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EXPERIMENTAL RESEARCH FOR PROMOTING LONGITUDINAL GROWTH OF THE LOWER EXTREMITIES BY IRRITATION OF THE GROWTH REGION OF FEMUR AND TIBIA

BY

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Numerous diseases and deformities result in a shortening of one of the lower limbs. We see this state appear after infantile paralysis, after an arthritis in childhood, after a badly united fracture, with congenital hypoplasia, with a defect of the lower extremity, and with some other affections.

For the treatment of this deformity in adults we have two methods: the lengthening of the affected leg or the shortening of the sound one, if we set aside the using of a raised shoe or an orthopedic apparatus. In very special cases we may apply the operation of *Borggreve,* which is indicated for very pronounced shortenings, particularly in cases of the existence of a congenital defect of the femur. In this case what matters is, that after resection, both of the pseudarthrosis and of the knee-joint, the foot is twisted 180° round the axis of the leg. On the forefoot a tibia-prothesis is fixed so that the twisted ankle-joint takes over the function of the knee.

The elongation of the diseased leg is certainly the most logical operation. However, its application is rather limited, the soft parts, viz. the vessels and nerves, allow but a limited amount of stretching. Many references are to be found in literature as to paresis and paralysis, as well as to circulatory troubles in the course of this treatment. With this operation which we apply by preference in the form of oblique osteotomy of the femur, eventually combined with a similar osteotomy of the tibia, we can obtain a lengthening of 4 cm.

Considerably better results are to be obtained with the shortening operation of *Heine,* in its modernized form, combined with osteosynthesis. Hereby we can easily neutralize a shortening from 4 to to 8 cm, and even larger, without detriment to the natural functioning. The technical conditions for this are a primary osteosynthesis, e.g. by a medullary pin of *Küntscher* and a thorough after-treatment of the muscles of the shortened leg with massage and Swedish gymnastics.

However, we consider it a disadvantage that these operations can only be successfully performed on adults, because otherwise growth would continue to be unequal. We also object to performing a fairly thorough operation on a sound leg, an objection which has been made before from different sides. One should not forget the fact that the muscles must adapt themselves in their functions to the new length of the skeleton. Though finally this happens without any permanent consequences, some muscular insufficiency may exist for a time.

There is still another way of treatment, i.e. the one by which, through affecting the growth during several years, successively an equalisation of the length of the leg is attained at last.

One of the most successful operations is the epiphyseodesis of *Phemister* in which the growth of the sound leg is stopped in order to enable the ailing leg to attain the length of the sound one. The only disadvantage may again be that the operation is performed on the sound leg. It is true that this small operation has not the same consequences for the muscular apparatus as the shortening operation.

Another possibility is to increase the growth of the shortened leg by stimulation of the growth region, so that the leg stunted in growth might overtake the length of the sound one. Perhaps this is only possible when the epiphyseal cartilage of the affected leg has not been destroyed by the pathologic process and have kept their potentiality for growth.

In literature different efforts have been described, in which it was tried to stimulate a pathologically shortened extremity to increased growth by inducing hyperaemia. It has been tried to make the shortened extremity grow faster by local applications of heat. *Froelich, Helfrich* and *Lange* tried to stimulate the growth of the retarded extremity by *Bier's* hyperaemia, without, however, obtaining definite results. *Harris* thought he could observe a lengthening of the extremity in the period of growth, by a lumbar sympathectomy, whereas *Bisgaard* has been able to show that this operation, performed on goats, does not yield the expected result.

Several authors, whose investigations will be discussed later on, have thought that they could correct genua valga by one-sided irritation of the growth region with metal and ivory pins and have published their results as successful.

Already in 1869 *von Langenbeck* made experiments in which he irritated the growth region of a dog 8 months old with ivory pins which he stuck into the metaphyses of femur and tibia. In this way he obtained a lengthening of the femur and the tibia of 5 mm. after 3½ months.

After World War I renewed interest has been taken in the experimental observations of the second half of the 19th century. In Europe there were *Königswieser* (1925), *Reschke* (1925 and 1928), *Ruschenberg* (1936) and *van Nes* (1938).

