasonable doubt.

Figure 1 is a schematic drawing of the posterior abdominal wall of an adult rabbit which was sketched at the time of dissection to show the left lumbar sympathetic trunk and ganglia.

By dissection and X-Ray it has been confirmed that the rabbit has seven or eight lumbar vertebrae. The last thoracic vertebra may have very rudimentary ribs but can be identified by the absence of well developed transverse processes.

The lower .....

POSTERIOR ABDOMINAL WALL OF THE RABBIT.

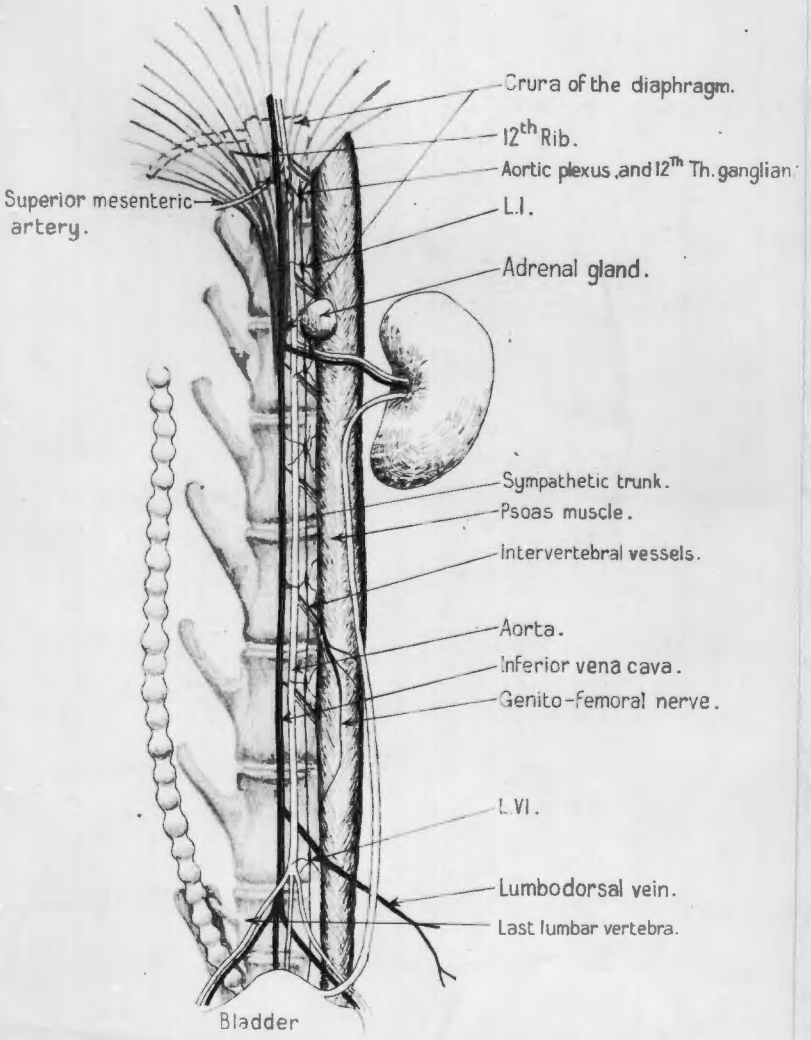


FIGURE 1.

The lower pole of the left kidney is opposite the disc between lumbar three and four. The renal vessels slant downwards and outwards, and the renal vein is a large structure if compared with the inferior vena cava.

The aorta lies behind the inferior vena cava, and is overlapped by the left psoas muscle. The bifurcation of the aorta takes place at the upper level of the last lumbar vertebra.

The left suprarenal gland is a pale pink structure, the size of a pea in small rabbits, and lies near the aorta on a higher level than the renal vessels, and does not approximate the kidney at all.

There is a long lumbodorsal vein to be seen and also the genitofemoral nerve on the medial side of the left psoas muscle.

The left lumbar sympathetic trunk lies behind the aorta. It is a very fine, thin structure, hardly thicker than a hair.

The right and left trunks are very close together, separated only by a thin film of tissue, and it is sometimes impossible to distinguish them without actually separating them.

All the ganglia lie opposite the lumbar vessels and the connecting fibres are seen dipping backwards between the psoas muscle and vertebral bodies towards the spinal nerves.

Small rami .....

Small rami from the ganglia can be followed in different directions, some passing towards the aorta and inferior vena cava.

The attempted dissections of the grey and white rami communicantes were unsatisfactory and I believe that it cannot be carried out for the smallness of the branches.

The first ganglion lies above the suprarenal gland to the left of the crus of the diaphragm.

The second ganglion lies behind the suprarenal gland and slightly above and in some cases below the renal vessels.

The sixth ganglion lies near the bifurcation of the aorta.

In order to perform the sympathectomies effectively it was essential to get a clear idea as to the connections of the sympathetic chain to the lumbo-sacral plexus. This was a painstaking operation but after numerous dissections it could be definitely established that the lowest outflow is commonly from L5. In one animal, however, it was found to be as low as from the sixth ganglion. This was confirmed by Prof. R.H. Goetz.

The lumbo-sacral plexus was dissected on two adult rabbits. One rabbit had seven lumbar vertebrae and the other one had eight.

The plexus is schematically reproduced on page 18, Figure 11.

The description of the lumbo-sacral plexus of the rabbit

by Libbie Hyman ....

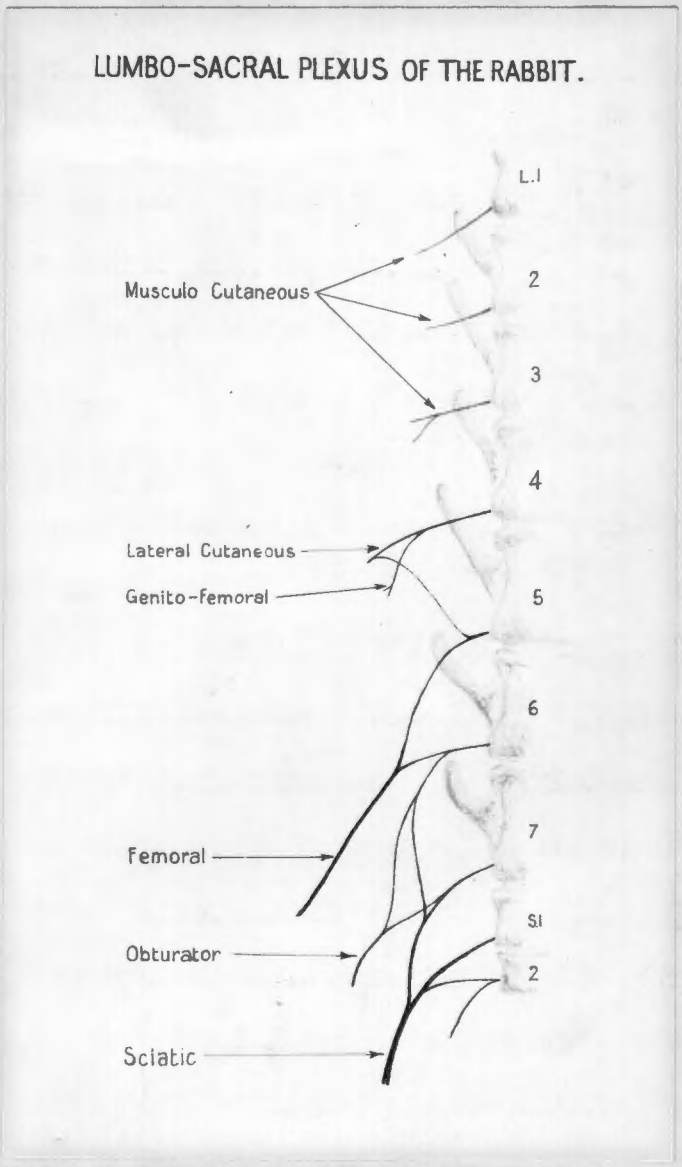

LUMBO-SACRAL PLEXUS OF THE RABBIT.
L.1
2
3
4
5
6
7
SI
2
Musculo Cutaneous
Lateral Cutaneous
Genito-femoral
Femoral
Obturator
Sciatic

FIGURE 11.

by Libbie Hyman (1944) was taken as a guide.

The ventral rami of the last four lumbar nerves and those of the sacral nerves form the lumbo-sacral plexus in the rabbit.

The fourth lumbar nerve is the first of the lumbar plexus. It has two main branches, the lateral cutaneous nerve and the genito-femoral nerve. The former is a stout trunk which emerges between the ilio-psoas and the psoas minor muscles and accompanies the course of the ilio-lumbar vessels passing to the thigh.

The genito-femoral nerve is a long slender nerve which runs along the medial border of the psoas muscle, lateral to the sympathetic trunk. The fifth lumbar contributes by means of its connection with the fourth to the lateral cutaneous and also forms a strong union with the sixth. The FEMORAL nerve is the union of branches from lumbar five to six.

THE OBTURATOR nerve arises from the sixth and seventh trunks.

The last lumbar and the first sacral unite to form the sciatic nerve. The second sacral and the sixth lumbar also contribute small branches.

GENERAL PHYSIOLOGICAL CONSIDERATION.

The sympathetic system of all animals follows a similar plan. There are cortical, diencephalic, bulber and spinal centres, the last named are situated in the lateral horns of the spinal grey matter.

In the medulla we find two important reflex centres the respiratory and the vasomoter centre, the latter lies in the medulla as a strip along the floor of the fourth ventricle.

So far as is known there is no parasympathetic supply to peripheral blood vessels. The major part of the large arteries and the smaller branches receive their innervation via reinforced strands, derived from the non-medullated fibres of peripheral nerves, supplying the chief vasoconstrictor control of the arteries and arterioles. These fibres come off at certain selective points from the peripheral nerves. Further the sympathetic supply to the vessels is from the ganglia to the large arteries via the aortic plexus and then along the peri-arterial tissue.

This conception that only the most proximal part of the large arteries to the limbs receive their sympathetic supply via the peri-aortic plexus and that the greater part is carried to the arteries by the peripheral nerves at many points along the length of the vessels,

have been .....

have been undoubtedly proved (Pollard H.H. and Morrich R.E. 1934, Kramer and Todd 1914, White and Smithwick 1941 review of literature).

Chemical agents are capable of producing vasoconstriction by its being widely distributed by the blood. It has been emphasized by Cannon 1939 that the point of action of the chemical mediators of the autonomic impulses lies between the nerve endings and the responsive mechanism in the smooth muscle cells. Numerous authors have demonstrated that following sympathectomy there occurs an increase in the sensitivity of the denervated structure to adrenaline. This is of fundamental clinical importance. Every sympathectomy to be efficient must denervate all the nerve endings in a given area, otherwise the secretion of chemical mediators at the remaining endings can reach the cells which have been denervated and cause them to react. The sympathetic pathway should be interrupted in its upper or pre-ganglionic motor neuron, in order to produce the minimum degree of sensitisation and the maximum reduction in tone. (White and Smithwick 1944, page 136).

The effect of these chemical agents on the vessels after sympathectomy has been investigated in rabbits and cats by le Compte 1941/42. He observed, among other things, two important facts

viz. (1) .....

viz. (1) The diameters of the denervated vessels, unlike those normally innervated, are not affected by moderate changes of body temperature. (2) Struggle induces constriction (cooling of the ears) of denervated vessels similar to the constriction caused by adrenaline.

In man the first lumbar sympathetic ganglion supplies the femoral and obturator nerves. It should, therefore, be removed in cases where an increased blood supply in the region of the epiphyses around the knee joint has to be obtained. Removal of lumbar 2 and 3 results in a vasodilatation in the region of the foot and the lower leg only. Consulting our chart of the lumbo-sacral plexus of the rabbit (page 18, Figure 11) it will be seen that the 4th lumbar nerve is the first to contribute to the plexus. The sciatic nerve originates from L6, 7 and S1, 2. In the rabbit the lowest sympathetic outflow comes from the 5th lumbar ganglion. In order, therefore, to perform a pre-ganglionic sympathectomy correctly, it is essential to remove the 5th lumbar ganglion.

In none of the papers on animal experiments studied by the author has an account of the anatomy and physiology been undertaken. Most of the papers on the effect of lumbar sympathectomy on bone growth in animals remark that they "removed ganglia and trunk from the renal vessels down to the pelvis". How and which ganglia were removed

are not .....

are not described.

This implies that the anatomical and physiological consequences were not fully appreciated.

Such a statement suggests that the first and second sacral ganglia may have been disturbed so that the post-ganglionic fibres to the foot were interrupted as well. This may have been the cause for the failure of these authors to obtain sustained vasodilatation because the vessels had become hypersensitive. Indeed no skin temperature differences were recorded by those authors. The same objection holds for the cervical sympathectomies which were performed to demonstrate bone growth of the upper limb. The operations performed by all authors were ganglionectomies, no effort being undertaken to perform preganglionic ramisection.

To my knowledge the pre-ganglionic outflow to the limbs in the rabbits has not previously been studied. To recapitulate the salient points :

(1) The lumbo-sacral plexus in the rabbit is derived from L4 to S2.

(2) The sympathetic pre-ganglionic outflow to the hind limb is via L4, 5 and L6 to S2 and consequently L4 and L5 have to be removed

to perform .....

to perform a pre-ganglionic sympathectomy. Occasionally the 3rd lumbar ganglion may contribute an outflow to the lumbar plexus and is, therefore, also removed. Removal of L1 and L2 is not essential.

(3) The author's original aim was to remove L1 to L5 because this last point was not appreciated.

(c) THE OPERATION OF LUMBAR SYMPATHECTOMY ON THE RABBIT AND A SUMMARY OF THE OPERATIONS.

Anaesthesia.

Premedication of Nembutal 40 mgm. per kilo of body weight is injected intra-peritoneally and the result observed for 15 - 30 minutes. If required a further 10 - 20 mgm. per kilo may be injected after 30 - 45 minutes. The rabbit is very sensitive and great care must be taken not to overdose. The rabbit's ears first become flabby and then the animal lies down. Ether by open improvised mask is commenced 15 - 30 minutes after the Nembutal injection. Breathing and movement of abdominal muscles are very carefully observed. Usually very little ether is required to keep the rabbit fully relaxed. In some cases no ether is required at all. The rabbits should be starved prior to operation because a full stomach not only interferes during the operation, but may easily be injected into instead of the peritoneum.

Operation.

The left lumbar sympathectomy is performed because at the preliminary dissections it was found easier to approach the left

chain .....

chain.

The rabbit's abdomen is shaved and surgical aseptic precautions employed.

The abdomen is opened along the midline and the large and small intestine retracted to the right in a hot pack, while the skin and muscles are kept pinned apart by sutures fixed to the board. A lens is required at this stage. With the fingers of the left hand spread inside the abdomen the aorta is slightly shifted to the right. The ureter and aorta are separated by opening the peritoneum.

The sympathetic ganglia are so closely approximated to the lumbar vessels that bleeding is often started, but this is easily overcome by pressure with a gauze swab. It is never necessary to ligate a vessel.

Often the trunk is severed in the process of removal, and this may be the cause of failure to remove, or, of an uncertainty of having removed all the necessary tissue, because it is sometimes impossible to find the trunk again due to its being so very fine. The right sympathetic trunk is separated from the left by a thin film only and great care has to be taken that it is not injured.

Another pitfall is the genito-femoral nerve which lies just lateral to the trunk. At the first operation, (Rabbit No. 20) it

was actually .....

was actually removed and thought to be the lumber sympathetic trunk.

The psoss muscle must be carefully retracted with the left index finger or with a blunt instrument because if the fibres are teased they can be mistaken for the trunk.

The removal of the sympathetic trunk and ganglia from L1 - L5 was originally aimed at, later L3 - L5 only. The first lumber ganglion is difficult to remove from below because the renal vein may be torn. During some of the operations the first lumber ganglion was not removed but it was found that the first lumber ganglion can best be approached from above the renal vessels by opening the peritoneum. The left crus of the diaphragm is a very good guide to the first ganglion.

Figure 111, page 28, is a photograph of some of the ganglionic chains removed. One ganglion of each chain was microscopically examined and in every case it was proved to be a sympathetic ganglion.

The 15 rabbits are grouped according to the survival period.

Group A.

Comprised of six rabbits (nos. 2, 7, 8, 10, 16 and 20). This group still survives and up to writing, the post-operative

period ranges .....

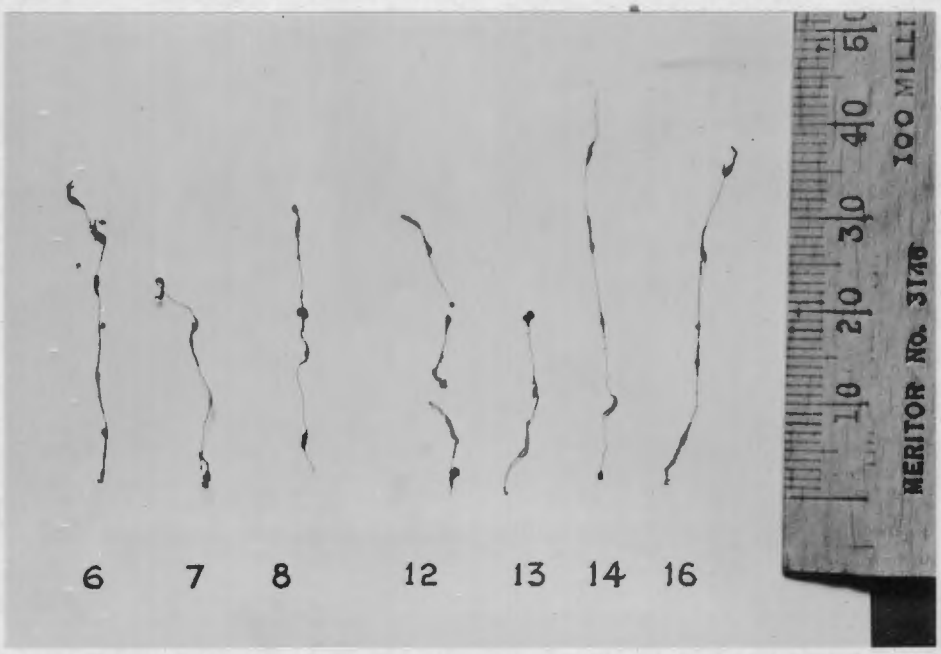


FIGURE 111.

period ranges from 96 - 124 days.

Rabbit No. 20 was the first rabbit to be operated on. On histological examination it was found that no sympathetic tissue had been removed. This rabbit, therefore, served only as a control.

Group B.

Four rabbits (nos. 11, 12, 13, 15 and control rabbit 17).

They all died within the period of 20 - 29 days post-operative.

Post-mortem examination revealed no organic cause. The region of the left lumbar ganglia was examined to verify the completeness of the operation.

The nights were exceptionally cold and it is possible that exposure accounted for the fatalities. A suggestion by a rabbit-keeper was that it might have been the oats on which they were fed. He had often had the experience that young rabbits died if they were fed on oats.

Rabbit No. 17 which was not operated on but kept as a control, also died at the same time as the others. None died because of sepsis and not a single rabbit had post-operative infection.

Group C.

Five rabbits (nos. 4, 5, 6, 9 and 14)

Four of .....

Four of the rabbits in this group died within the first 24 hours after operation, probably from shock. The anaesthetic, 70 mgm. (Nembutal) per kilo of body weight, was a definite contributing factor in two earlier cases. 40 mgm. per kilogram of body weight was found to be the optimum dose. The remaining animal died of strangulation of the small bowel.

This group will not be referred to again. They are mentioned because valuable experience was gained concerning the best anaesthetic and the operative procedure.

(d) METHODS UTILIZED TO DEMONSTRATE THE SKIN TEMPERATURE OF THE FEET AFTER LUMBAR SYMPATHECTOMY.

To compare the changes taking place after sympathectomy numerous normal rabbits were first tested, of which graph No. 1V is an example - Page 39.

It is important to point out that the previous authors found great difficulties to demonstrate differences in the skin temperatures between the normal and sympathectomized limbs in their animals. These authors, therefore, had hardly any control as to the fact whether their animals were really completely sympathectomized, and do not mention any other method employed by them to make sure about this point. We have, therefore, no conclusive evidence that they succeeded in proving a successful sympathectomy and of increasing the bloodflow. Therefore, if no increase in growth of bone was recorded it is not conclusive evidence that sympathectomy does not influence bone growth.

It is our contention that unless we could prove that our animals were really sympathectomized our study would also fail to convince and bring the subject nearer solution. Of the methods available in man to prove this point, few can be applied in animals. Skin resistance, which is hailed as a very good method (Richter) by numerous authors,

cannot be .....

cannot be applied because the rabbit lacks sweat glands. Sweating tests, so instructive in man, is therefore also out of the question.

Despite the failure of previous investigators, however, means had to be found to observe skin temperature changes after sympathectomy.

The following procedure was therefore adopted :

At the outset the rectal temperature was taken. It varied in our animals between 38.5°C - 40°C.

The skin temperatures of the paws were recorded by means of thermocouples. Hair interferes with the taking of temperatures and was removed by plucking, which was found easy and time saving. The hair had to be plucked before each reading and some rabbits were plucked 4 - 5 times during the period of observation. No definite difference in the length of hair was noticed in the two feet following operation and no difference could be observed in the texture of the hair by naked eye.

After removing the hair the skin temperatures were tested at room temperature. Temperature readings are always taken at the same spots, one at the ankle and another between the 1st and 2nd metacarpals.

The vessels of both feet were regularly found to be well dilated when the rabbits were removed from the cage. This can be seen from the graphs .....

the graphs, the initial temperatures being 30 - 32°C. It slowly dropped to about 27°C on exposure to room temperature and because of vasoconstriction which was the result of handling the animals.

It is, therefore, apparent that the skin temperatures taken under ordinary laboratory conditions did not always show a striking difference, and in most cases, if it was not known that one leg had been sympathectomized, no hint of its having been done could be gained from the skin temperature readings. In this, our experience coincides with the findings of previous investigators (Bisgard 1933, Harris & McDonald 1936).

It was then argued that if both limbs were equally cooled first, then the rate of warming will depend on the arterial bloodflow through the skin. If, therefore, one limb was constantly and significantly warming faster than the other, that limb could be regarded as being better supplied by blood. If this was found to occur to the sympathectomized limb, it could be strong evidence indicating successful operation.

To demonstrate this we developed a special technique, as follows : To reduce the skin temperature vasoconstriction is induced by making the animals stand in cold water (4 - 14°C) for 3 minutes and after drying the feet, temperature readings are recorded every two or three minutes

for about .....

for about 10 - 15 minutes and then at longer intervals up to 60 minutes after the immersion. These graphic results were recorded every three weeks.

Immediately after drying the feet the temperatures are practically the same, but the left (sympathectomized) foot soon afterwards, 5 - 10 minutes, shows an increase which mostly is about 6 - 10°C above that of the right foot. It usually takes 15 - 60 minutes longer for the right foot to reach its pre-cooling temperature in relation to that of the left sympathectomized foot.

If struggling is induced the temperature drops temporarily, due to the liberation of adrenaline into the circulation.

By the method developed, marked increase in skin temperature could, therefore, for the first time constantly be demonstrated in favour of the sympathectomized limb, and, for the first time be definitely established that the limb of the experimental animal was really sympathectomized.

(a) THE METHODS OF INVESTIGATING THE EFFECT ON LUMBAR SYMPATHECTOMY ON THE GROWTH OF BONE IN RABBITS.

After lumbar sympathectomy, dilatation of the vessels of the hind limb takes place but it is not certain up to what level this would occur.

The hind feet were selected as the special bones to be observed because it is uncertain whether hyperaemia would occur in the region of the epiphyses around the knee joint. Increased tibial growth was therefore problematical, and the uncertainty was further strengthened by the preliminary skin temperature readings, where it was noticed that, following cooling, a difference in skin temperature between the two feet was always very well marked below the ankle while above it hardly any difference could be demonstrated.

The whole foot was X-Rayed from the calcaneus to the tips of the nails. It was found inaccurate and laborious to draw every bone to scale on graph paper as was originally tried, and this plan was discarded. The new programme was to draw 4 mm. squares in indian ink on white paper. This paper was photographed and reduced by half, i.e. squares of 2 mm. This negative is incorporated in the copy of every

X-Ray to .....

X-Ray to give a rough indication of the comparative lengths. It is impossible to hold the rabbit in such a way that the angle of the bone to the graph paper is always correct and, therefore, the actual measurements were done by means of a graduated caliper whereby greater accuracy was obtained.

The caliper was found accurate up to 0.1 mm.

Measurements have to be carefully carried out and depend on the recognition of joint lines. Exactly the same spot is employed on each bone.

The length of the whole foot is measured from the tip of the calcaneus to the first interphalangeal joint, but the points for comparison were only decided upon after all the relevant X-Rays had been carefully studied. Unless the joint lines and other points of measurement were clearly seen the X-Ray was discarded in order to avoid errors. X-Rays of the bones were taken before or soon after operation when the rabbits were over the dangers resulting from the operation, thereafter at regular intervals.

The tibiae of all rabbits were also X-Rayed at the end of the experimental observation.

V. RESULTS.

The rabbit has a poorly developed sympathetic system as compared with other animals, e.g. the cat. The ganglia are much smaller and the lumbar sympathetic trunk not so obvious. Even the guinea pig has bigger ganglia.

Young rabbits can be operated on and with experience the operative mortality is not high. Of the fifteen rabbits operated only four of the earlier ones died as a result of the operation.

The first point which had to be established before the results could be evaluated was whether the operation was successfully performed. As pointed out earlier a special test was developed to ascertain the completeness of the operation as judged by the effect of the sympathectomy on the temperature of the precooled feet.

The results will be discussed under two headings :

(a) The effect of sympathectomy on skin temperature readings,

(b) The effect of sympathectomy on osseous growth.

(a) The effect of sympathectomy on skin temperatures.

On routine examination of the operated rabbits striking differences were not observed. When the rabbits are taken out of

the cage .....

the cage very little, if any, difference in temperature can be demonstrated by the thermocouples. This is explained by the fact that the rabbit keeps both feet folded under the body and covered by the fur, consequently both feet are warm and the vessels usually well dilated. The result is that, under ordinary circumstances, skin temperature readings are not able to demonstrate whether the operation has been effective. However, it was found that if vasoconstriction was induced by immersing both hind limbs in iced water for a few minutes, definite differences in the temperature of the feet could be demonstrated. Following the immediate drop in temperature of both feet, it is seen that after 5 - 10 minutes the skin temperatures of both feet rise but the sympathectomized foot has a steeper immediate rise to remain considerably warmer than the normal foot.

We will first examine the graph of an unoperated rabbit of the same age. (Figure IV, page 39).

Following cooling, the temperatures of both feet behave in exactly the same way. Small differences up to 1.5°C are noticed which can be expected. But these differences between the two feet are negligible, if they are averaged. It is further noticed that the temperature drops and does not regain the pre-immersion level in the first hour.

Let us compare this result with the results in operated rabbits.

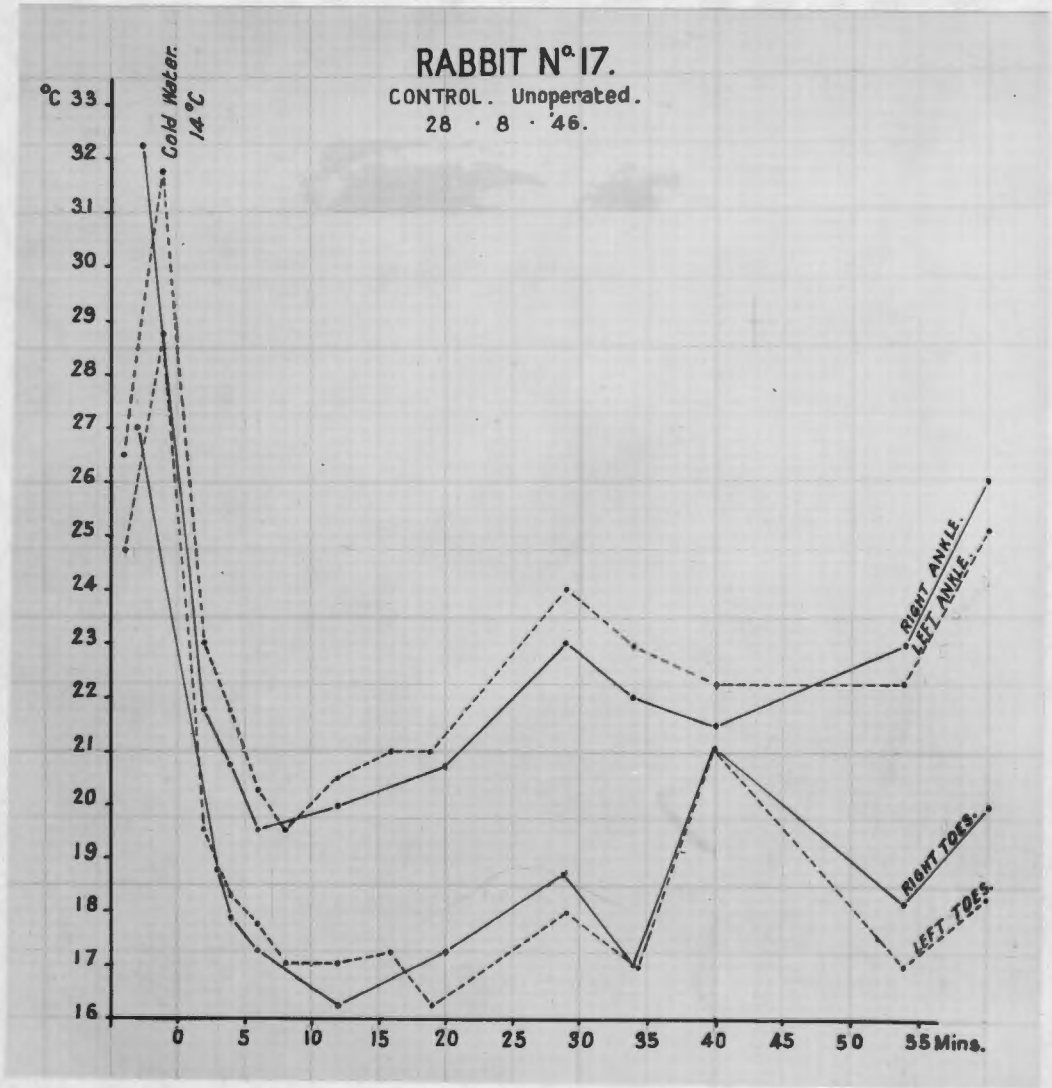

RABBIT N°17.
CONTROL. Unoperated.
28 · 8 · 46.
°C 33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
Cold Water. 14°C
RIGHT ANKLE.
LEFT ANKLE.
RIGHT TOES.
LEFT TOES.
0 5 10 15 20 25 30 35 40 45 50 55 Mins.

FIGURE 1V.

RABBIT NO. 2.

Lumbar ganglia 2, 3, 4 and 5 were removed and four temperature graphs were recorded after the operation. Figures V, Vl, Vll and Vlll, (pages nos. 42, 43, 44 and 45).

They all demonstrate a marked difference in skin temperature of the two feet.

Figure V,(page No. 42) for instance shows an immediate steep rise of the temperature on the left foot while the right foot shows a tendency to remain at a more constant level or even dropping further. In this way the left foot steadily increases the difference up to 24 minutes when the maximum difference of 8°C is registered.

In Figure Vl, (page No. 43), the left foot is colder than the right foot up to 17 minutes when suddenly in the space of three minutes the left toes and left ankle rise 13.5°C and 10°C respectively. Struggling causes an immediate drop in temperature on both sides.

The sympathectomized foot regains its pre-immersion level within 20 minutes while the non-sympathectomized foot still shows a drop of the temperature after 60 minutes. A maximum difference of nearly 10°C was registered.

In Figure Vll, (page No. 44), a fairly sudden rise in temperature of both .....

of both feet can be seen after 17 minutes. Struggling again affects the temperatures of both feet but the right foot continues to drop. The left foot regains its pre-immersion level within 25 minutes. After 124 days the rabbit (Figure VIII, page No. 45), still demonstrates the difference in skin temperature. Even before the immersion there was a difference (2.3°C), and again the left foot remains cooler than the pre-immersion temperature. The temperatures are more stable than in the previous graphs.

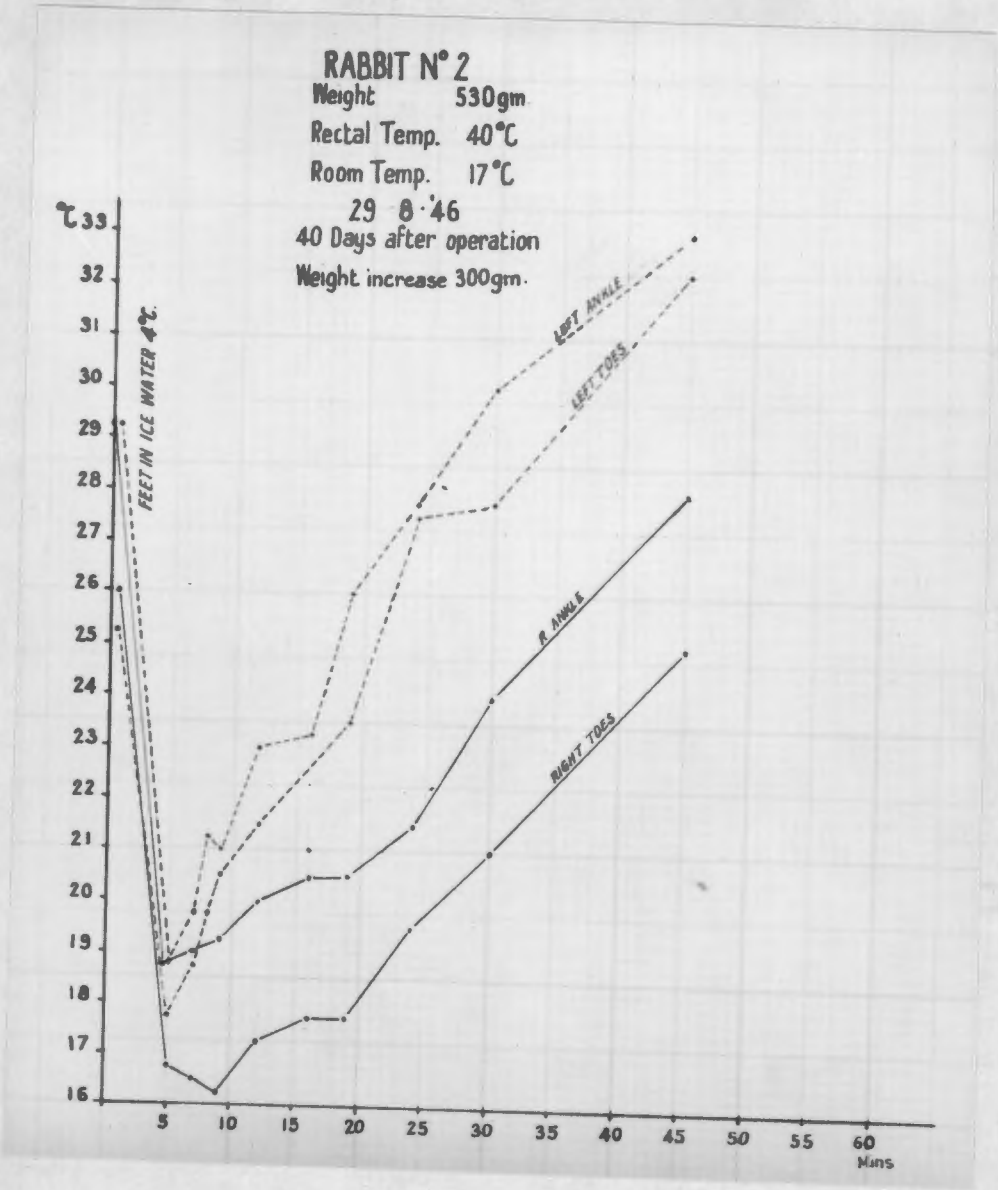


FIGURE V.

The left foot was sympathectomised and is indicated by the interrupted line.

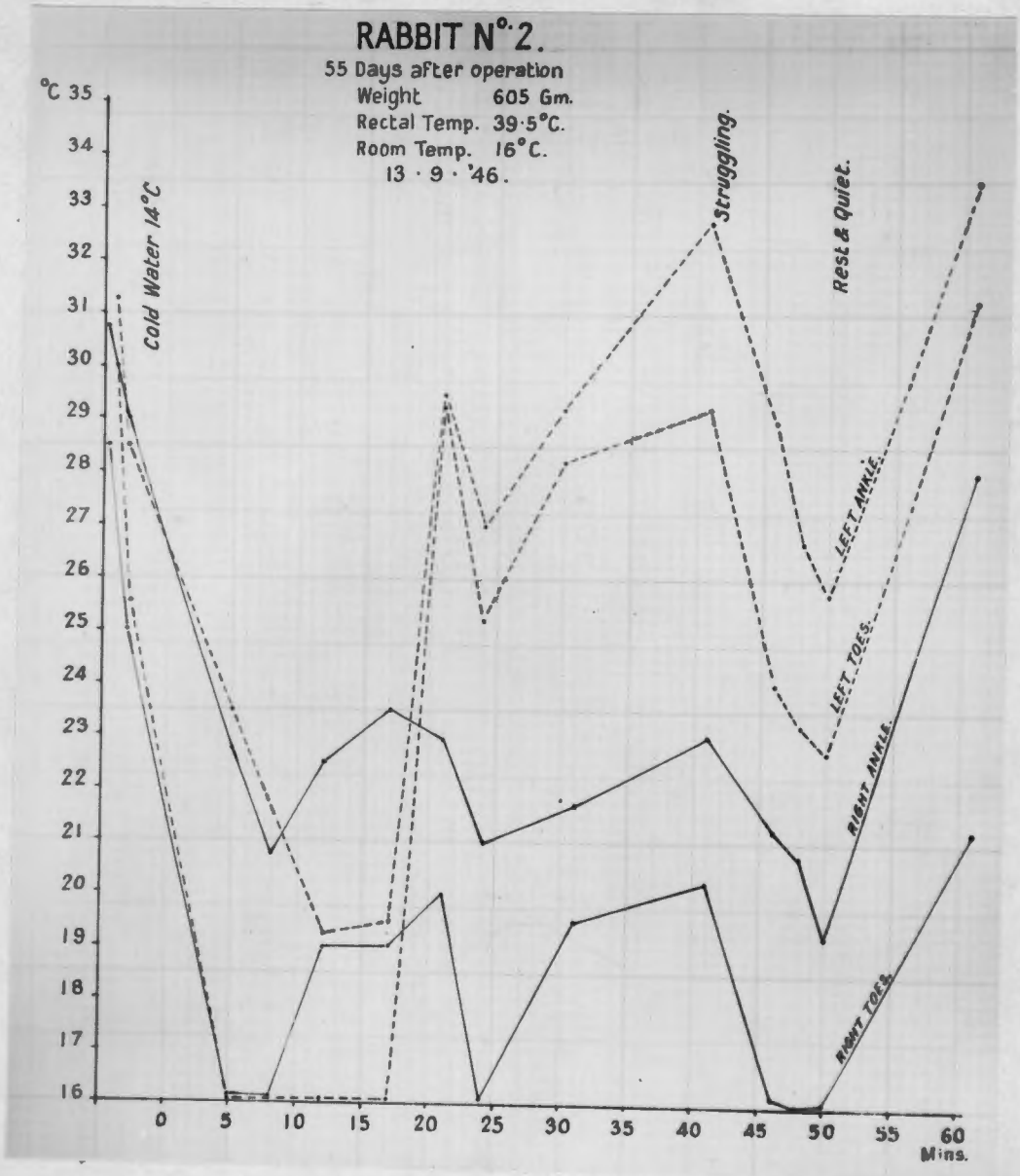

RABBIT N°2.
55 Days after operation
Weight 605 Gm.
Rectal Temp. 39·5°C.
Room Temp. 16°C.
13 · 9 · '46.
°C 35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
Cold Water 14°C
Struggling.
Rest & Quiet.
LEFT ANKLE.
LEFT TOES.
RIGHT ANKLE.
RIGHT TOES.
0
5
10
15
20
25
30
35
40
45
50
55
60
Mins.

FIGURE V1.

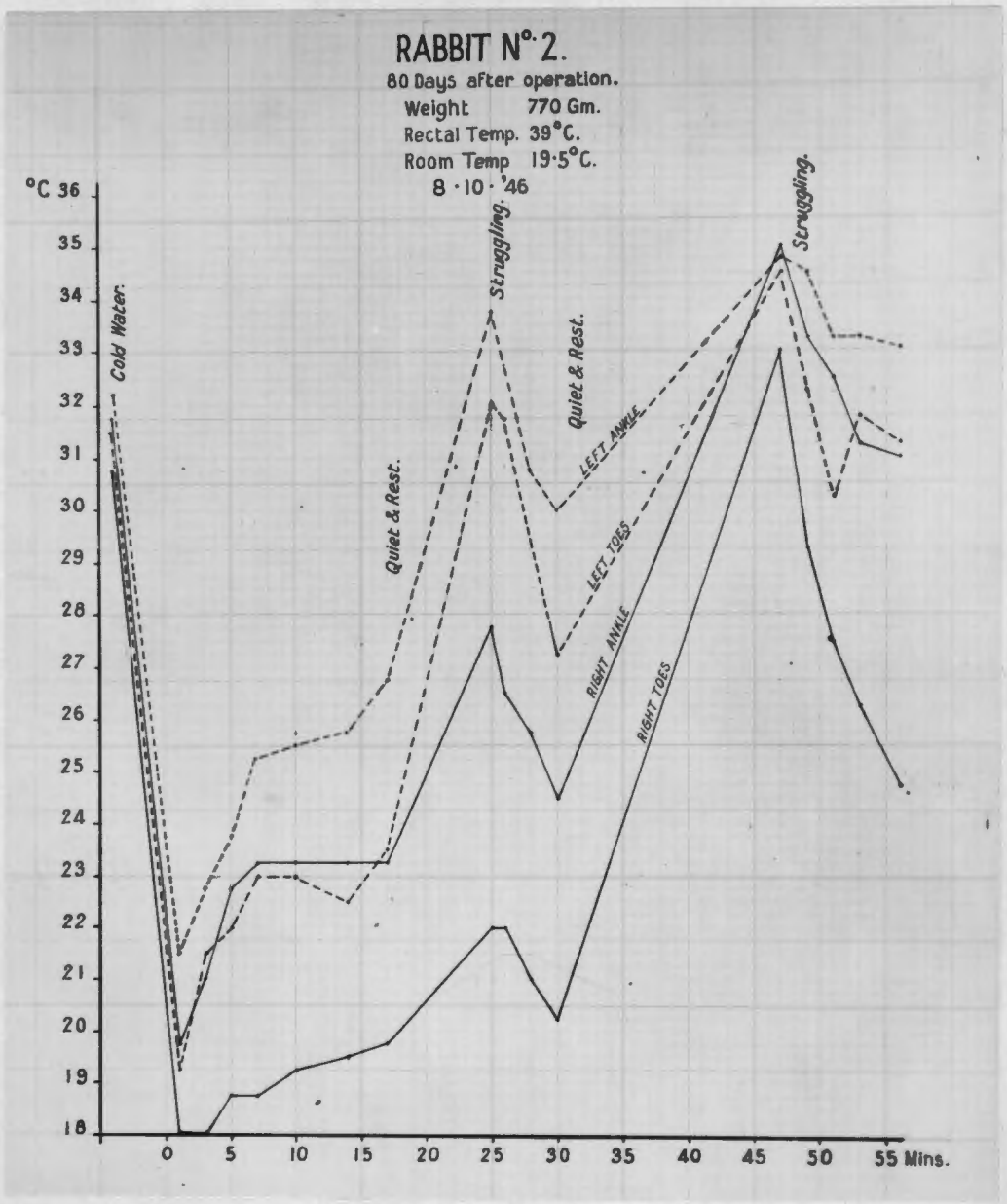

RABBIT N°. 2.
80 Days after operation.
Weight 770 Gm.
Rectal Temp. 39°C.
Room Temp 19·5°C.
8·10·'46
°C 36
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
Cold Water.
Struggling.
Quiet & Rest.
Quiet & Rest.
Struggling.
LEFT ANKLE
LEFT TOES
RIGHT ANKLE
RIGHT TOES
0
5
10
15
20
25
30
35
40
45
50
55 Mins.

FIGURE V11.

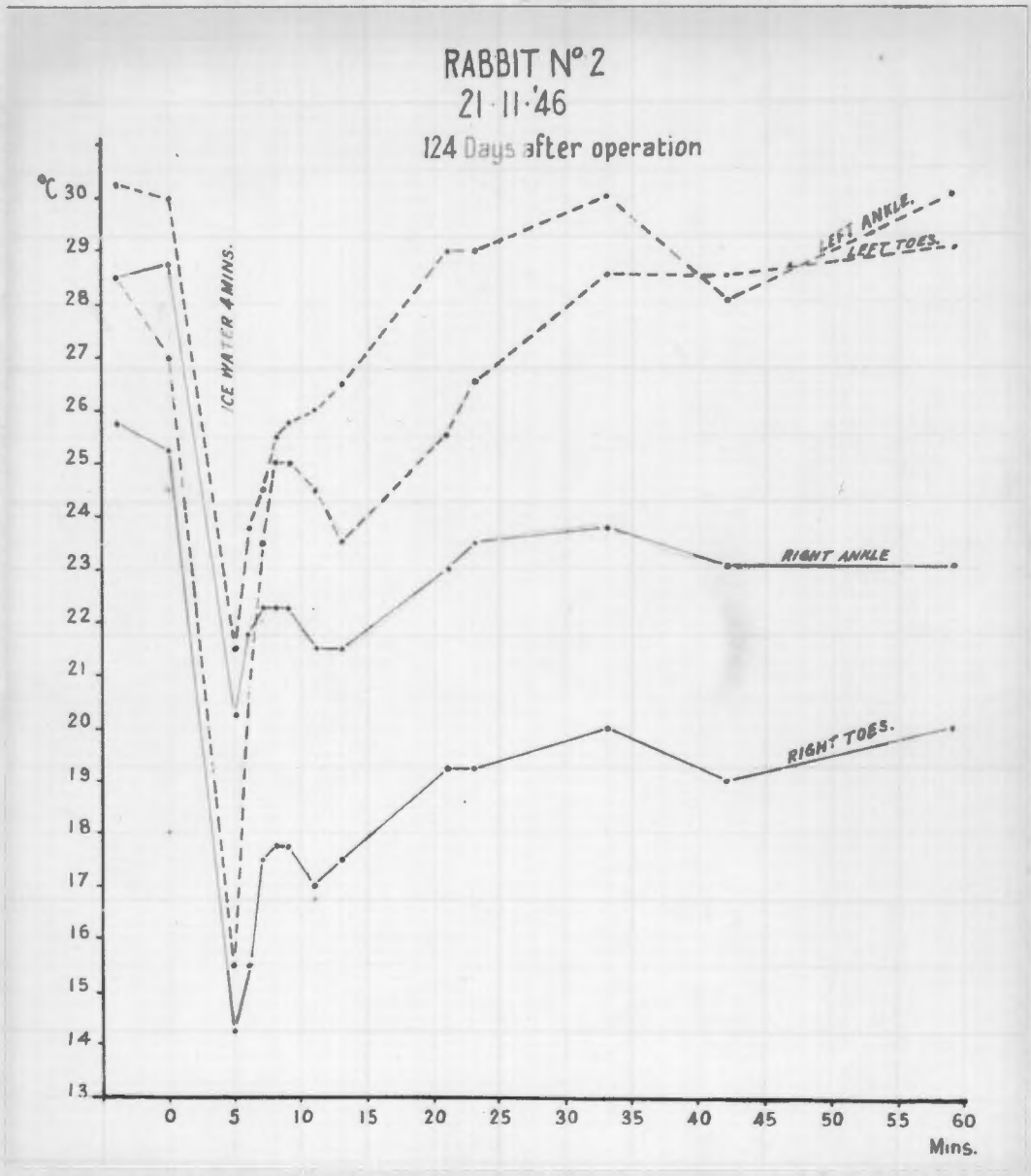

RABBIT N° 2
21·11·'46
124 Days after operation
°C
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
ICE WATER 4 MINS.
LEFT ANKLE.
LEFT TOES.
RIGHT ANKLE
RIGHT TOES.
0
5
10
15
20
25
30
35
40
45
50
55
60
Mins.