These attempts were a reason for us to study the possibilities of lengthening the bones by operative irritation of their epiphyseal cartilage, in order to arrive at a definite opinion about their possibilities, the more so as the results were doubtful, and no systematic summing up and verification of these existed.

The basis of experimental research.

In our experiments, which we made in the years 1942, 1943 and 1944 under difficult war circumstances during the occupation, cut off from modern literature and other sources, we started from the well-known observation that pathologic processes in the vicinity of the epiphyseal cartilage, which do not touch them, may result in a stimulation of longitudinal growth of bones by local hyperaemia. We found some statements about this made by *Stanley* (1849), *Paget* (1853), *von Bergmann* (1868) and *von Langenbeck* (1869). The observations on increased longitudinal growth in inflammations of the bone tissue near the epiphyseal cartilage, in inflammation of the joint, in

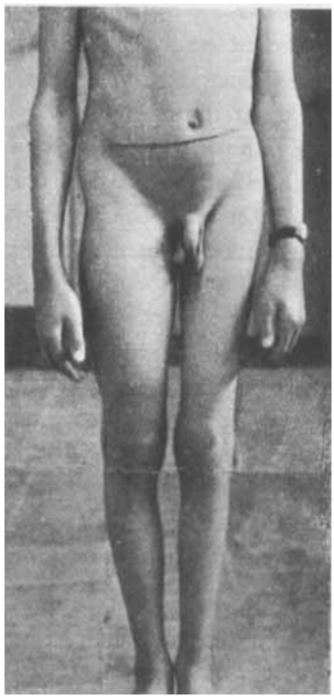

Fig. 1.
Increase of growth of 2 cm due to a tuberculosis of the left knee.

fractures and in osteosynthesis of the bones in the vicinity of the growth region, have increased and are generally known, so that we need not dwell longer upon this. To sum up, all processes in the vicinity of the epiphyseal cartilage of a bacterial inflammatory or aseptic nature may bring about an increase of longitudinal growth by hyperaemia. To illustrate this we reproduce here a photograph of a 15 year old boy (Fig. 1), who in childhood suffered from tuberculosis of the left knee, which was cured, however, without destruction of the joint, so that this boy has only been left with a slightly impaired flexion of the knee joint, besides an atrophy with a lengthening of the affected leg of more than 2 cms.

The experiments which have been undertaken to stimulate the growth region in order to increase the longitudinal growth arose from the idea of causing a sterile reaction in the vicinity of the epiphyseal cartilage. This has been tried with different irritating substances, by putting in ivory pins, which would be absorbed in course of time, or by metal pins by which reaction with local hyperaemia would be brought about. *Helferich* obtained some lengthening of the legs of rabbits, after having put in splinters of wood drenched with tct. cantharidis into the medullary cavity. *Helger* saw the same after filling up the medullary cavity of the metaphysis with a fluor-calcium plug. *Königswieser* made similar experiments, in the course of which he observed a small longitudinal increase during bacterial irritation; he obtained the best results by filling the medullary cavity of the metaphysis with a plug of camphor and nitrate of silver. Although he could not observe a permanent increase of length, these experiments sufficiently proved that irritation of bone tissue in the vicinity of the epiphyseal cartilage may cause a lengthening of the bone.

Experiments to stimulate longitudinal growth of bones by irritating the epiphyseal cartilage by means of ivory and metal pins:

The oldest experiments are those of *von Langenbeck* who, as described above, used ivory pins to stimulate the growth region. He obtained a positive result with these and has recommended applying this process to men.