FIGURE V111.

RABBIT NO. 7.

L2 - L5 were removed in this case. (Figures IX, X and XI, pages Nos. 47, 48 and 49).

Figure IX, (page No. 47), shows the ankle temperatures before and after immersion of the feet in cold water (15°C). The right foot showing a marked drop in skin temperature and the usual slow warming. The left sympathectomized foot, however, after an initial slight drop in temperature soon regains its original temperature and even surpasses it.

From Figure X, (page No. 48), it can be seen that there was a marked drop in temperature of the right foot which remained very cold for over 35 minutes when it suddenly rises to the same level as the left foot within 20 minutes, viz. 53 minutes after cooling.

After 121 days the effect of the sympathectomy on Rabbit No. 7 (Figure XI, page No. 49), is still very obvious and it is a typical example of what has been the author's experience during these experiments.

Initially the left foot is approximately 2°C warmer. When after cooling a sudden drop in the temperature of both feet occurs. The left foot warms up suddenly and remains 6 - 10°C higher. The right foot also warms up slightly after the initial sudden rise at 5 - 10 minutes after cooling, but has only gained 4 degrees from the 15th - 65th minute, although the difference is 8 - 10°C in favour of the sympathectomized limb.

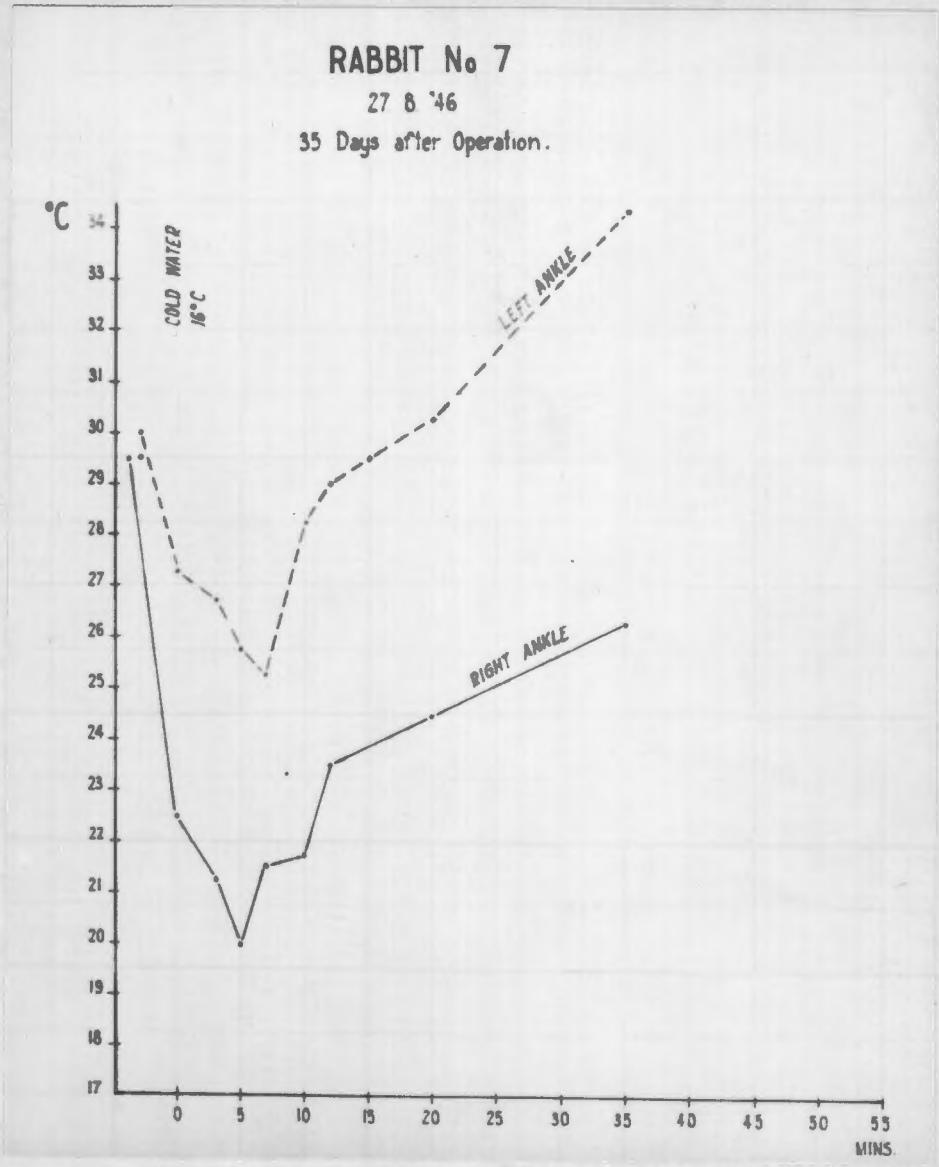


FIGURE 1X.

The interrupted line indicates the temperature of the sympathectomised foot.

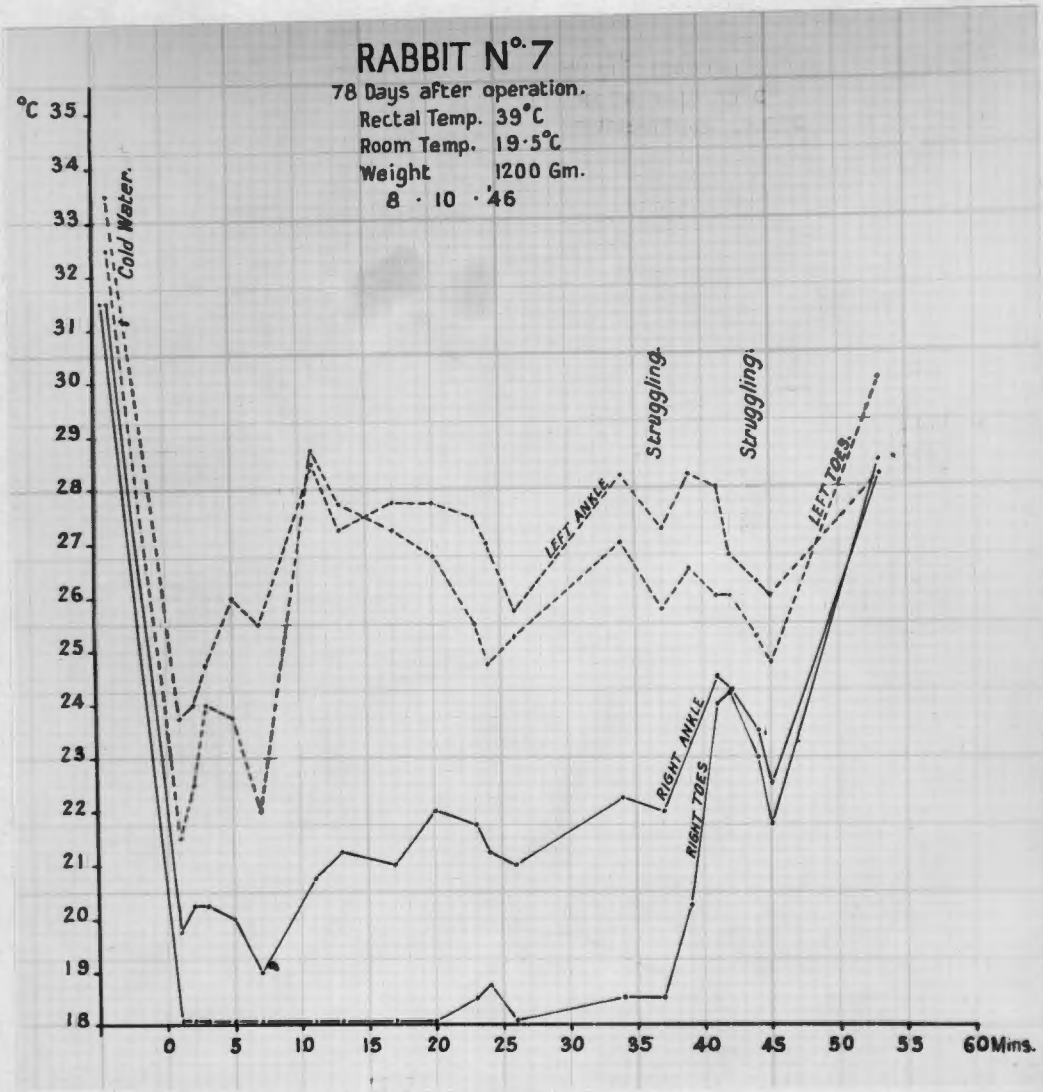

RABBIT N°. 7
78 Days after operation.
Rectal Temp. 39°C
Room Temp. 19·5°C
Weight 1200 Gm.
8 · 10 · 46
°C 35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
Cold Water.
Struggling.
Struggling.
LEFT ANKLE
LEFT TOES
RIGHT ANKLE
RIGHT TOES
0
5
10
15
20
25
30
35
40
45
50
55
60Mins.

FIGURE X.

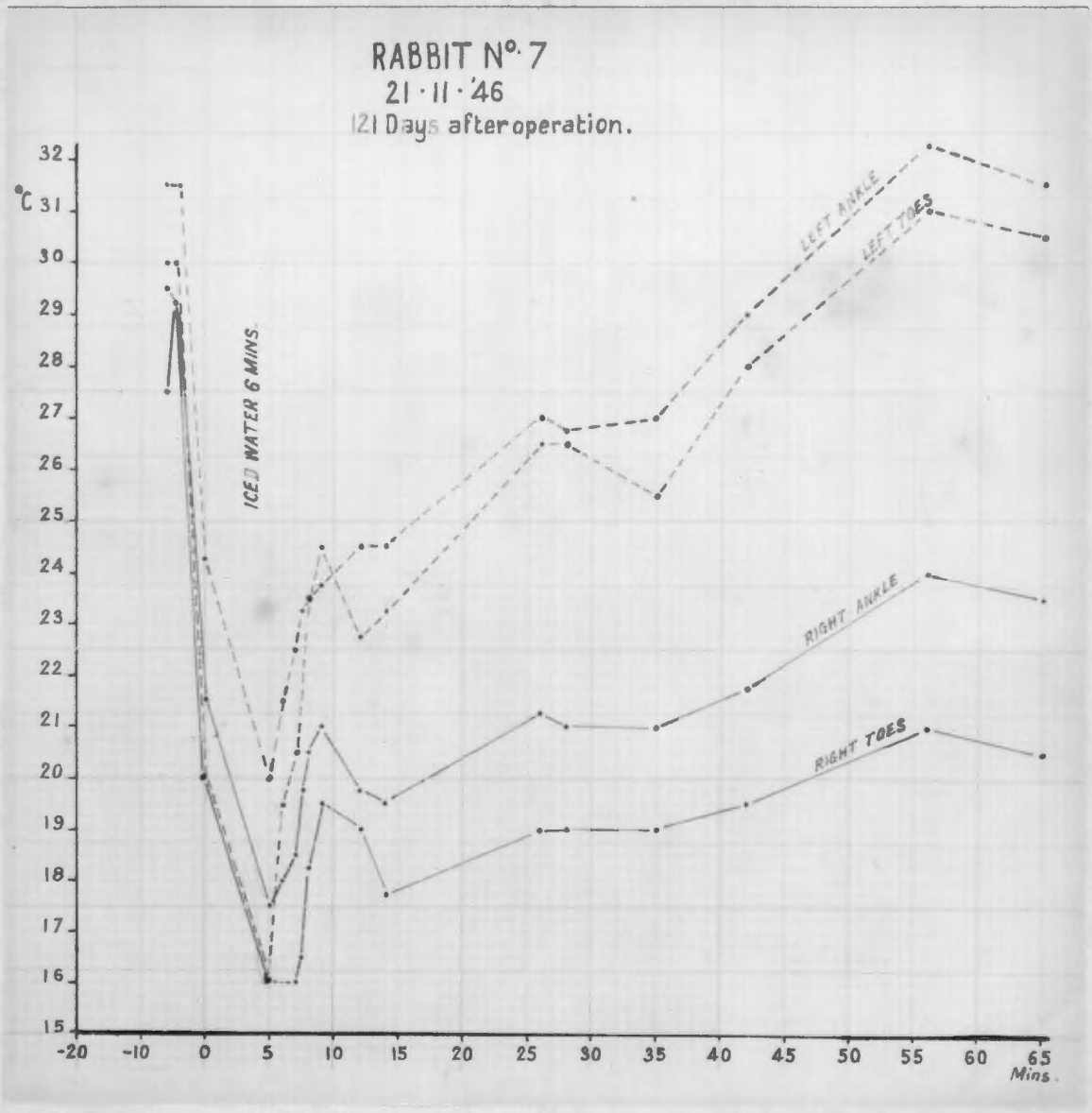

RABBIT N°. 7
21 · 11 · '46
121 Days after operation.
°C
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
ICED WATER 6 MINS.
LEFT ANKLE
LEFT TOES
RIGHT ANKLE
RIGHT TOES
-20
-10
0
5
10
15
20
25
30
35
40
45
50
55
60
65
Mins.

FIGURE X1.

RABBIT NO. 8.

Ganglia L2 - L6 were removed. Three temperature charts are included. (Figures XII, XIII and XIV), pages Nos. 51, 52 and 53.

Figure XII, (page No. 51), the feet were immersed into 15°C water. The initial temperature of the right foot continues to drop while the left side demonstrates that some disturbance of the heat regulation has occurred. Although definite and constant, the differences in temperature were never so marked in this animal as in previous cases.

Figures XIII and XIV, (pages Nos. 52 and 53), show that the toes of both feet have exactly the same temperature, while the left ankle remains slightly warmer than the right.

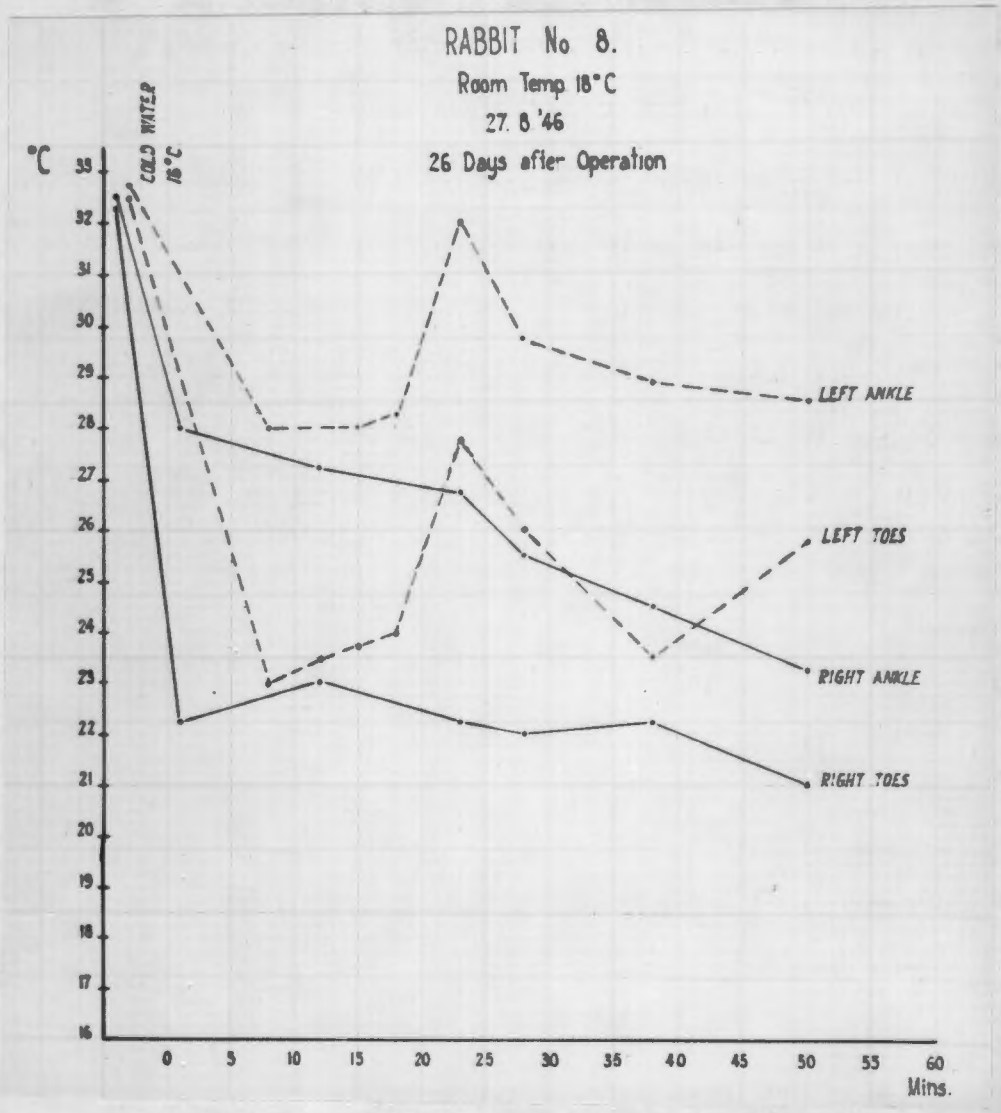


FIGURE X11.

Left foot was sympathectomized.

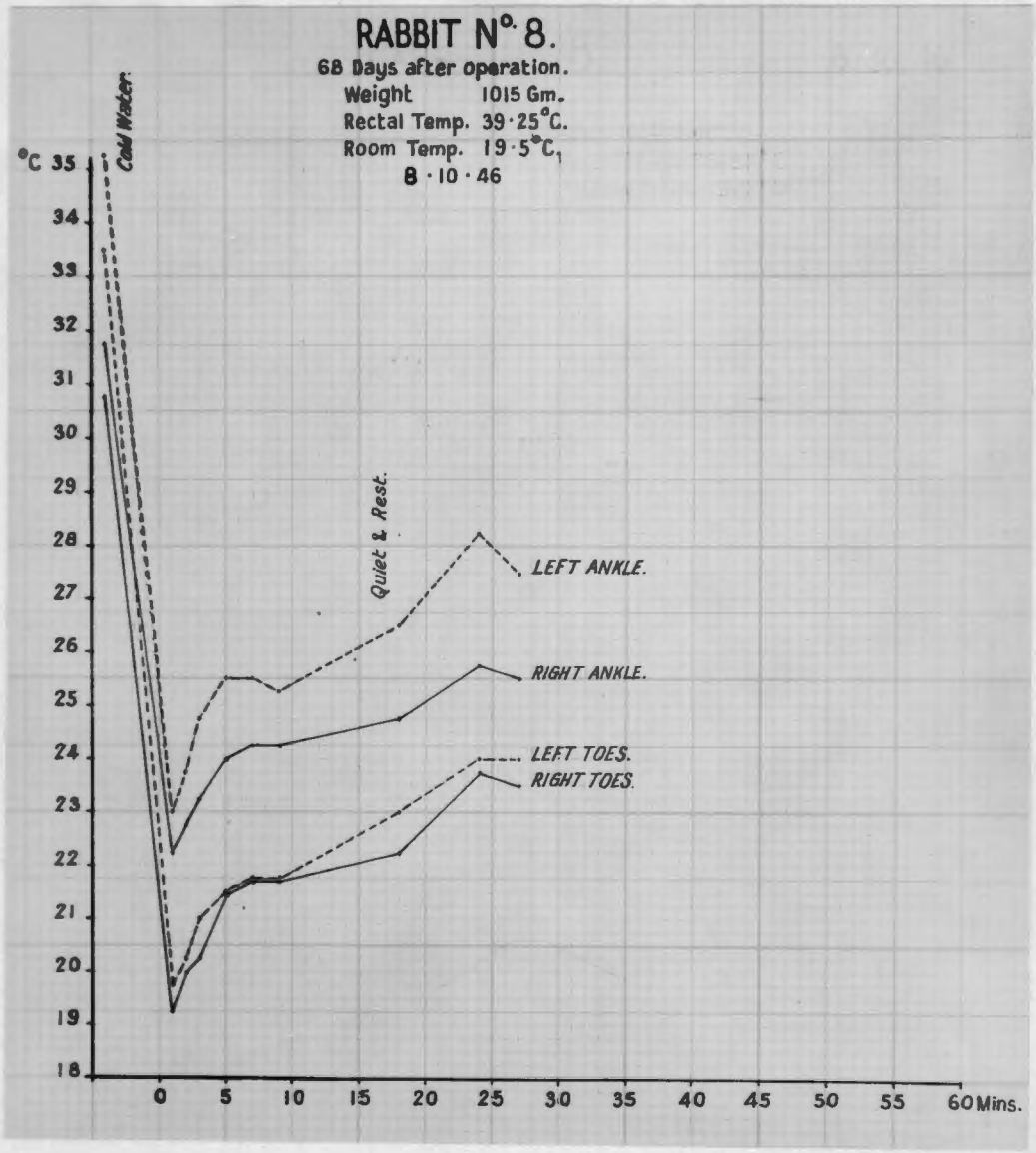

RABBIT N°. 8.
68 Days after operation.
Weight 1015 Gm.
Rectal Temp. 39·25°C.
Room Temp. 19·5°C.
8 · 10 · 46
°C 35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
Cold Water.
Quiet & Rest.
LEFT ANKLE.
RIGHT ANKLE.
LEFT TOES.
RIGHT TOES.
0 5 10 15 20 25 30 35 40 45 50 55 60 Mins.

FIGURE XIII.

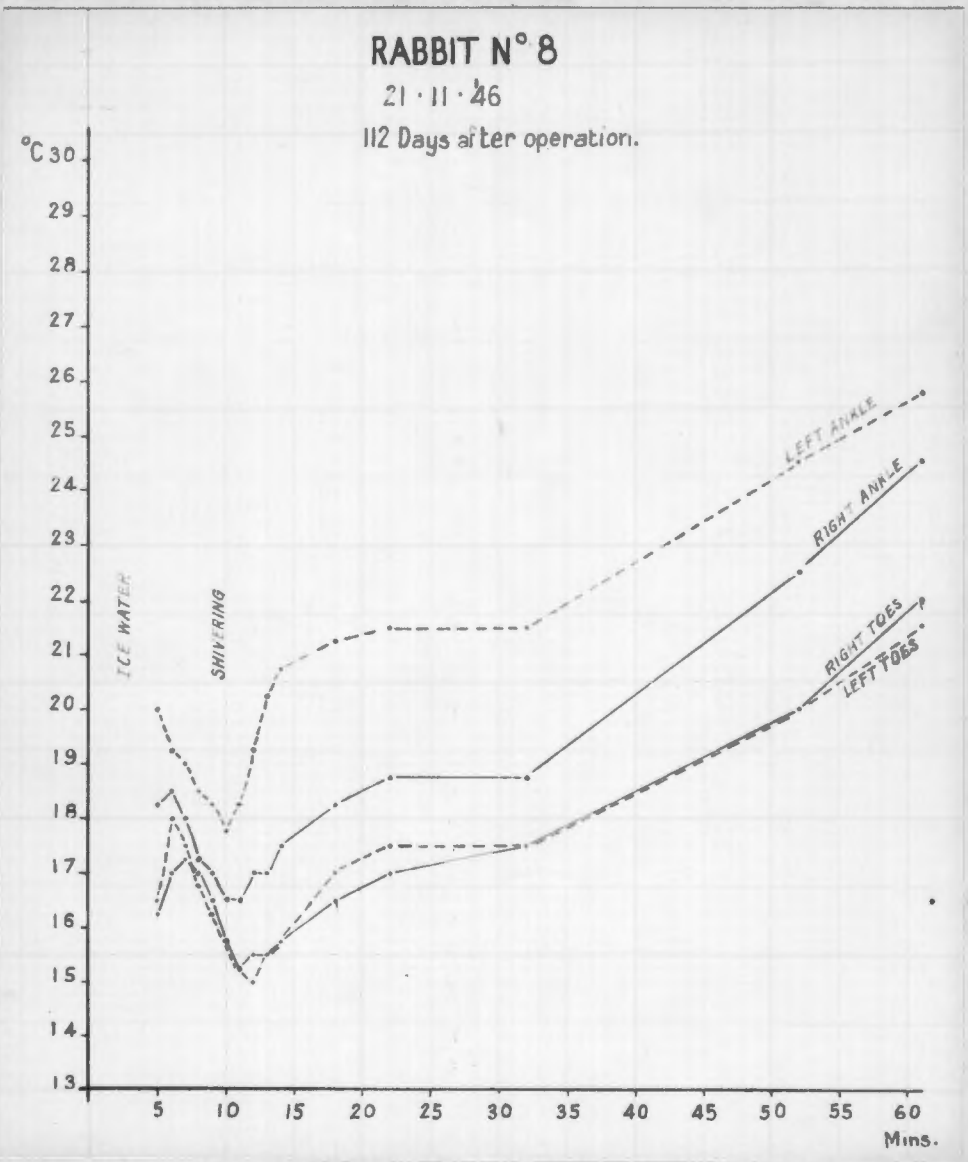

RABBIT N° 8
21 · 11 · 46
112 Days after operation.
°C 30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
ICE WATER
SHIVERING
LEFT ANKLE
RIGHT ANKLE
RIGHT TOES
LEFT TOES
5
10
15
20
25
30
35
40
45
50
55
60
Mins.

FIGURE XIV.

RABBIT NO. 10.

This rabbit had five ganglia removed viz. L1, 2, 3, 4 and 5.

Four temperature graphs are included.

Figure XV, (page No. 55) demonstrated a drop in the temperature of the right foot which continues for 20 minutes after cooling. The left foot shows a sudden rise in skin temperature with no appreciable rise for the first 30 minutes whereafter the temperature of both feet rises to a much higher level than before the experiment was commenced.

Figure XV1, (page No. 56), needs no special comment.

Figure XV11, (page No. 57), demonstrates a very marked difference in skin temperature. The pre-cooling temperature level is reached within 16 minutes in the sympathectomized foot.

The right foot remains cold for 55 minutes.

After 104 days (Figure XV111), page No. 58, this rabbit still demonstrates a marked hyperaemia of the left limb proving that the animal was properly sympathectomized.

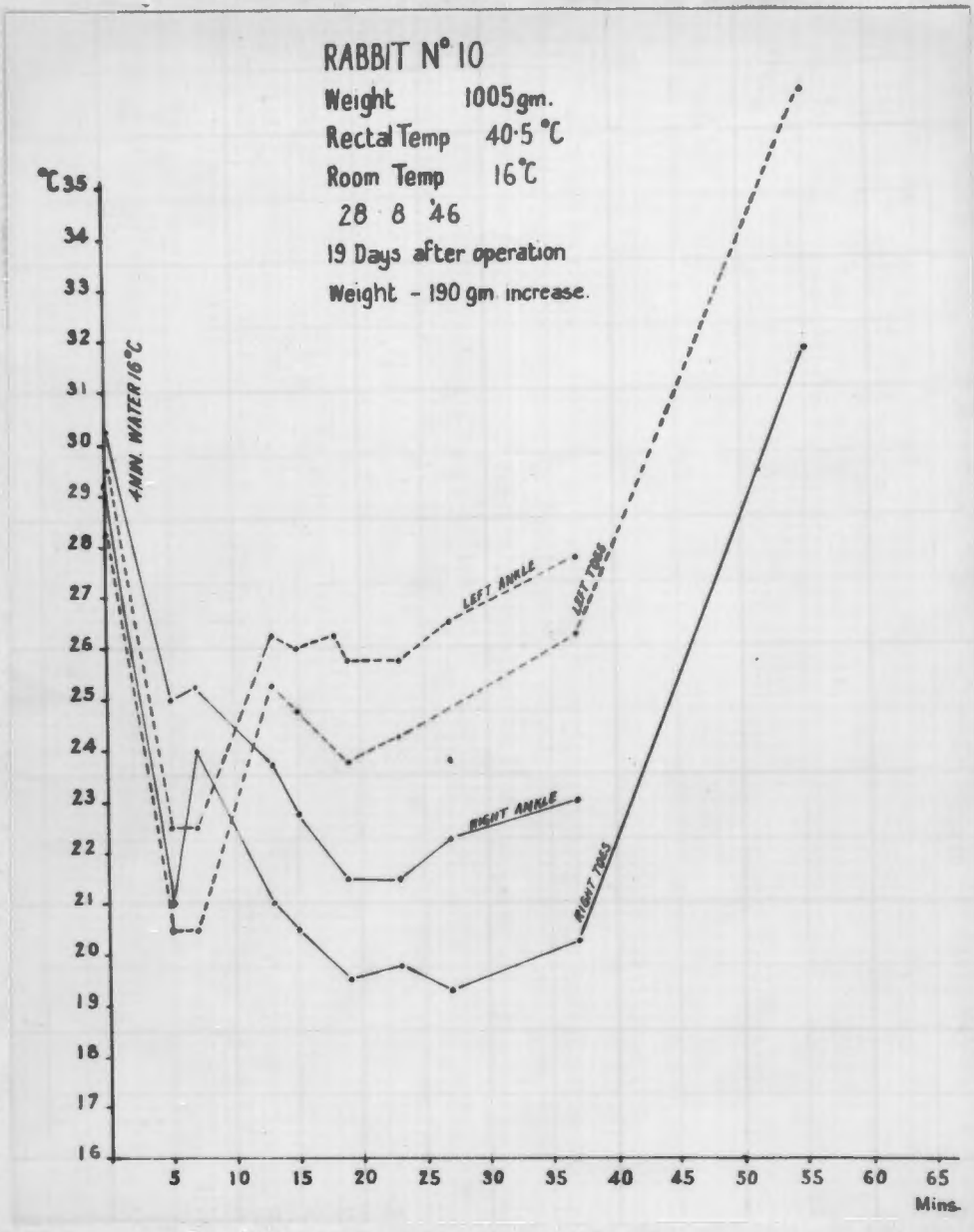


FIGURE XV.

Left foot was sympathectomized.

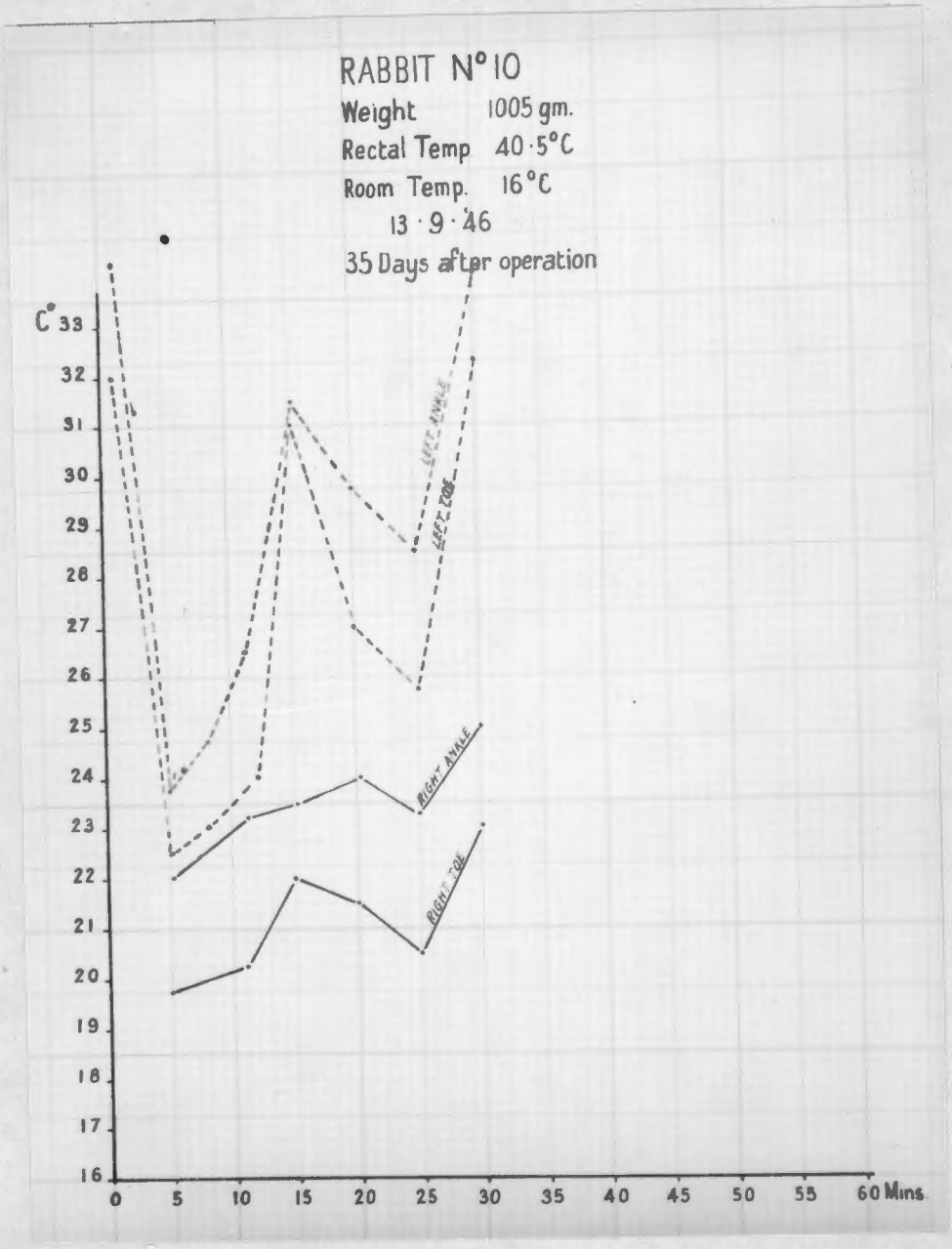

RABBIT N° 10
Weight 1005 gm.
Rectal Temp 40·5°C
Room Temp. 16°C
13·9·46
35 Days after operation
C°
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
0
5
10
15
20
25
30
35
40
45
50
55
60 Mins.
LEFT ANKLE
LEFT TOE
RIGHT ANKLE
RIGHT TOE

FIGURE XVI.

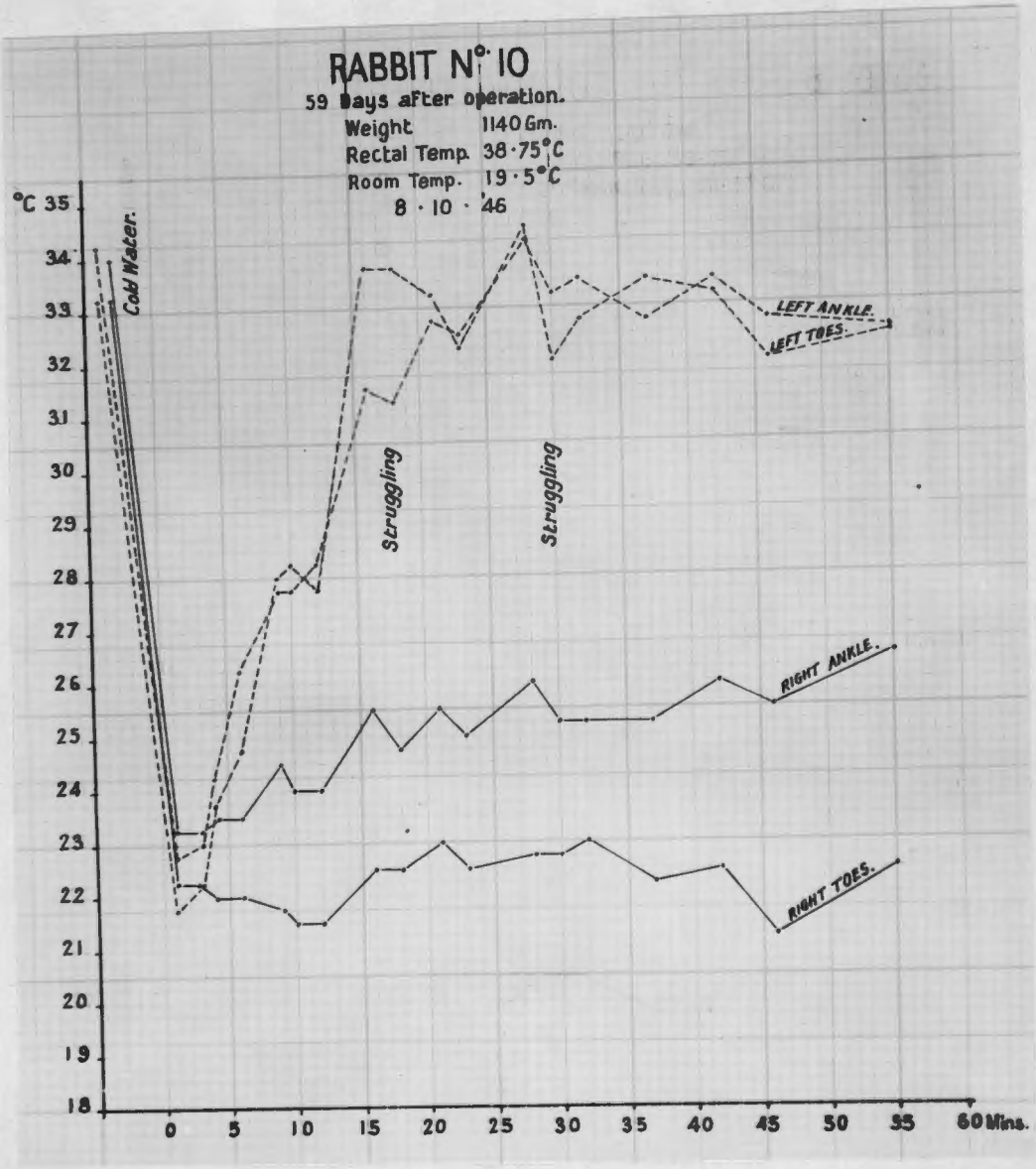

RABBIT N° 10
59 Days after operation.
Weight 1140 Gm.
Rectal Temp. 38·75°C
Room Temp. 19·5°C
8 · 10 · 46
°C 35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
Cold Water.
Struggling
Struggling
LEFT ANKLE.
LEFT TOES.
RIGHT ANKLE.
RIGHT TOES.
0 5 10 15 20 25 30 35 40 45 50 55 60 Mins.

FIGURE XV11.

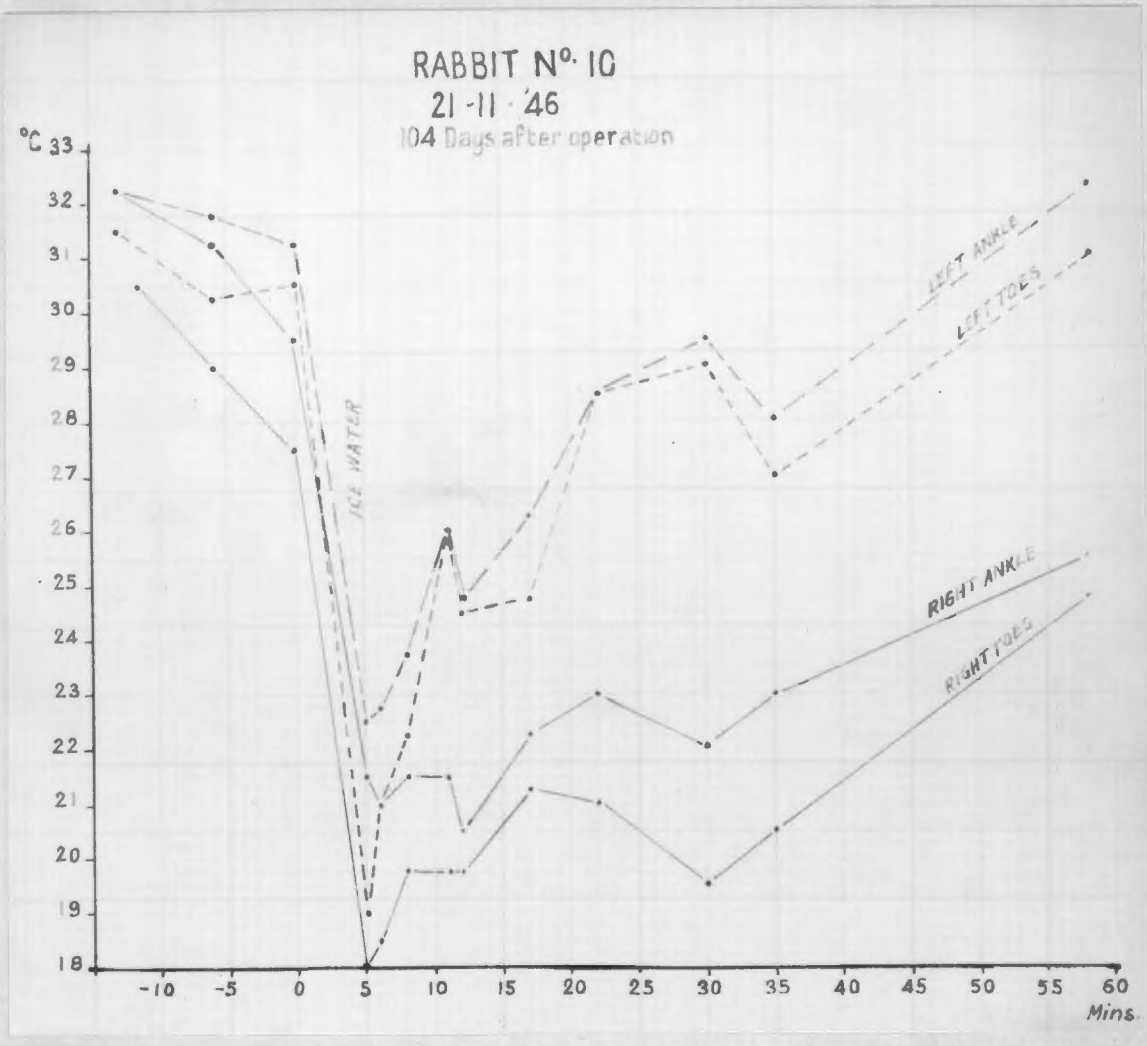


FIGURE XVIII.

RABBIT NO. 16.

L1 - L6 were removed with a fair result as far as temperature differences are concerned. (Figure XIX, page No. 60).

The right ankle regaining the pre-cooling level but the temperature of the right toes remaining low.

In Figure XX, (page No. 61), the temperature differences are small but the vasoconstriction in the right toes is clearly seen to be more permanent than in the sympathectomized foot.

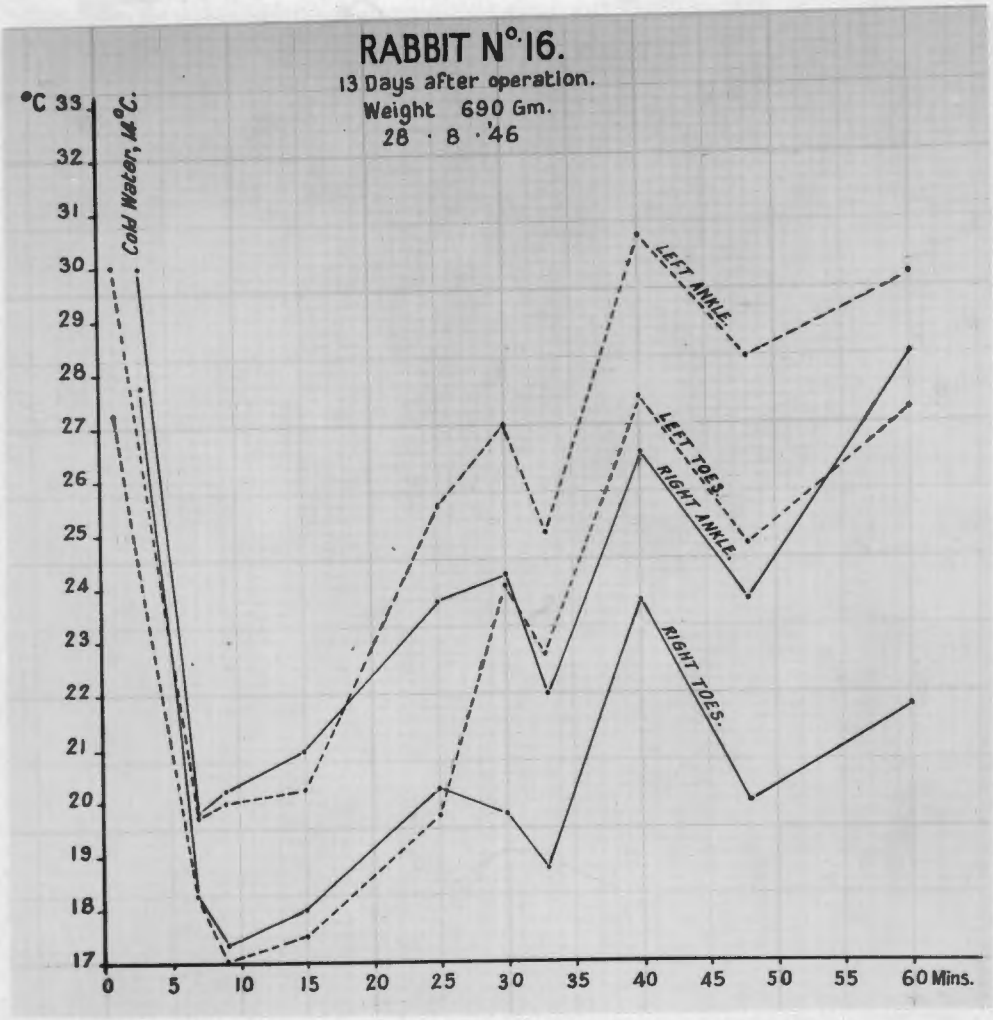


FIGURE XIX.

Left foot was sympathectomized.