In 1881 *Riedinger* made analogous experiments. He placed two sizeable ivory pins in the vicinity of the growth region into the diaphysis of a dog which he killed 3 months later. The irritated tibia showed a length of 99½ mms. against the normal one 95½ mms. long. After the insertion of the pins a strong reaction appeared, as a result the pins worked their way out with pus formation. He could observe on the tibia a circumscript osteitis with a local increase in thickness of 5 mms. The femur had not been irritated, but through the reaction in the joint, it had become 2½ mms. longer, standing a reactive increase of cell growth of the epiphyseal cartilage plate. His experiences agree with the results of the experiments of *Weinlechner* and *Schott*. These experiments, like those of *Bidder* who checked the growth by driving metal needles into or beside the epiphyseal cartilage in rabbits, show clearly from the protocols that the asepsis had not been perfect, so that purulent reactions had developed on the spot. From this fact it follows that we are unable to attach much importance to these experiments. So we must assume that the increase of the growth is to be ascribed to the purulent reaction. In itself an aseptic reaction by sticking ivory pins in the vicinity of the epiphyseal cartilage with a certain amount of influence on the growth is quite possible, as we can clearly conclude from the experiments of *Rauch* (1927) that after the introduction of ivory pins first a light bone-necrosis arises on the spot. Months or even years afterwards the absorption of the ivory then begins, and after that a local recovery of the bone processes which cause sufficient reaction and hyperaemia. With young, growing individuals, these processes end quicker so that the ivory is absorbed more quickly and a stronger reaction is brought about. This method has been applied in human practice. While *Ollier* was the first to propose a correction of the genu valgum by one-sided destruction of the epiphyseal cartilage; *Schüller* was the first to introduce a metal pin in the vicinity of the growth region on the lateral side for its stimulation to achieve a correction of a genu valgum. He left this pin in for a time to irritate one side of the epiphyseal cartilage, and removed it after the lapse of a certain time, and observed a favorable result of this treatment. *Reschke* likewise implanted ivory pins of a length of 3-4 cms. for the correction of genua valga, and obtained good results (1925 and 1928). *Ruschenberg*, too, (1936) mentions a number of 6 young patients, whom he treated in a similar way with a like object, and likewise attained good results. He placed the pins laterally, so that they partly protruded from the bone in order also to obtain a stimulation of the periost. *Van Nes* (1938) describes 2 cases, in which he placed ivory pins in the metaphysis for the stimulation of the longitudinal growth of bones, without publishing the results.

Influence of X-rays on longitudinal growth of bones:

Apart from these efforts to influence the growth, further experiments have been tried to use X-rays for the same purpose. That through X-rays the normal growth of the bone can be injured has been demonstrated by *Perthes* on chickens. Since the observations of *W. Müller, Stordem, Grassmann, Beck, Ombredanne, Hueck* and *Spies, Schmidt, Anschütz* and *Beck* and others this is a generally known fact.

The experiments of *Fürsterling, Krukenberg, Iselin,* and others on dogs, rabbits, goats, mice, rats, etc. followed. *Hoffman* has made systematic investigations, and demonstrated by these (1922) that with rabbits of 3 or 4 weeks old an injury of the bone already appears with a dose of 25 % S R D, whereas older rabbits need a dose of 40 % S R D for a similar injury of the bone. In his experiments *Baunach* has shown that with 1650 r necrosis of the bone can be attained; a checking of the growth has, however, already appeared at doses of 550-880 r given in fractions. After a pause of 1-2 months, however, a recovery may appear. At an irradiation with 165 r a temporary stimulation of the growth was observed. This has also been pointed out by *Simons. Bisgaard* and *Hunt* relate that with rabbits they attained an injury of the cells of the epiphyseal cartilage plate at 50-100 % S R D, whilst a dose of 25 % S R D resulted in an injury of the haematopoetic tissues. With 400 r they obtained a shortening of 5 mms. in the femur of a rabbit. From this it appears that with X-rays one may attain an arrest or a considerable check in growth of the bone, whereas the results of the experiments for stimulating the growth are uncertain.

Checking the growth by X-rays is a dangerous enterprise, and offers no advantages over the operative treatment. Consequently only a possible stimulation of the growth by X-rays would be of interest. The experimental results, however, already point to their usefulness. We have also tried to attain either the checking or stimulation of growth in rabbits experimentally. It was our intention to obtain eventually a clinically usable method so that we had to restrict ourselves to a moderate dose in order not to produce a general injury of the body. The results of our sporadic examinations were all negative. With a stimulating X-raying on rabbits we could not fix a lengthening of the irradiated leg. With a checking X-raying with a moderate dose, a periostitis of the bone indeed appeared, but there was no check in growth. Very soon, however, we gave up these experiments, and restricted ourselves to others, stimulating the growth by means of metal and ivory pins.