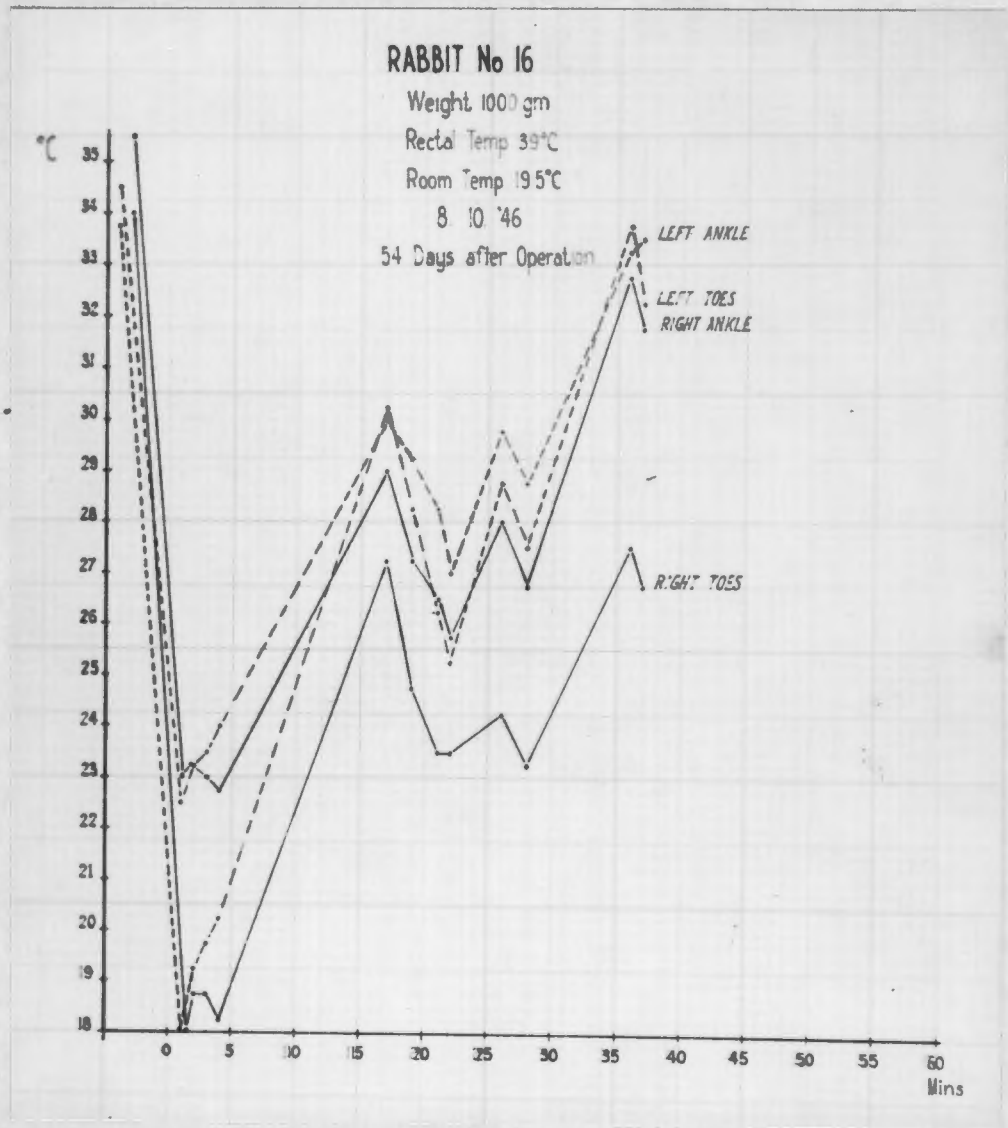

RABBIT No 16
Weight 1000 gm
Rectal Temp 39°C
Room Temp 19.5°C
8 10 '46
54 Days after Operation
°C
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
LEFT ANKLE
LEFT TOES
RIGHT ANKLE
RIGHT TOES
0
5
10
15
20
25
30
35
40
45
50
55
60
Mins

FIGURE XX.

RABBIT NO. 20.

This rabbit, (Figure XXI, page No. 63), belongs to the group (Group A) which survived up to the time of writing.

Sympathectomy was unsuccessful since on histological examination no ganglia could be demonstrated. The graphs are included to indicate the value of our method in demonstrating whether a limb is sympathectomized or not. The skin temperatures of both feet behave in the same way following cooling. Compare this reaction with that in an unoperated animal (Figure IV, page No. 39) on the one hand, and a successfully operated one (Figure XVII, page No. 57) on the other, and notice that Rabbit No. 20 reacted like the unoperated animals.

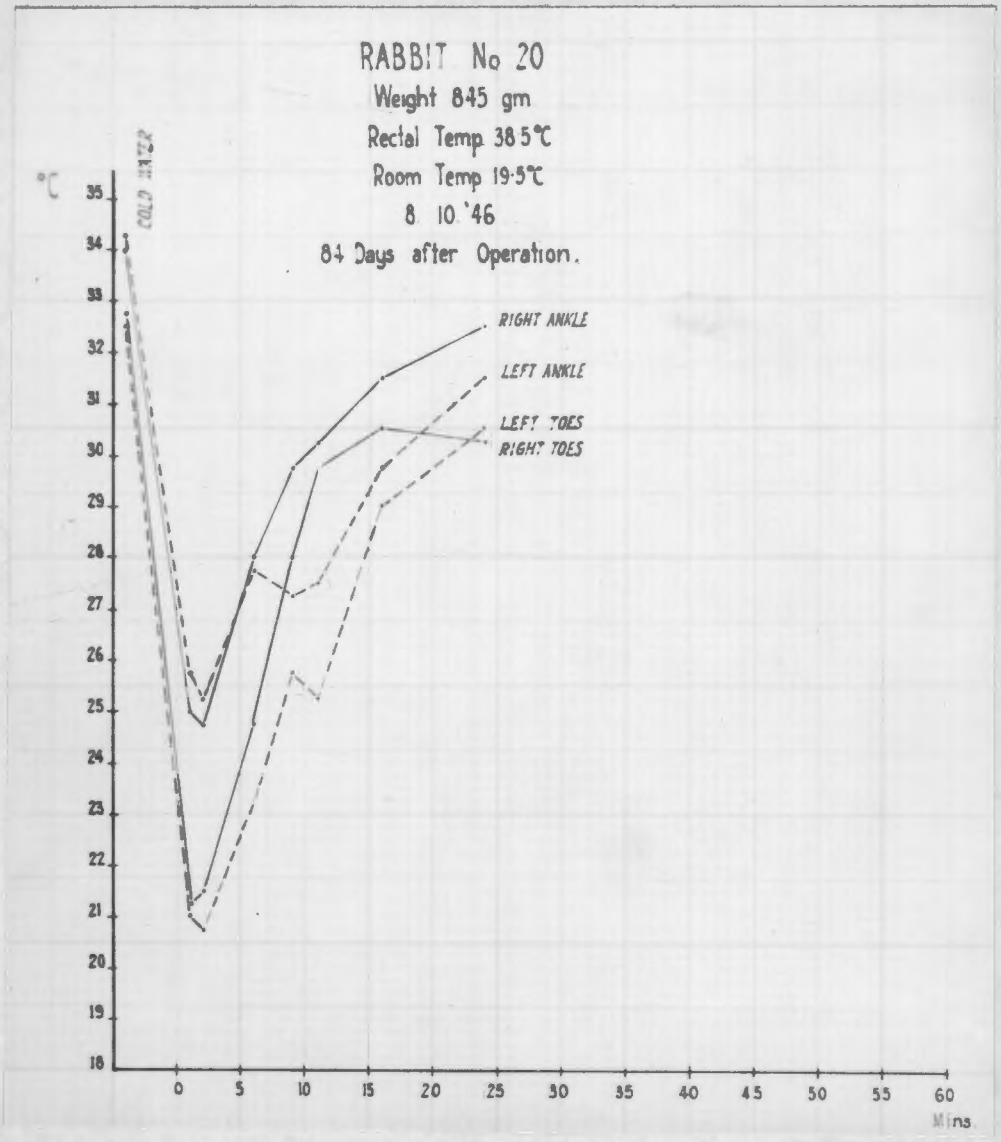


FIGURE XX1.

No sympathetic tissue was removed.

Rabbits Nos. 11, 12 and 13 belong to Group B. Only one postoperative graph is available in each case because the animals died between 20 and 29 days following operation.

RABBIT NO. 11. (Figure XXII, page No. 65).

L2 - L6 were removed. This is the only rabbit that ever demonstrated a temperature difference in favour of the unoperated foot although on histological examination sympathetic ganglia were demonstrated and the operation at the time appeared to be successful. Unfortunately the animal died and, therefore, could not be followed up. The reason for this unusual behaviour could therefore never be ascertained.

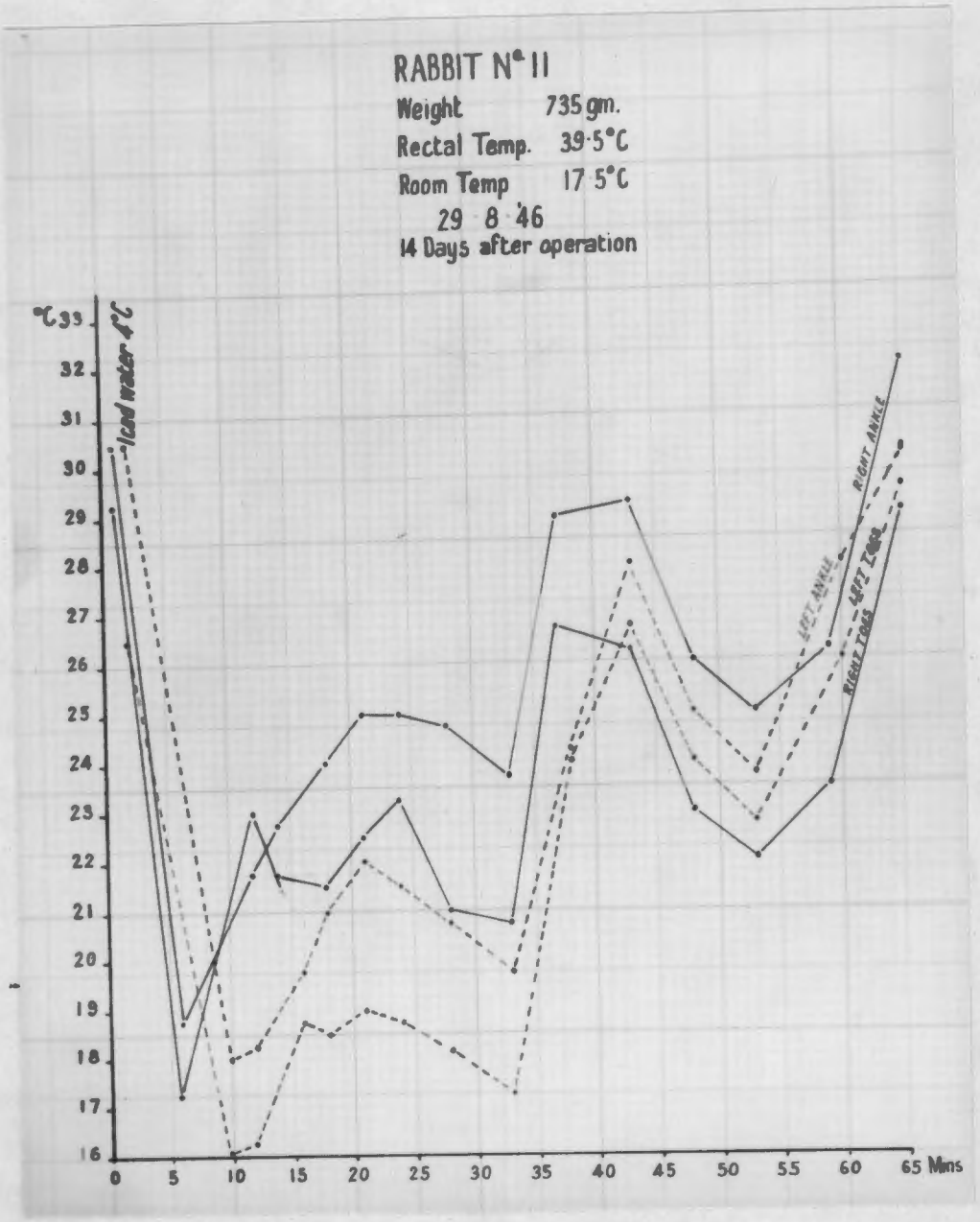


FIGURE XXII.

Left foot was sympathectomized.

RABBIT NO. 12. (Figure XXIII, page No. 67).

L1 - L6 removed. This rabbit shows the usual sudden rise in the 5 - 10 minutes period, the left foot only exceeding the right foot after 14 minutes. After 44 minutes the right foot suddenly warms up to the pre-cooling level and equals the left foot at 55 minutes.

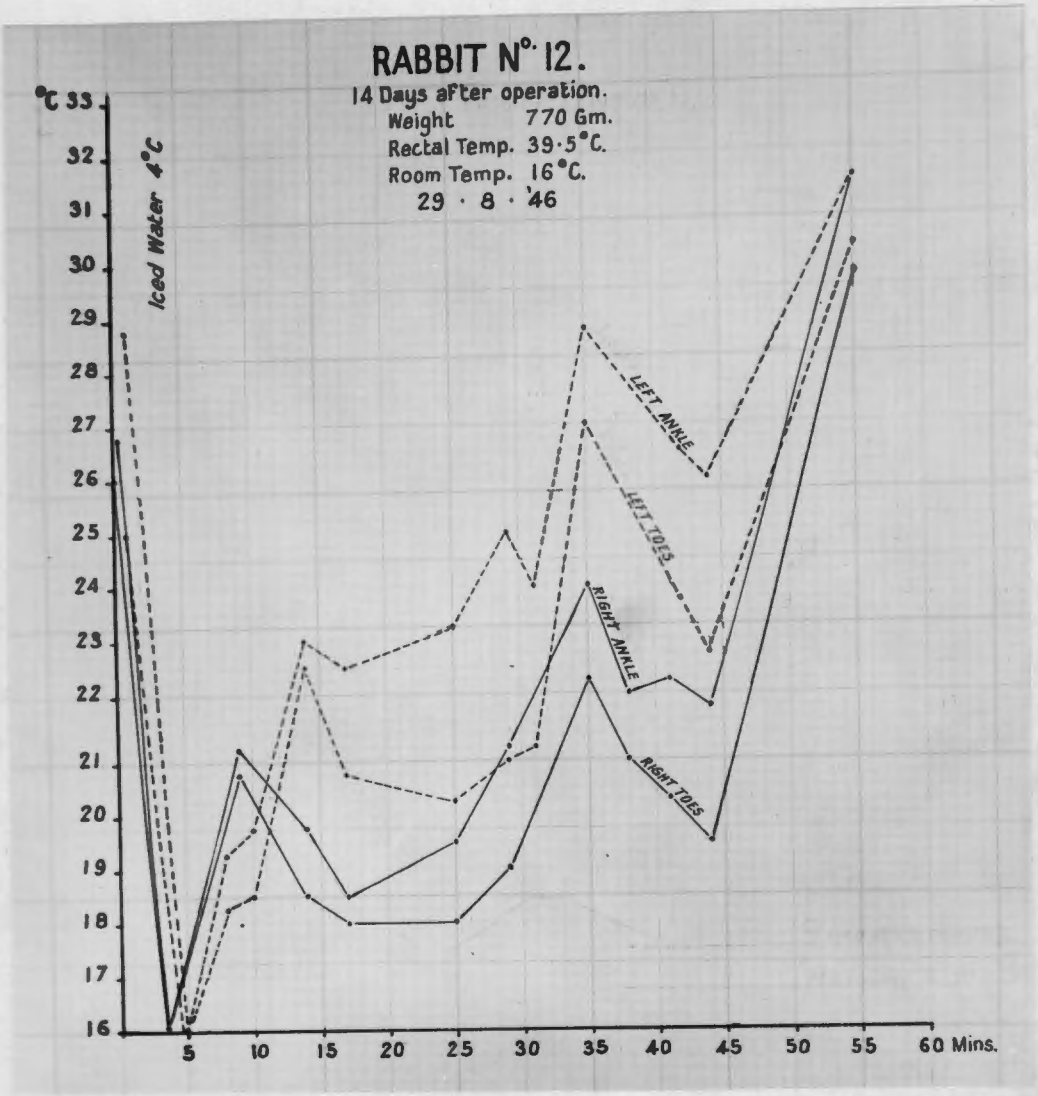


FIGURE XXIII.

RABBIT NO. 13.

This was a very good case because of the marked difference in the temperatures of the feet (Figure XXIV, page No. 69), even under laboratory circumstances and without the cold stimulus to produce a vasoconstriction.

L2 - L5 were removed. From the 15th - 52nd minute period the temperature differences are well marked and then the temperatures equalise.

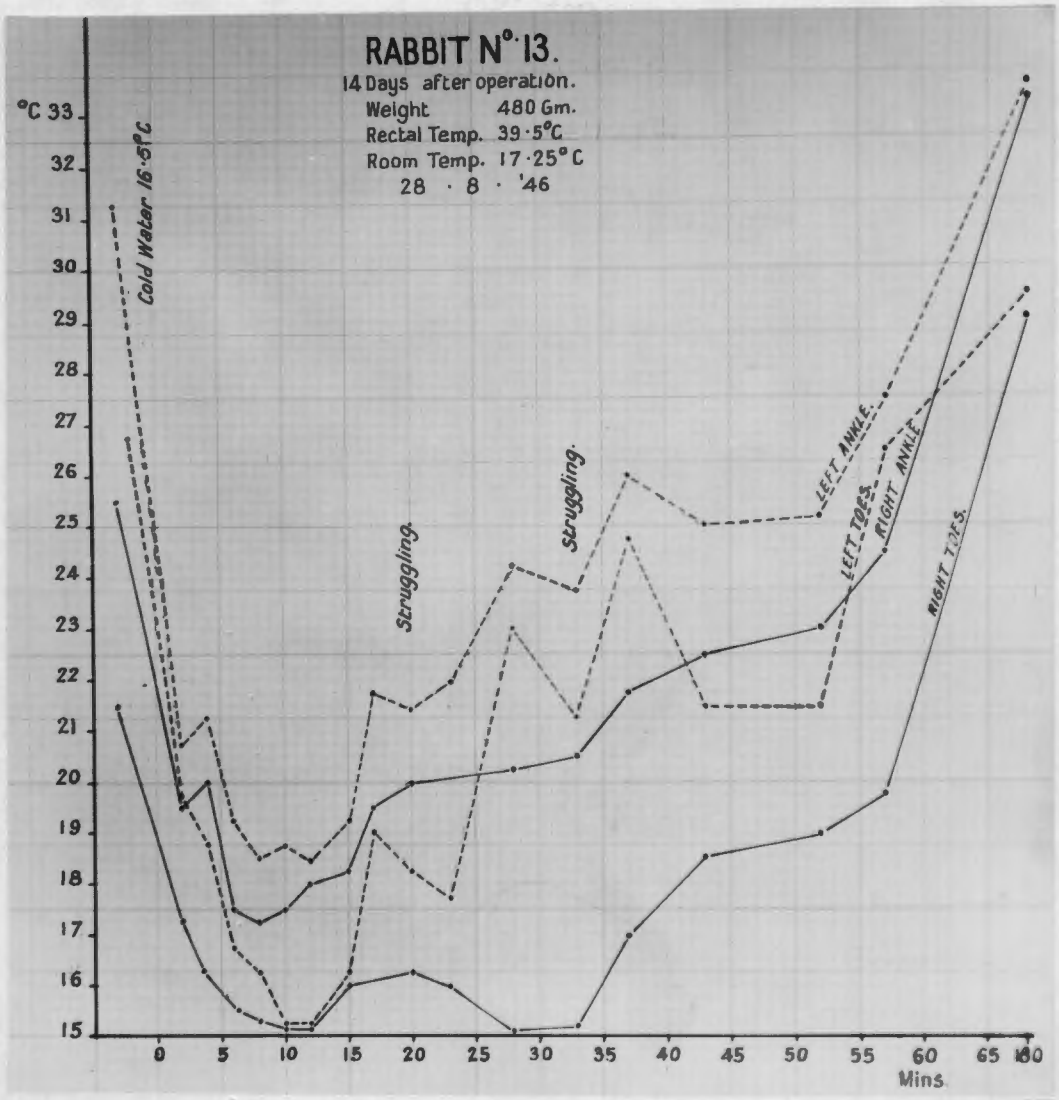

RABBIT N°13.
14 Days after operation.
Weight 480 Gm.
Rectal Temp. 39·5°C
Room Temp. 17·25°C
28 · 8 · '46
°C 33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
Cold Water 16·5°C
Struggling.
Struggling.
LEFT ANKLE.
LEFT TOES.
RIGHT ANKLE.
RIGHT TOES.
0 5 10 15 20 25 30 35 40 45 50 55 60 65 80
Mins.

FIGURE XXIV.

(b) THE EFFECT OF SYMPATHECTOMY ON OSSEOUS GROWTH.

From the foregoing chapter it is apparent that there can be no doubt that vasomotor paralysis did occur in the rabbits following successful lumber sympathectomy.

As we have pointed out previously the question arises whether this is sufficient to stimulate bone growth, whether the hyperaemia produced by vasoconstrictor paralysis is a strong enough stimulus to produce increased bone growth.

We have five rabbits, which survived the experiment, to be properly investigated. (Rabbits Nos. 2, 7, 8, 10 and 16).

The tibiae were X-Rayed in each case at the end of the observation period (Figures XXV - XXIX, pages Nos. 72 - 76), but no significant difference in length was demonstrated. Although the lengths of the tibiae were equal, marked differences in growth of the feet could be seen on the same X-Ray. The increase being in favour of the sympathectomized limb.

It can here also be mentioned that, as control, all these rabbits were X-Rayed in the first fortnight after operation and that the feet did not show any difference.

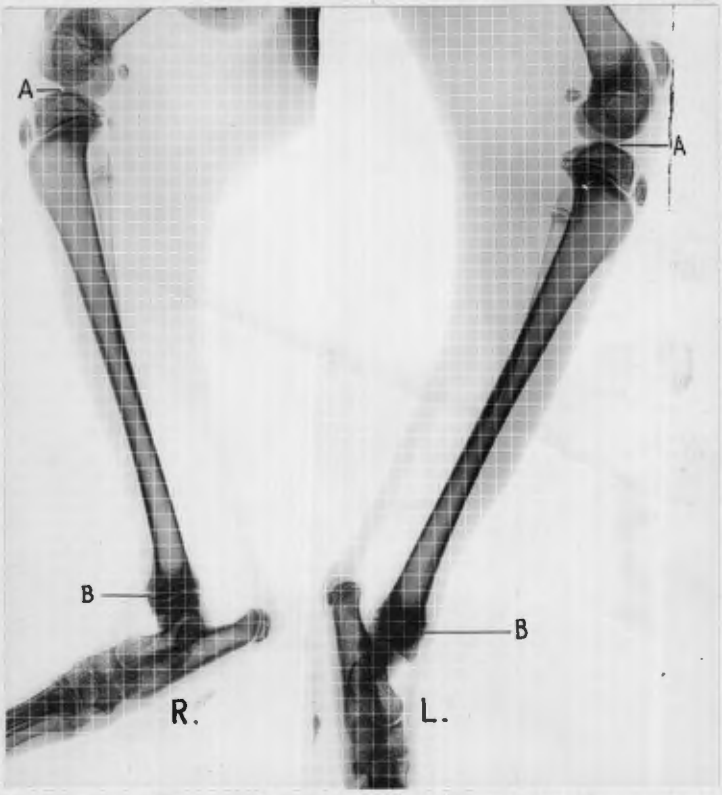
Although it is realised that it would have been better to use as controls .....

as controls, X-Rays of the feet obtained before operation, this could not be done on account of extreme difficulties of getting repeated X-Rays due to lack of adequate research facilities. In order to minimize unnecessary X-Raying the animals were X-Rayed for the first time immediately after they recovered from the operation or at least within 14 days following the operation. Thus no X-Ray was wasted on an animal that subsequently died during operation and the X-Ray examinations were reduced to a minimum. It was found that on the X-Rays taken within 14 days following operation no differences in the length of bone were recorded. Figure XXXIIa, page No. 82, is an example.

RABBIT NO. 2.

Date of X-Ray: 22.9.46.

64 DAYS AFTER OPERATION.



Right.

AB. 68.1

Left.

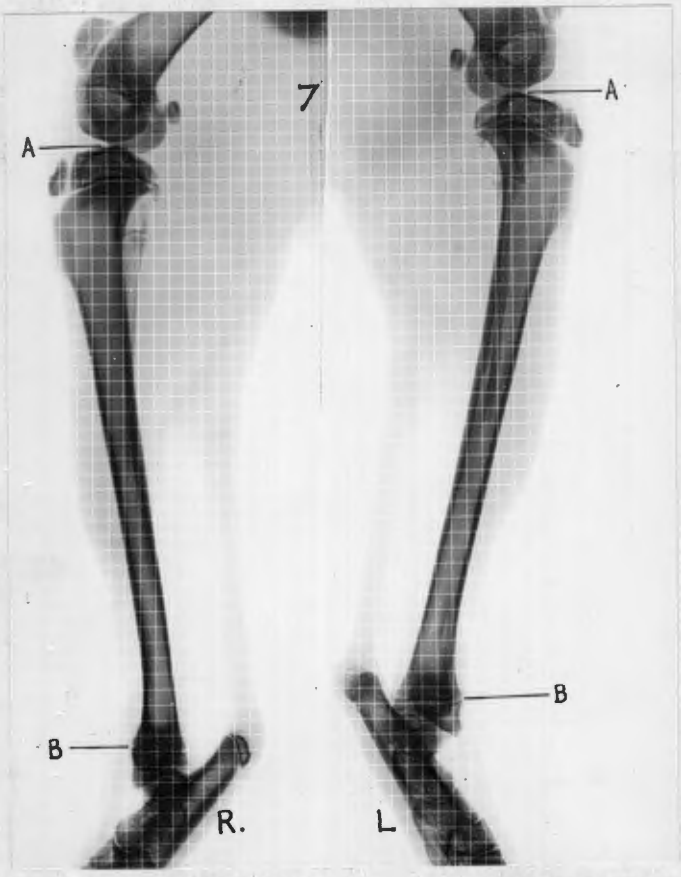
AB. 69.1 mm.

FIGURE XXV.

RABBIT NO. 7.

Date of X-Ray: 22.9.46.

61 DAYS AFTER OPERATION.



Right.

AB. 84.2

Left.

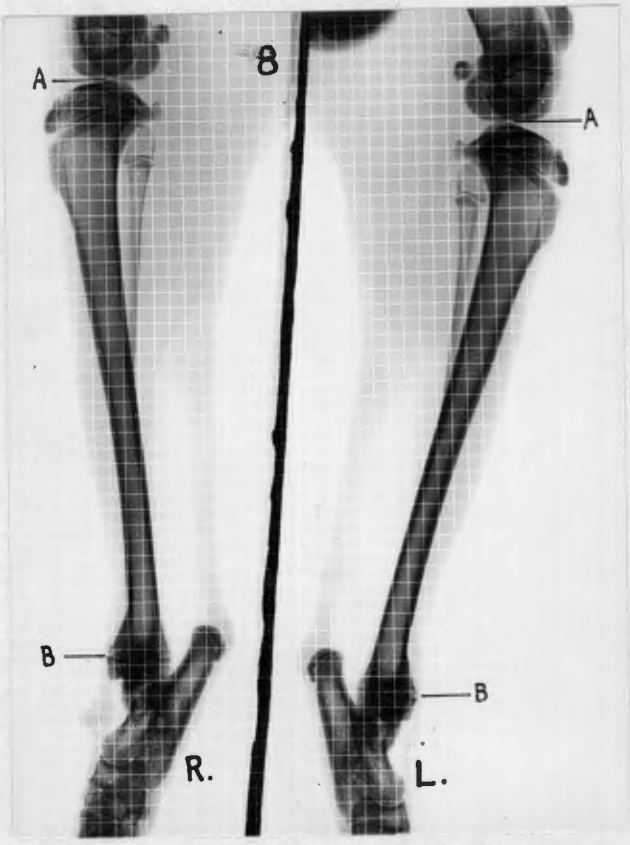
AB. 84.8 m.m.

FIGURE XXVI.

RABBIT NO. 8.

Date of X-Ray: 22.9.46.

52 DAYS AFTER OPERATION.



Right.

AB. 75.6

Left.

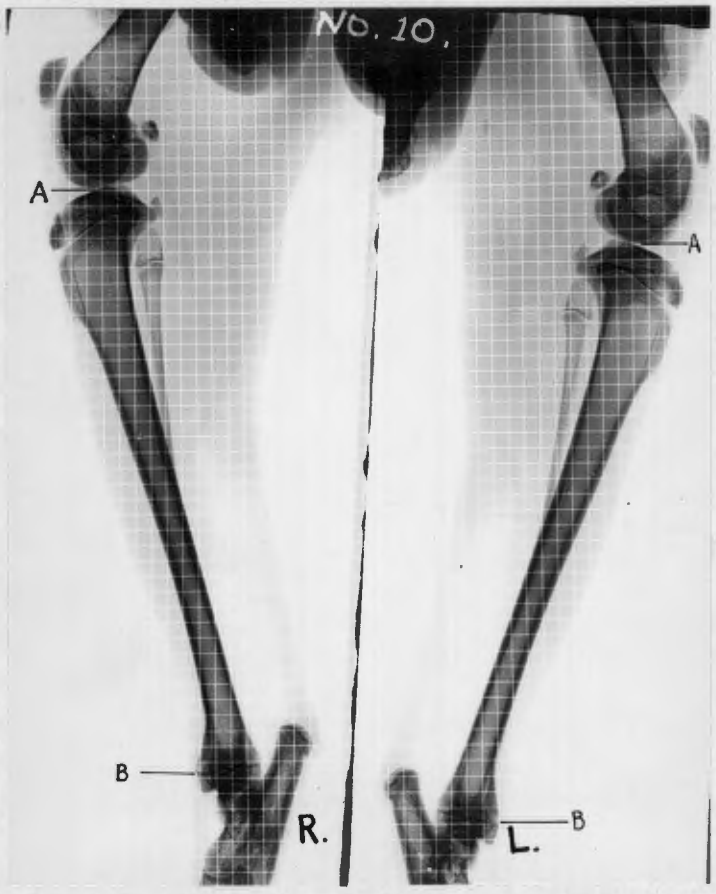
AB. 76.4 mm.

FIGURE XXVII.

RABBIT NO. 10.

Date of X-Ray: 22.9.46.

44 DAYS AFTER OPERATION.



Right.

AB. 78.2

Left.

AB. 78.7 mm.

FIGURE XXVIII.

RABBIT NO. 2.

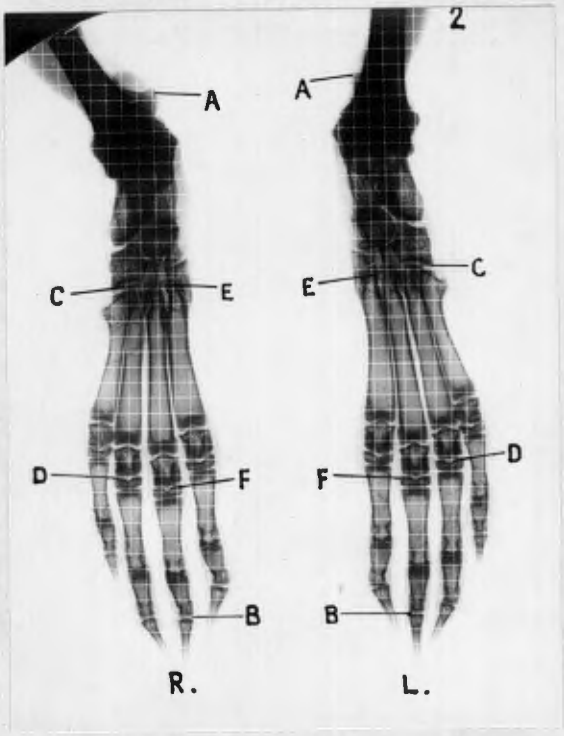
The three X-Rays of Rabbit No. 2 taken 29, 64 and 80 days after the operation, demonstrate a difference of 1.9 mm. (Figure XXX, page No. 78), 3.1 mm. (Figure XXXl, page No. 79), and 3.1 (Figure XXXll, page No. 80), in favour of the left foot. This corresponds to 2.74%, 4% and 4.25% respectively.

The metatarsal bones show a difference in length, the 2nd metatarsal of the left foot giving the greatest growth increase, viz. 2 mm. (Figure XXXll E.F., page No. 80).

RABBIT NO. 2.

Date of X-Ray: 18.8.46.

29 DAYS AFTER OPERATION.



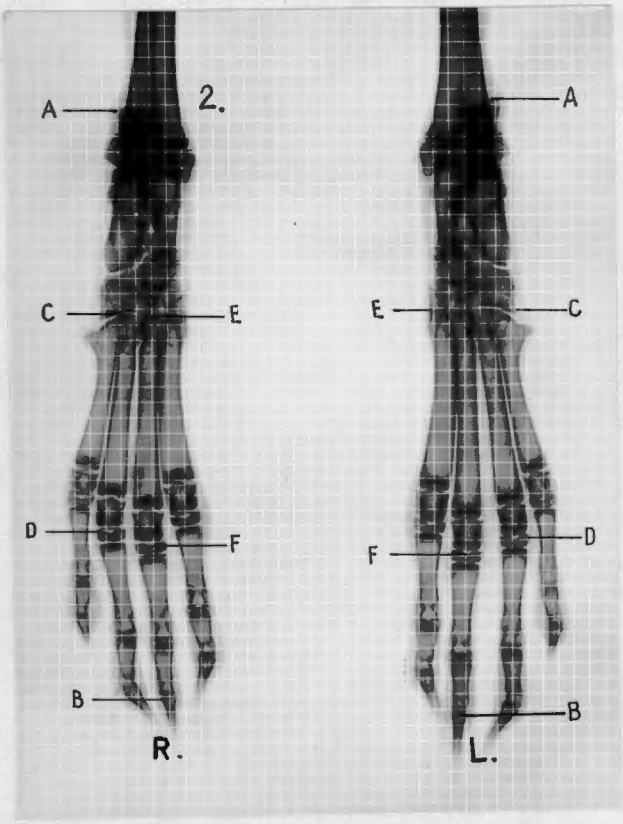
Right.		Left.
AB. 69.4		AB. 71.3 mm.
CD. 25.7	Third Metatarsal.	CD. 26.3 mm.
EF. 26.5	Second Metatarsal.	EF. 27.3 mm.

FIGURE XXX.

RABBIT NO. 2.

Date of X-Ray: 22.9.46.

64 DAYS AFTER OPERATION.



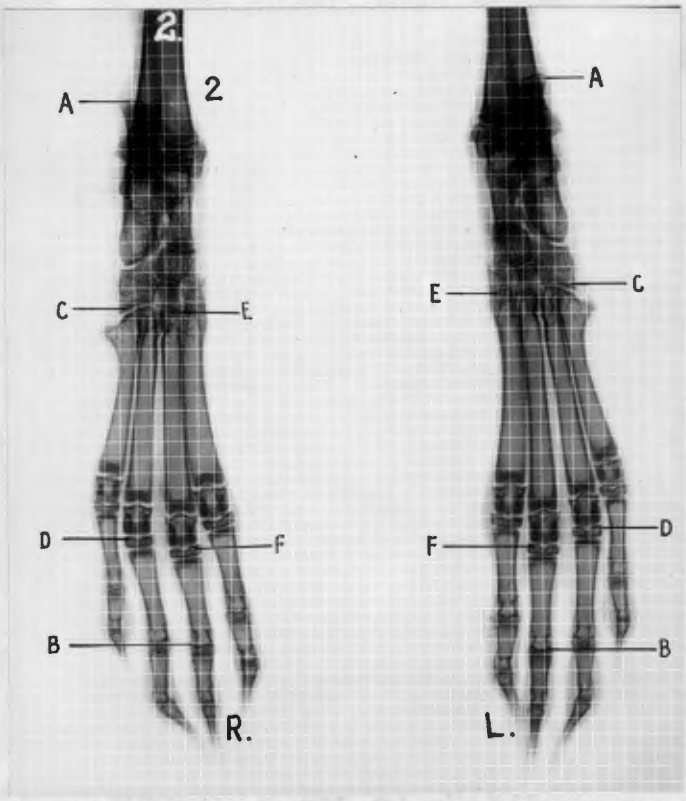
Right.	Left.
AB. 77.4	AB. 80.5 mm.
CD. 28.6 Third Metatarsal.	CD. 30.2 mm.
EF. 29.7 Second Metatarsal.	EF. 31.5 mm.

FIGURE XXXI.

RABBIT NO. 2.

Date of X-Ray: 8.10.46.

80 DAYS AFTER OPERATION.



Right.		Left.
AB. 72.9		AB. 76.0 mm.
CD. 30.5	Third Metatarsal.	CD. 31.8 mm.
EF. 31.2	Second Metatarsal.	EF. 33.2 mm.

FIGURE XXXII.

RABBIT NO. 7.

Three X-Ray photographs of Rabbit No. 7 are included. (Figures XXXIIa, XXXIII and XXXIV, pages Nos. 82, 83 and 84). On the third day after the operation the feet were of the same length. (Figure XXXIIa, page No. 82).

61 days after the operation the left foot was longer than the right by 1.7 mm. which corresponds to 2%. (AB Figure XXXIII, page No. 83).

The first toe of the left foot (CD Figure XXXIII, page No. 83) was slightly longer (.9 mm.) than the corresponding toe on the right foot.

After 78 days, the left foot is longer then the right by 1.2 mm. (AB Figure XXXIV, page No. 84). This represents an excess growth of 1.33%. The Third toe of the left foot is 1.1 mm. longer than that of the right foot. This represents 2% excess growth.

RABBIT NO. 7.

Date of X-Ray: 18.8.46.

3 DAYS AFTER OPERATION.

Right.

AB. 66.8

Left.

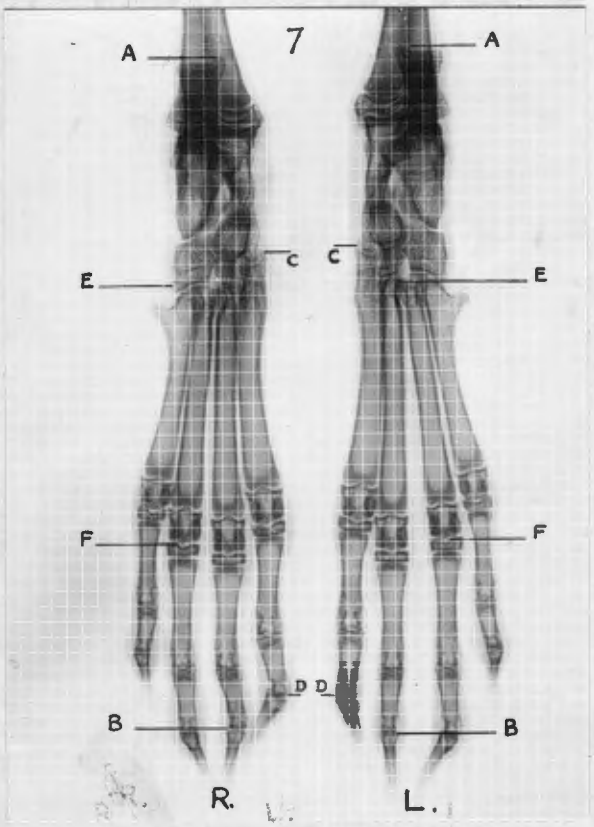
AB. 66.8 mm.

FIGURE XXXIIa.

RABBIT NO. 7.

Date of X-Rays: 22.9.46.

61 DAYS AFTER OPERATION.



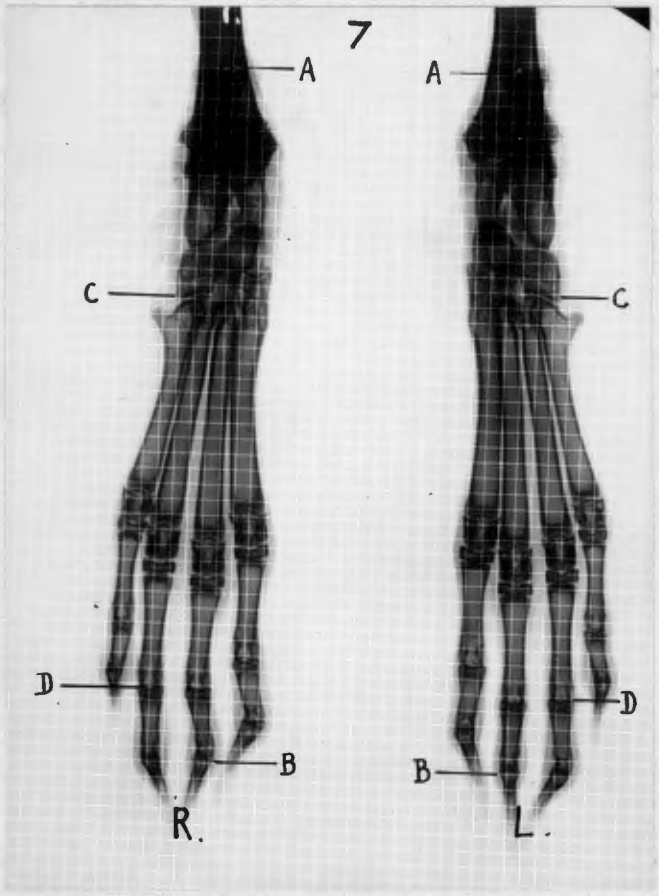
Right.		Left.
AB. 87.8		AB. 89.5 mm.
CD. 57.9	First Toe.	CD. 58.8 mm.
EF. 34.2	Third Metatarsal.	EF. 34.9 mm.

FIGURE XXXIII.

RABBIT NO. 7.

Date of X-Ray: 8.10.46.

78 DAYS AFTER OPERATION.



Right.	Left.
AB. 90.4	AB. 91.6 mm.
CD. 52.5	CD. 53.6 mm.

FIGURE XXXIV.

RABBIT NO. 8.

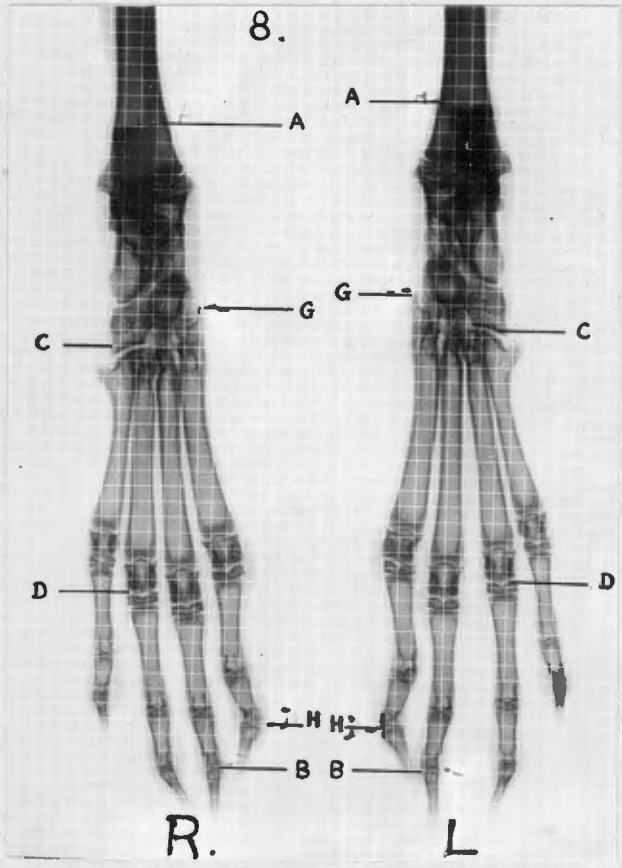
Photographs are included of Rabbit No. 8 taken 52 days and 68 days after the operation.

In Figure XXXV, (page No. 86), the growth in the left foot is 2.3 mm. greater than that in the right, and in Figure XXXVI, (page No. 87), 2.4 mm. greater. This represents an excess growth in the left foot of 2.72% and 3.07% respectively.

RABBIT NO. 8.

Date of X-Ray: 22.9.46.

52 DAYS AFTER OPERATION.



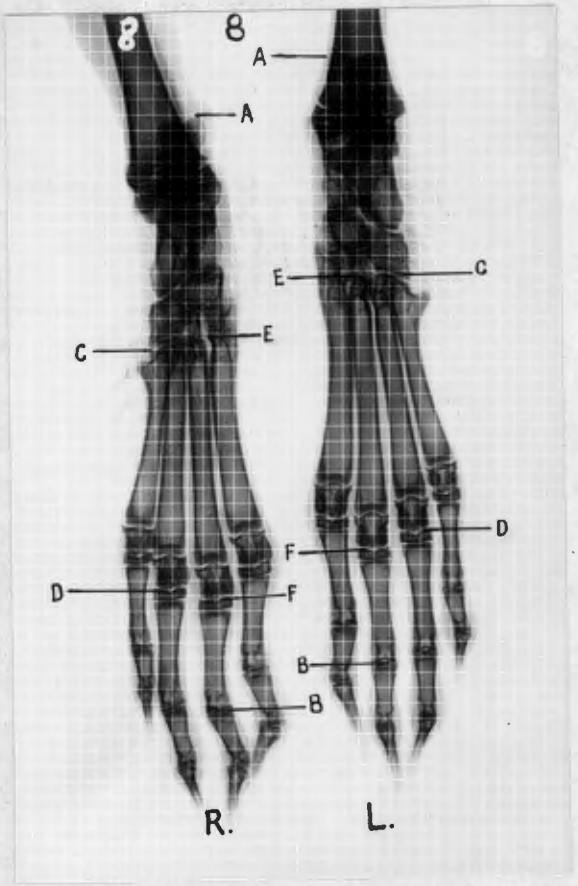
AB. 84.4		AB. 86.7
CD. 32.2	Third Metatarsal	CD. 33.3
GH. 55.1	First toe	GH. 56.9

FIGURE XXXV.

RABBIT NO. 8.

Date of X-Ray: 8.10.46.

68 DAYS AFTER OPERATION.



Right.		Left.
AB. 78.3		AB. 80.7 mm.
CD. 33.2	Third Metatarsal	CD. 34.2 mm.
EF. 34.4	Second Metatarsal	EF. 35.6 mm.

FIGURE XXXVI.

RABBIT NO. 10.

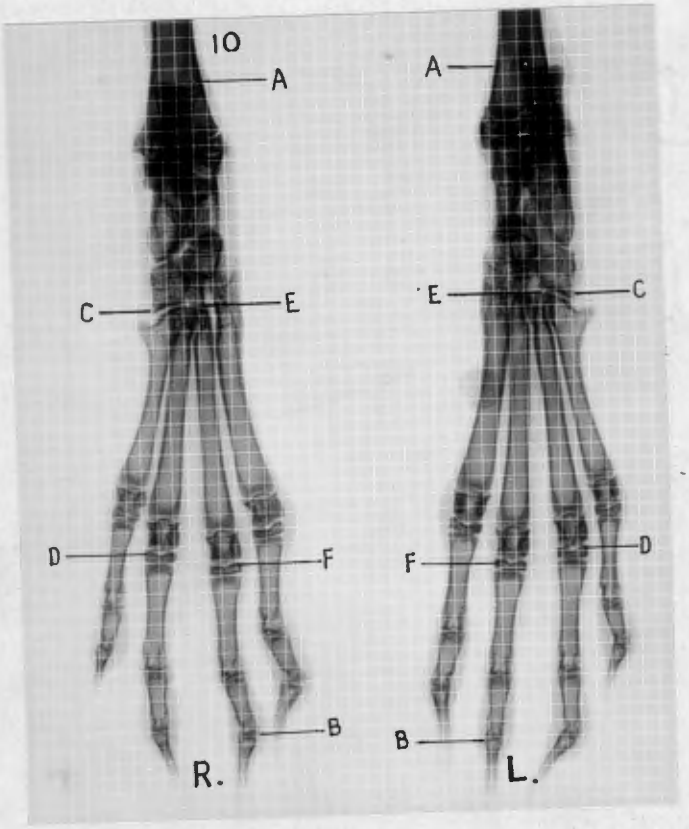
The left foot of Rabbit No. 10 also shows a very definite growth in excess of that of the right foot - 2.20% excess 44 days after the operation and 1.95% 59 days after operation. (AB in Figure XXXVII, page No. 89, and AB in Figure XXXVIII, page No. 90 respectively.