OUR EXPERIMENTS AND RESULTS

The basic idea of the experiments:

We based our experiments on the observation that reactive processes, as already described, can give a lengthening of the bone. We proceeded from the premise, that when metal pins in the vicinity of the epiphyseal cartilage cause a slight bone necrosis which reacts into hyperaemia, this reaction can stimulate the growth. On the basis of this we decided to deposit pins near the growth region and expected this to result in a lengthening of the extremity.

The choice of the material which was used to stimulate the growth.

Smook and *Gaillard* describe in their research that different metals produce different reactions in the bone, *i.e.*, some metals are toxic with respect to the growth of bone cells and others are not. They used in their experiments osteoblasts of fowl-embryos which they raised during a certain time with various metals deposited in the cultures. Certain cultures experienced a checking influence by the toxic action of the metal and were retarded in growth with respect to control cultures. Eventually they succeeded in setting up a series of toxicity which we reproduce here. By comparative measurements of the diameter of growth and surface, they found a growth-constant, which they calculated from the following formula:

$$K = \frac{Ln}{L(n-1)} \cdot \sqrt{S_n}$$

L = the radial extension of culture.
S_n = surface of culture after n days.

Metal	Maximal radiate extension 1st day		growth constant K	
	control culture	trial culture	control culture	trial culture
phosphorbronze	0.97	0.00	5.91	0.00
copper	1.70	0.70	7.35	0.00
bronze	1.26	0.30	7.02	0.45
Cr-Ni-steel	1.30	0.53	7.63	1.47
brass	1.97	1.84	8.30	5.67
iron	0.79	0.47	4.00	3.51
aluminium	2.29	1.78	7.30	6.50
nickel	1.52	1.50	7.91	6.79
V2A-steel	1.10	1.18	6.51	6.53

Smook and *Gaillard:* Influence of metals on the growth of bone tissue. (Table abridged.)

So when various metals exercise a different toxic action on the growth of osteoblasts and check the growth by this action, then after introduction of the metal a reaction of the bone must appear. This reaction must be strongest with metals working extremely toxically. The stronger the toxic reaction appearing in the bone tissue, resulting in local necrosis, the stronger the reparative reaction with hyperaemia will be. So we can use this reaction as a stimulus for growth by introducing metal, acting toxically in the vicinity of the growth region, and let the destructive and reparative processes end there. This was for that matter the basic idea of our experiments. With V2A-steel pins we cannot get any reaction, V2A-steel being indifferent to bone tissue; growth constant of the test culture is 6.53 against the control culture 6.51 when checked. The difference of 0.02 falls within the margin of error. Therefore no increase of the growth in length can be expected, if the ground plan of our experiments is correct. Should we however observe any change in the rate of growth, then other elements would play a part. The fact is that, through the presence of galvanic current between the pins a necrotic zone appears round each of them. This could produce sufficient reaction to stimulate longitudinal growth. Therefore it was decided to deposit pins of different metals in the bone so that a current could be raised between them. *Smook* and *Gaillard* observe that when fixing a fracture of the neck of the femur with a metal pin a decalcified zone can be observed round the pin by X-rays. This is not based on osteoporosis, but rather on the appearance of a capsule of fibrous tissue round the nail. It is to be assumed that this capsule arises through necrobiotic processes resulting from galvanic current generated on the spot. The metal pin works as a galvanic element, electrochemical processes result, when the metal is not homogenous, or when the pin lies in different media, with a difference of oxygen concentration. So if a pin lies in the bone, projecting into another surrounding, e.g. muscular tissue, then the result is, that the part which lies in the bone and finds itself in surroundings poor in 0_2, works as an anode, while the projecting part lying in surroundings rich in 0_2, works as a cathode. These simple reasonings have for that matter furnished the basis for further experiments in which the pins were not fully introduced into the bone-tissue. Further experiments are based on the fact that absorbable materials cause a protracted reaction. We need not dwell any longer on this fact here, as this has already been discussed before and has been proved by the experiments of others. We used ivory for our experiments, which is an absorbable material and brings about a protracted reaction, so that it might reasonably be supposed that sufficient hyperaemia would take place to stimulate the longitudinal growth.