Up to 1.2 mm. excess growth is demonstrable in the third metatarsal of the left foot (CD in Figure XXXVII, page No. 89), which amounts to 3.26% over the right foot.

RABBIT NO. 10.

Date of X-Ray: 22.9.46.

44 DAYS AFTER OPERATION.



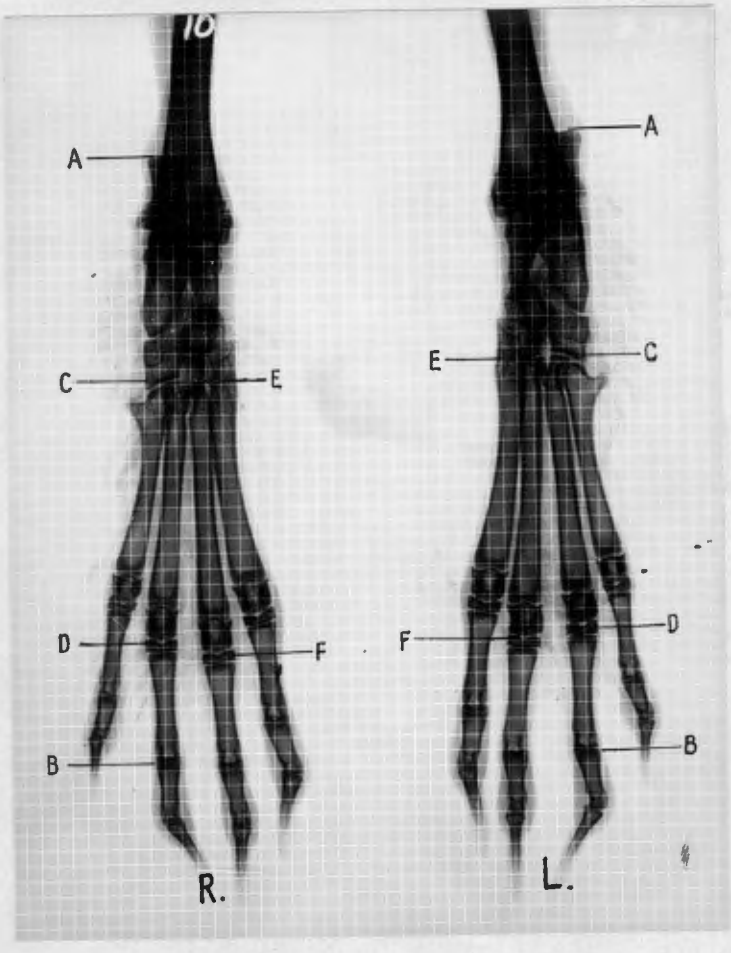
Right.		Left.
AB. 86.3		AB. 88.3 mm.
CD. 32.6	Third Metatarsal.	CD. 33.8 mm.
EF. 34.3	Second Metatarsal.	EF. 35.3 mm.

FIGURE XXXVII.

RABBIT NO. 10.

Date of X-Ray: 8.10.46.

59 DAYS AFTER OPERATION.



Right.		Left.
AB. 79.7		AB. 81.2 mm.
CD. 34.3	Third Metatarsal.	CD. 35.4 mm.
EF. 36.	Second Metatarsal.	EF. 36.7 mm.

FIGURE XXXVIII.

RABBIT NO. 16.

This Rabbit does not show any excess increase in bone growth of the left foot as a whole. (Figure XXXIX and XL, pages Nos. 92 and 93).

RABBIT NO. 20.

In this case no growth above the normal was expected because, as explained, no sympathetic tissue was removed at operation. And no hyperaemia of the vessels on the operated side could be demonstrated. This animal, therefore, served as a control.

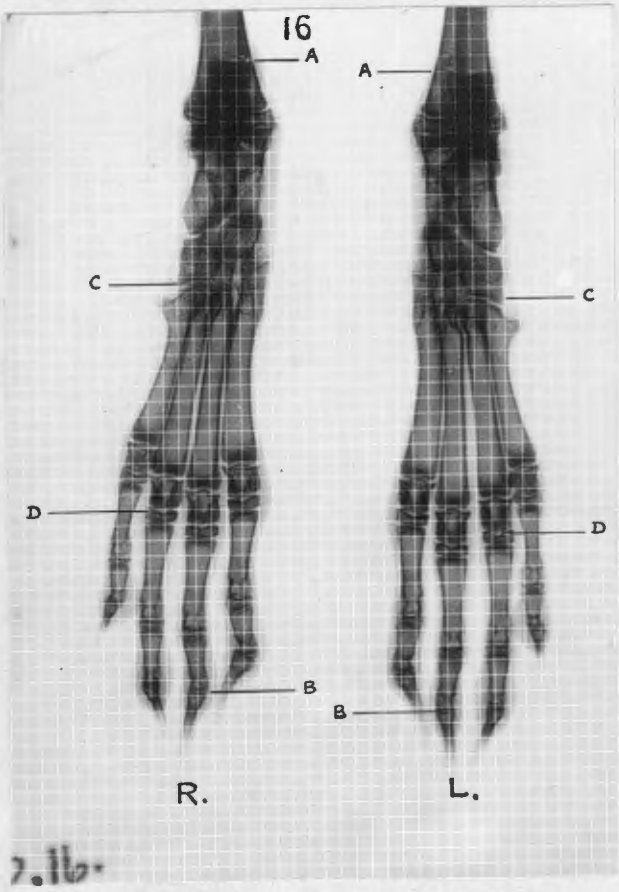
RABBITS NOS. 11, 12 and 13.

These rabbits had feet of equal size when X-Rayed 3 days after operation. They unfortunately died 20 - 29 days later. Therefore the X-Rays can serve as controls only.

RABBIT NO. 16.

Date of X-Ray: 22.9.46.

38 DAYS AFTER OPERATION.



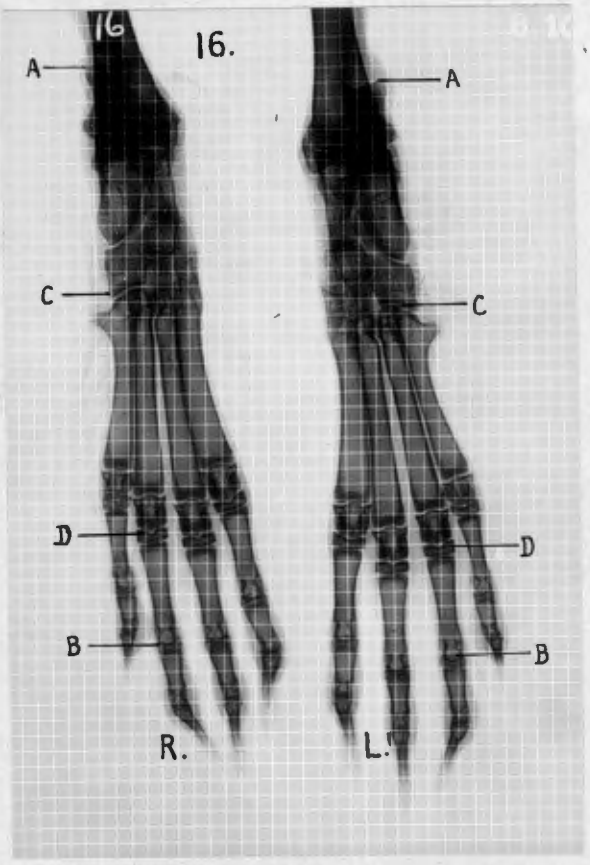
Right.		Left.
AB. 83.3		AB. 84.2 mm.
CD. 30.9	Third Metatarsal.	CD. 31.5 mm.

FIGURE XXXIX.

RABBIT NO. 16.

Date of X-Ray: 8.10.46.

54 DAYS AFTER OPERATION.



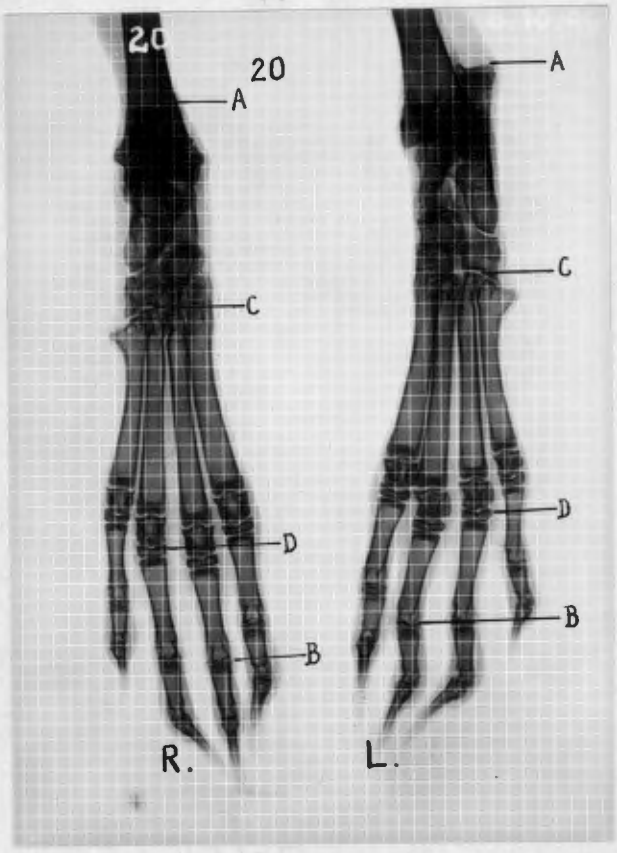
Right.		Left.
AB. 76.9		AB. 76. 9 mm
CD. 32.7	Third Metatarsal.	CD. 32.5 mm.

FIGURE XL.

RABBIT NO. 20.

Date of X-Ray: 8.10.46.

84 DAYS AFTER OPERATION.



Right.	Left.
AB. 74.3	AB. 74.6 mm.
CD. 31.7	CD. 31.6 mm.

FIGURE XL1.

SUMMARISING WHAT HAS BEEN SAID IN THIS CHAPTER :

Repeated roentgenographic records of the feet of 5 animals were taken at various intervals after the operation, and the bones measured by means of a graduated caliper. The results were compared with the X-Rays obtained in all animals immediately after operation and animals Nos. 20 and 17, who had no sympathectomies. No significant differences could be demonstrated in the controls, while in the others the X-Rays taken from 29 to 80 days following the operation, differences in growth between the two feet, constantly in favour of the sympathectomized limb, were demonstrated.

In Table Page 96, the results of the four animals who showed increase in growth are compared with X-Rays of four controls and the percentages of excess growth is calculated.

In measuring the bones, it will be noticed that AB represents the whole length of the foot from the calcaneus to the 1st or 2nd interphalangeal joint.

The exact points of measurement were decided on after inspection of the X-Rays, as it is sometimes impossible to identify a particular interphalangeal joint, making it difficult to compare points chosen on the earlier X-Ray with exactly the same points when the rabbit is re-X-Rayed. This explains why 3.1 mm. growth in the case of Rabbit No. 2 represents 4% after 64 days and 4.2% after 80 days.

RABBIT NO.	DAYS AFTER OPERATION.	EXCESS GROWTH IN LEFT FOOT IN M.M.	PERCENTAGE INCREASE.
2.	29 64 80	1.9 3.1 3.1	2.74 4 4.25
7.	61 78	1.7 1.2	2 1.33
8.	52 68	2.3 2.4	2.72 3.07
10.	44 59	2.0 1.5	2.20 1.92
CONTROL X-RAYS.			
20.	84	0.3	(No ganglia removed).
12.	3	0.2	(Died too soon).
13.	3	0	(Died too soon).
17.	-	0.1	(Not operated).

VI. DISCUSSION.

In the introduction it has been pointed out that the surgeon may be called upon to consider the various methods of leg equilization, and also how the growth of a limb may be stimulated. As previously mentioned, growth of a bone depends upon the activity of the cells at the epiphyseal lines. These are stimulated by various factors. Only one is of special interest to us in this paper, i.e. increased bloodflow, which we believe can stimulate bone growth above that which would occur from the normal blood supply.

After lumbar sympathectomy, the loss of vasomotor tone of the vessels of the lower limb results in an increased bloodflow in which the region of the epiphyseal lines also partakes.

Constriction and dilatation are the normal functions of the blood vessels, their state depending on the circumstances of which environmental temperature is one of the most important. The conservation and dissipation of heat to meet the environmental changes in temperature are primary functions required by the warm-blooded animal.

In the human this adjustment is accomplished by the amount of heat which is dissipated from the skin, particularly of the hands and the feet. As Goetz 1940 has remarked, the hands and the feet serve virtually as our [illegible].

as our radiators. By adjusting the bloodflow through them man keeps his body temperature constant.

The tone of normal blood-vessels is constantly regulated by the higher centres, probably situated in the hypothalamus, and, depending on the needs of the body as a whole, the superficial vessels constrict or dilate. It appears, further, that the integrity of the sympathetic pathway is essential for the fulfilment of this constant readjustment.

After sympathectomy the vasomotor tone is paralysed and vasoconstriction does not result from central stimuli. Sympathectomy leaves the vessels in an autonomous state, i.e. they respond solely to local changes in the surroundings as, for instance, changes in the tissue metabolites, changes in the local environmental temperature or to substances circulating in the blood, such as adrenaline, acetycholine etc.

Vasoconstriction as produced by the local application of cold - a phenomenon which we observe daily - was utilized in these experiments to demonstrate differences in vasomotor tone following sympathectomy.

Different animals have different mechanisms for heat regulation. In man, as has been pointed out, the hands and the feet play the major rôle, in the dog, the tongue, and in the ox, its nose. In the rabbit, our test animal, it is certain that the feet do not play that important rôle in

in body .....

in body temperature regulation as they do in man. It is the ear of the rabbit, more than any other part, that serves as a radiator for body temperature control, being extremely well supplied by an enormous network of capillaries.

Therefore, in studying the growth in a rabbit's foot, we are limited to results which would be inferior for the purposes of our experiment to those which could possibly be obtained from the study of the human limb. As a matter of fact, investigators have been uniformly unsuccessful in promoting growth of bone by lumbar sympathectomy in the rabbit and other test animals.

An increased bloodflow for the purpose of stimulating bone growth must be sustained during the growth period. That means that a prolonged hyperaemia is essential. Prolonged vasomotor paralysis follows on the correct type of sympathectomy. It has been stressed repeatedly by experts on peripheral vascular diseases that a pre-ganglionic sympathectomy is essential to maintain a prolonged vasodilatation, since a post-ganglionic sympathectomy renders the vessels much more sensitive to adrenaline than the pre-ganglionic type.

A marked increase in bloodflow through the superficial vessels is regularly observed after sympathectomy. But it is more difficult to prove whether the vessels of the deeper structures, i.e. the muscles and

bone are .....

bone are affected in the same way or not as the vessels of the skin. Indeed, the blood vessels of the muscles may not respond in the same manner to a stimulus as the vessels of the skin and, actually, opposite changes in them have been observed. (Goetz 1940).

We know that the vessels to the muscles are greatly influenced by the tissue metabolites produced during exercise, causing full vasodilatation. Thus, Barcroft et al 1943 found that, after complete sympathectomy, the dilatation of vessels is only 1/13 of the dilatation that can be produced by metabolites.

The bones' nutrient vessels are branches of the muscular vessels, thus we can reasonably expect them to be innervated in the same way as the latter. Furthermore, muscle and bone are both mesodermal structures and are functionally related. For these reasons we would hesitate to accept the statement of Harris and Wright (1931) that the nutrient vessels are not affected by sympathetic denervation.

That sympathetic innervation plays an important part in the pathology of bone is well demonstrated in e.g. Sudeck's atrophy, in which improvement after sympathectomy is remarkable. Thus Leriche and Fontaine (1930 and 1935), who demonstrated in Sudeck's atrophy a constant association with vasomotor disorders, also reported the effectiveness of sympathectomy in its treatment. The bones returned to normal, as seen in their roentgenographs.

On the .....

On the other hand, it may be true that the nutrient vessels are not influenced to the same extent by sympathectomy as the superficial vessels. It is, therefore, understood that skin temperature readings may be misleading as regards the bloodflow to the deeper structures.

In the case of the rabbit's feet, the skin is very closely associated with the bones and the muscle tissue is very poorly developed. The network of arterioles of the skin anastomoses with the periosteal arteries of the bone (Blair 1938). A measurable change of bloodflow through the superficial structures can, therefore, reasonably be expected to affect the deeper circulation as well.

Harris and Wright (1931) in discussing the case of a boy of 10 years with a congenital arteriovenous fistula in the region of the right knee, describe their experiments on kittens and rabbits in trying to find an explanation for the increase in growth.

They demonstrated hardly any increase in temperature (1.67° to 2.85°) on the side on which they performed a cervical sympathectomy. They were forced to conclude ".....that some other explanation than simple increase in blood supply to the part must be found to account for the hyperthrophy of the limb as seen in this case".

They suggest two possibilities.

(a) That sympathetic denervation does not effect the nutrient arteries to ....

arteries to the bone.

(b) That the temperature differences, as shown, are only superficial and do not effect the bone.

Both these points have already been discussed and we do not consider that they meet the facts. It is, of course, important to be certain that the sympathectomy in the test animal has been properly performed. We have, already, demonstrated that our results regarding skin temperatures agree with those of other authors, namely, that after sympathectomy, skin temperature readings, under o r d i n a r y circumstances, are hardly different in the legs. Although everybody knows that in man marked differences in skin temperature between the normal and sympathectomized limbs do occur, none of the authors has tried to look for reasons why, in their animals, this should not be the case. Our operation were carefully carried out and histologically controlled and a reason for this lack of difference in skin temperature had, therefore, to be sought.

It appears that the rabbit, when sitting, covers the legs with its body and its fur, with the result that the vessels in the limbs are not exposed to dissipate heat. It must be borne in mind, as has been previously pointed out, that the skin of the feet are not of primary importance in body temperature regulation. Therefore, skin temperature readings, taken under ordinary circumstances, cannot furnish us with

information as .....

information as to the completeness of the operation in the physiological sense. Therefore, there are no means of proving whether the animals of previous authors were really sympathectomized. No effort was made by these authors to clarify this point. Only when we are certain that sympathectomy has been successfully performed can we conclude regarding its effect on bone growth.

To prove that there was loss of sympathetic vasomotor activity in our animals, a special experimental technique was devised. If the limbs are first cooled sympathetic vasomotor paralysis can successfully be demonstrated in the rabbit's limb by means of skin temperature measurements.

There can be no doubt that vasomotor paralysis did occur in our rabbits after lumbar sympathectomy. The other authors did not appreciate the fact that the vessels can only show a difference in vasomotor response after vasoconstriction has been induced by cold.

Therefore, the fact that the skin temperature readings were the same in both limbs under ordinary circumstances after sympathectomy in the animals of the other authors, does not necessarily mean that these sympathectomies were not correctly performed, but we have no proof that they were.

Grant (1935) in carefully controlled experiments, has shown that, if a rabbit with one sympathectomized ear is chilled, the vessels in the

normal ear .....

normal ear start to constrict when a certain crucial level of rectal temperature (38.5°C) is reached, while the vessels of the sympathectomized ear remain dilated. These results conform well with our own observations.

Under experimental conditions, where the rabbits are kept warm and in small cages, marked and prolonged differences in the blood supply to both limbs cannot be expected. These unnatural and sedentary habits will, therefore, actually tend to defy the purpose for which our operations were performed. It is anticipated that a more marked growth difference would occur under natural conditions.

It must be appreciated that by lumbar sympathectomy abnormal vasodilatation is not produced, but it is only a vasoconstrictor paralysis which accounts for the warmth. The increased bloodflow in the sympathectomized foot is, therefore, only periodic, viz. at times when vasoconstriction should be evident. In this it differs vastly from cases of arterio-venous fistula and vascular tumours in that here the abnormality is continuously present. In arterio-venous fistula, we have invariably a difference in surface temperature of many degrees as compared with the corresponding normal region. The temperature fluctuations are very small and hardly affected by environmental temperature (Horton, Sheard and Roth 1940). The well balanced physiological control of the vessels is completely upset.

There are other factors why vasodilatation following sympathectomy may not .....

may not be so constant in producing an increased bloodflow. We have already mentioned that the vessels become sensitive to circulating adrenaline, particularly following a post-ganglionic sympathectomy. This is why we have done the hind limb, where sympathectomy is by necessity pre-ganglionic in type. The ganglia entering the synapses to the sciatic nerve were not removed but the pre-ganglionic fibres were interrupted.

Consequently our results on the growth of bone in animals produced by increased bloodflow after sympathectomy were, therefore, not expected to be anything like those seen in humans with arterio-venous fistulae. For the sake of interesting comparison, let us examine the details of a few cases of congenital arterio-venous fistula in humans.

I am indebted to Prof. Goetz for the following cases :

CASE 1.

PHILIP MOSES. Non-European boy aged 16 years.

This is a case of congenital arterio-venous fistula of the left leg with changes in skin temperature, a marked enlargement of the left leg and foot, and a slight difference in size between the two thighs. (Figure A, page No. 108).

HISTORY.

The left leg has been bigger than the right ever since he can remember. The swelling of the affected leg increases on walking and the limb also becomes painful. No history of trauma.

ON EXAMINATION.

The left leg is larger and longer than the right one especially from the knee downwards. (Figures A and B, pages Nos. 108 and 109).

The left leg is much warmer than the right.

In the left groin the femoral pulsation is rather pronounced and there is a well marked systolic bruit, not heard on the right side.

Skin temperature readings of this case can be seen in Case 1 Figure C, page No. 110, where we notice a difference from 2 - 6°C.

In Figures D and E, pages Nos. 111 and 112, we have X-Rayed photographs of this case's Femora and Tibiae, in each of these it can be seen that .....

seen that there is an excess growth of bone on the affected (left) side, in the case of the Femora 4.7% and in the Tibiae 9%.

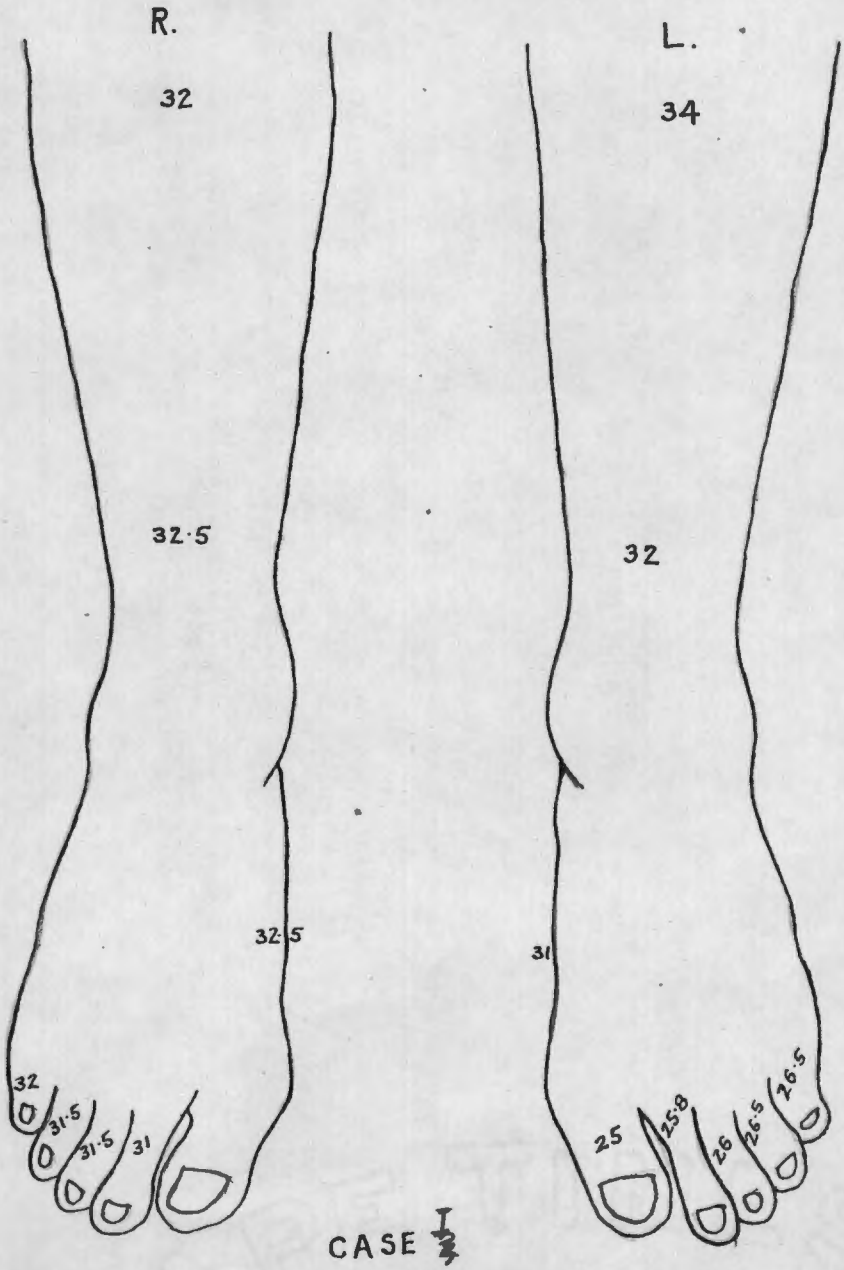
These proportions are approximate, being adjudged from the reduced X-Ray photographs.

CASE 1.

FIGURE A.

CASE 1.

FIGURE B.



CASE I
Fig. C.

CASE 1.

FIGURE D.

4.7% excess growth in left femur.

CASE 1.

FIGURE E.

9% excess growth in the left tibia.

CASE 11.

LUCY ADAMS. A non-European female aged 17 years.

HISTORY.

Ever since she can remember the right leg has been bigger than the left one and the right foot takes a bigger shoe. She has also noticed that the right leg is usually warmer than the left one.

There is no history of injury.

PHYSICAL EXAMINATION.

There is pitting oedema of the right leg and the whole of this leg is longer and thicker than the left one. (See Figure F, page No.114), and has a blueish to purple colour.

The pulses of the right leg are not perceptible.

No bruit can be detected on auscultation.

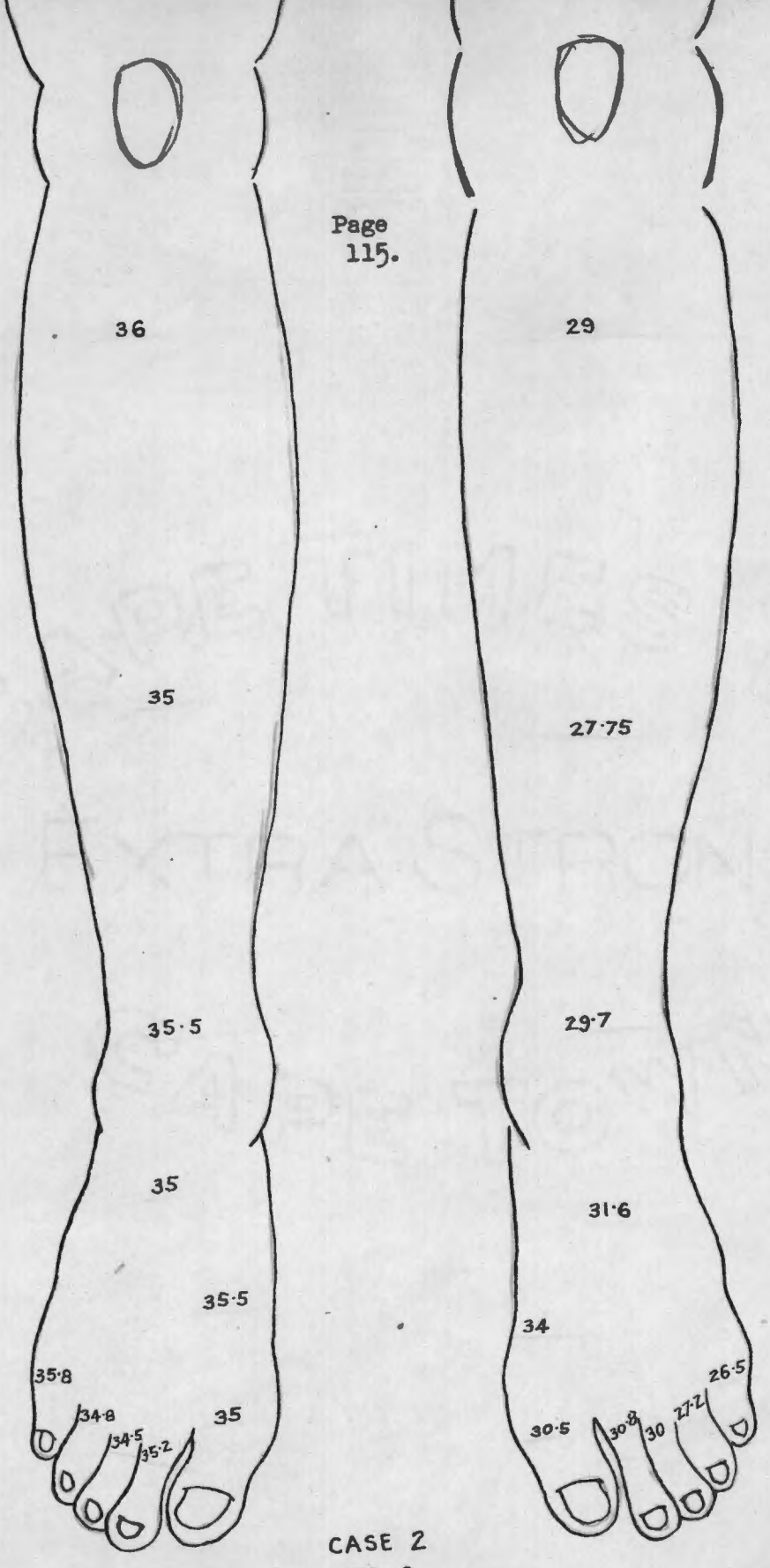
The temperature readings are recorded. (See Figure G, page No. 115), and the skin temperature of the right leg is obviously higher.

Brenhams sign was positive.

The X-Ray (Figure H, page No. 116) of the fibulae were measured and the diseased leg had a fibula which is 6.2% longer than the normal one. The interesting fact was that, in this case, no bruit was heard and it was obvious we were dealing with many small openings and the bloodflow not so much increased.

CASE 11.

FIGURE F.


36
35
35·5
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35·2
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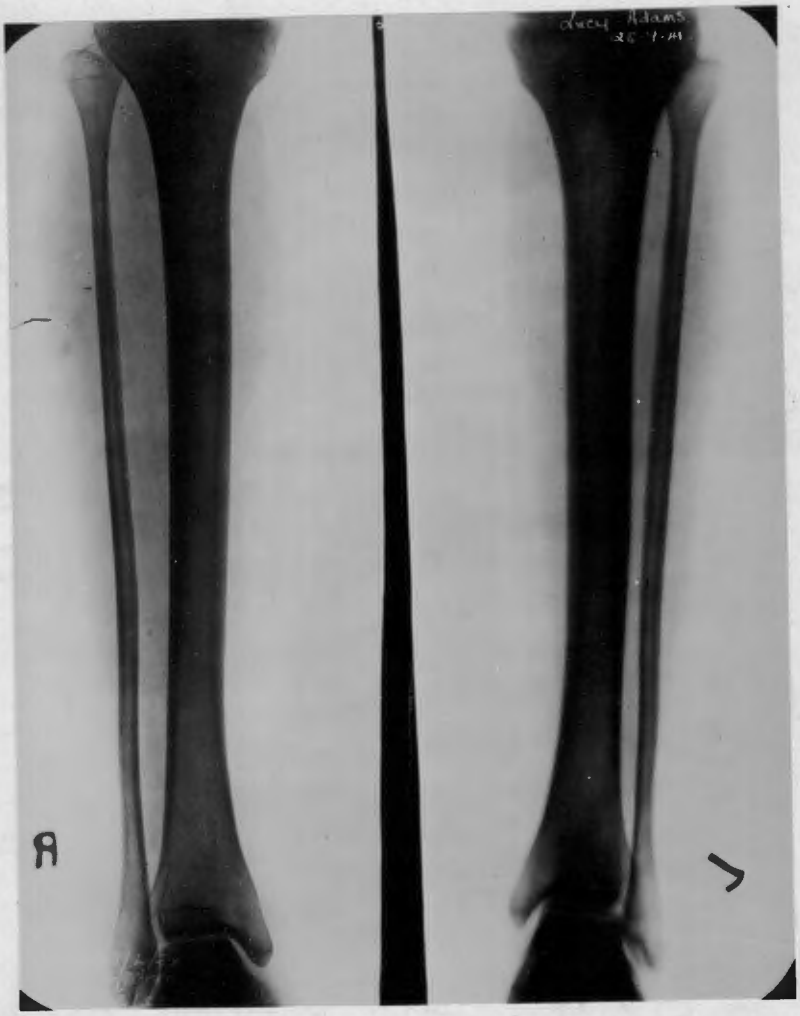
CASE 2
Fig. G.



CASE 11.

FIGURE H.

CASE 111.

MRS. SHACH aged 42 years.

HISTORY.

Since her youth she had noticed that the 4th left finger is thicker than the others (Figures 1(a) and 1(b), pages Nos. 118 and 119).

EXAMINATION.

The whole of the left 4th finger pulsates. There is a souffle heard and a thrill felt. There is a humming noise at the base of the 4th finger.

COMMENT.

This is a case where the patient has noticed the fistula or, at any rate, an abnormality since her youth.

The skin temperature readings indicate a difference of up to 10° C (Figure J, page No. 120).

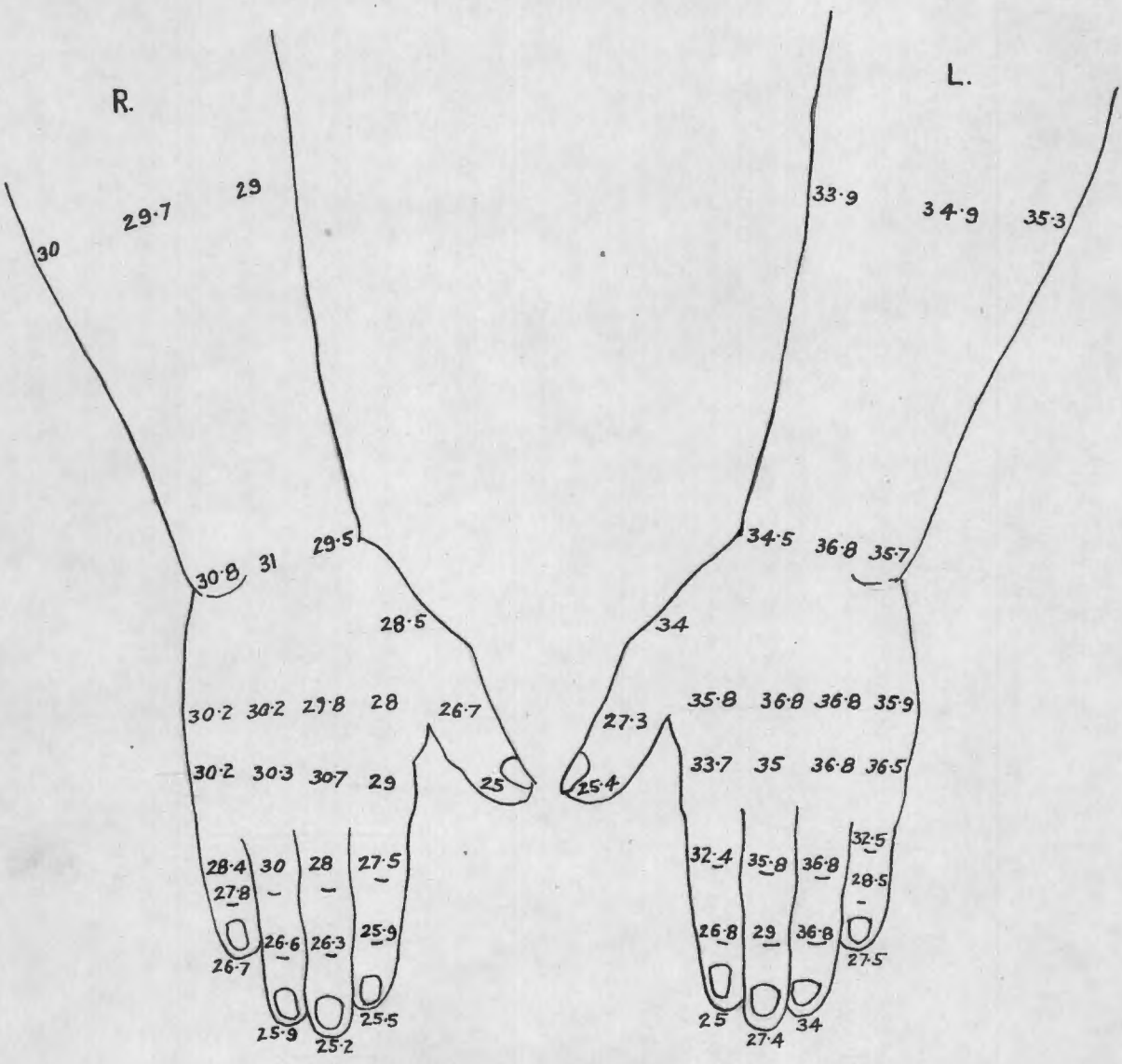
The growth in excess of the normal hand is not so striking in this case. The left 4th finger is 3% longer than the right hand.

CASE 111.

FIGURE I (a).

CASE 111.

FIGURE I (b).


R.
L.
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26·6
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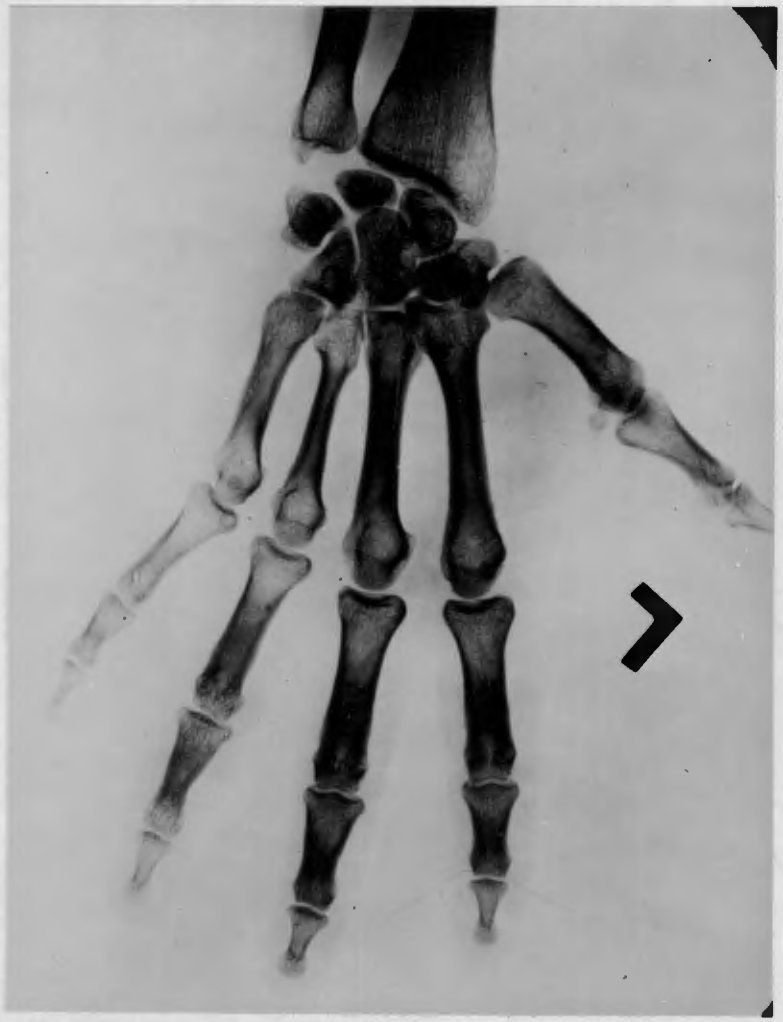
CASE 3
Fig. J

CASE 111.

FIGURE K.

RIGHT HAND.



CASE 111.

FIGURE L.

LEFT HAND.

In all these cases of arterio-venous fistula can we demonstrate a growth increase which is also very apparent clinically, especially in the cases with the pathology in the region of long bones.

A definite growth increase therefore follows on hyperaemia which we were able to demonstrate experimentally in rabbits.

For comparison the following table is included :

The excess bone growth over the normal side is expressed as percentage.

ARTERIO-VENOUS FISTULAE CASES.			RABBITS.	
Case 1 :	Femur Tibia	9% 6.2%	No. 2	4.25%
Case 11 :	Fibula	6.5%	No. 7	2%
Case 111 :	4th Finger	3%	No. 8	3.01%
			No. 10	2.2%

The experimental results compare favourably with these cases. In the rabbit the highest increase was 4.25% and the average 2.88%.

The question arises whether the increase obtained in the rabbit is significant. This I answer in the affirmative. The increase was always in .....

always in favour of the left (sympathectomized)side, and the values obtained compare favourably with the human cases under discussion, and also with those discussed by Wilson and Thompson (1939) where, in children, following sympathectomy an increase up to one inch is seen on the operated side as compared with the normal side. Furthermore in the control animals as well as in the X-Rays of the animals taken immediately after operation, hardly any differences could be demonstrated.

In a human limb of 30 inches measured from the ground to the greater trochanter of the femur, one inch represents 3.33% and a $\frac{1}{2}$ inch difference in length of the tibiae measuring 12 inches represents 4.1%. Clinically such a growth difference would be detectable and considered pathological. Therefore we feel that our results compare favourably with the amount of growth obtained in children after lumbar sympathectomy. A definite increase in bone growth after lumbar sympathectomy in rabbits, as demonstrated in our experiments, is contrary to the general consensus of opinion as reported in the literature but confirm Wilson & Thompson's view on this subject.

Wilson & Thompson (1939) in their paper on equalizing of leg length, remark "The problem of producing an increased blood supply over a prolonged period presents great difficulties. Lumbar sympathectomy apparently accomplishes ....

apparently accomplishes this better than any local procedure yet devised. Although the experimental attempts to stimulate growth by lumbar sympathectomy in animals have been uniformly unsuccessful, in children it is known to produce a lasting hyperaemia and many of these patients show definite gain in the rate of growth on the operated side".

The conditions under which we observe retarded growth are usually associated with vasospasm e.g. Anterior Poliomyelitis and pyramidal tract diseases; the victims complain of coldness and cyanosis of the paralysed legs. Sometimes also of pain and ulceration. All these manifestations are usually of vasospastic origin and relieved by sympathectomy. With the added advantage of increase in bone growth lumbar sympathectomy becomes all the more important.

The results in this type of case have not been wholly satisfactory if there is extensive paralysis, but recently, with extra-peritoneal approach and the knowledge of the value of removing the first lumbar ganglion, results have been more satisfactory (White and Smithwick, (1944), page No.134).

In selecting a suitable type of case for operation, with a view to increasing bone growth, a few facts must be kept in mind :

(a) The paralysis must not be too extensive because the contraction of muscle is the most important factor in assisting the bloodflow.

An underdeveloped and paralysed musculature carries with it a

deficient type .....

deficient type of bloodvessel. (du Toit, 1945). Furthermore, a poorly developed type of bloodvessel cannot respond in a normal way to the physiological stimuli of vasodilatation.

(b) The shortening of the leg must not be too great because there are better methods of leg lenthening or leg equilization. Methods can be employed which are more exact and where the results are more predictable.

(c) The amount of growth to be expected depends on the age of the child. Older children may not have a long enough growth period ahead.

The greatest benefit from lumbar sympathectomy seems to be gained by children with shortening up to 1½ inches, where a growth handicap, which is obvious, may be reduced to ½ inch difference which cannot be detected clinically.

VII. SUMMARY AND CONCLUSION.

Of fifteen normal young rabbits, each subjected to a left lumbar sympathectomy, five survived a properly performed operation up to time of writing.

The following are the surviving rabbits :-

No. 2	-	124 days.
No. 7	-	121 days.
No. 8	-	112 days.
No. 10	-	104 days.
No. 16	-	97 days.

The results confirm the findings of other authors that, under ordinary circumstances, there is hardly any difference in skin temperature between the normal and sympathectomized rabbit's foot. The reason for this is discussed, and it is pointed out that hyperaemia, after sympathectomy, can only become noticeable after some stimulus has occurred to produce vaso-constriction on the normal side.

A special test was devised to demonstrate vasomotor paralysis in the operated limb. Both feet were cooled for three minutes by immersion into water of 4 - 14°C in order to induce vasoconstriction. Following this, the rise in the skin temperature of the sympathectomized foot is

constantly steeper .....

constantly steeper and earlier than in the normal. This has been demonstrated to be true with all the rabbits on which the sympathetic chain was removed. This difference in temperature was repeatedly demonstrated, as may be seen from the graphs, and in some cases seems to be a permanent effect, as it is still evident after 120 days have elapsed.

The effect on the growth of bone was unequivocal and amounted to 2 - 4.25%. This is in contrast to reports on animals in the literature but confirms findings on humans.

The hyperaemia, in order to induce bone growth, must be prolonged or at least very often induced, but because the rabbits are normally kept warm and protected vasodilatation in both feet is at an optimum under experimental conditions. It seems reasonable, therefore, to expect that if these rabbits, after sympathectomy, were subjected to more natural conditions the growth discrepancy would be more apparent.

The value of sympathectomy in certain selected cases of poliomyelitis is well known and with the additional factor of possible increase in bone growth the plea for sympathectomy in suitable cases is certainly strengthened.

VIII RECOMMENDATIONS FOR FURTHER STUDY.

The study of this subject is not yet complete and, although convincing, further data should be obtained in order to have an unshakeable scientific standard.

(1) The rabbit has a very poorly developed sympathetic system and it is, therefore, suggested that other animals such as kittens or lambs should be subjected to a similar investigation.

(2) The type of operation should be carefully planned and therefore the anatomical details of the particular animal studied meticulously. The lowest sympathetic outflow should be determined with certainty in order to devise a proper preganglionic sympathectomy.

(3) It is recommended that the growth curve of the type of animal selected for the experiment, be plotted at the outset in order to ascertain the period of greatest growth.

(4) The animals should all be of the same age at the time of operation. Their ages should be such that the operation is performed early in the period of greatest growth.

(5) From each litter of animals at least one animal should be kept as a .....

as a control and for comparison.

(6) Plethysmographic records to demonstrate the state of the vessels will be convincing and valuable in addition to the thermocouple records.

(7) Cases of Anterior Poliomyelitis and cases of Hirschsprung's disease on which lumbar sympathectomies were performed in childhood, should be collected and carefully investigated and followed up.

ACKNOWLEDGMENTS.

I am beholden to Professor R.H. Goetz of the Department of Surgery of the University of Cape Town, for his wholehearted interest, his valuable assistance and suggestions, and for his having placed his laboratory and equipment at my disposal; to Miss D. Malan for the typing of this script; to Miss Mackay of the Groote Schuur Hospital for her help in obtaining the X-Ray negatives; to Mr. T.G. Rolling for the execution of the sketches and skin graphs; and to Mr. M. Taylor of the Pathology Department for histology slides which he so willingly prepared.

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