The technique of the experiments:

In our experiments we have used dogs, guinea-pigs and rabbits. The experiments with dogs had to be soon stopped on account of war conditions. Caviae did not prove suitable for these experiments, as the skeleton is too thin. We succeeded in breeding a series of rabbits of a strong and big breed in the University Pathological Institute at Leyden, and used them for our purpose. We made our experiments on 22 animals; only 14 produced results to form an opinion on. (6 animals died of infectious diseases, before a proper opinion of the result could be formed.) All the animals were operated on quite young, so that a long period of growth could be counted on. With rabbits the age at which the experiments commenced ranged from 6 to 12 weeks. After 12 weeks they were X-rayed. The length of the paw had been fixed by X-rays before the operation. The experiments were all made on one side, so that the other hindleg could serve for comparison. We tried to stimulate the lower growth region of the femur and the upper one of the tibia, as it appears clearly from *Campbell's* figures that the growth regions of the knee give by far the most growth in length: 77 % of the length of the femur and 56 % of the tibia. In one case the upper growing cartilage of the femur was stimulated too. The measurements were made direct on the X-ray photographs, which were all taken with the same technique. For this the animals were laid on their bellies, and the legs extended equally. The distance between object and tube amounted to 65 cms. The X-ray photographs were consequently taken dorso-ventrally.

The experiments were made under narcosis, and performed under the most aseptic circumstances. Here we manipulated exclusively with instruments in the wound, and the pins were likewise exclusively handled with forceps. The pins were introduced from a straight incision opening the knee, after a hole had been made on the desired spot. It must be noted that the pins were introduced from medial, lateral and bilateral. Some of the pins were deposited entirely in the bone, others with a small part of their length protruding from the bone. To eliminate the possible disturbing influence of the unstimulated fibula, it was resected beforehand for a distance of 2-3 cms in some of the animals. The healing of the wounds of all the animals was undisturbed. The function of the joints remained intact. Optimal feeding of the animals was cared for. A number of the animals was killed when the experiments were finished, and their legs were examined histologically.

The growth in length of long tubular bones occurs towards the epiphysis. Causing the stimulation in the epiphysis has the advantage, that the

TABLE OF EXPERIMENTS (1) In this table only subjects, which were observed and controled from the operation until at least 3 months afterwards, have been included.

No.		animal no.	age in weeks	Side	date	length in mm				technique		
						femur		tibia		site		material
						r	l	r	l	E	M	
1	o	D 1	9-10	l	12/5 -42	—	83.5	—	73.0	+		V2A-steel
	c	D 1	appr. 12	l	1/6 -42	90.5	91.0	95.0	95.0	+		
	c	D 1	„ 16	l	24/6 -42	117.0	118.0	107.0	111.0	+		
	c	D 1	„ 27	l	?/9 -42	144.0	144.0	—	—	+		
2	o	D 2	10-12	r	29/1 -43	100.0	100.0	95.0	95.0	+	+	ivory
	c	D 2	17-19	r	19/3 -43	110.0	110.0	108.0	108.0	+	+	
	c	D 2	27-29	r	29/5 -43	125.0	128.0	123.0	123.0	+	+	
3	o	C 4	?	r	2/9 -42	32.0	—	38.0	—		+	copper
	c	C 4	?+1	r	2/10-42	32.0	32.5	38.0	38.0		+	
	c	C 4	?+3	r	10/12-42	33.0	35.0	43.5	44.0		+	
4	o	R 1	appr. 12	r	5/3 -43	89.0	91.0	105.0	105.0		+	iron
	c	R 1	„ 26	r	4/6 -43	86.5	89.5	108.0	108.0		+	
5	o	R 2	„ 12	r	5/3 -43	89.0	90.0	115.0	115.0	+	+	copper + zinc
	c	R 2	„ 26	r	4/6 -43	108.0	107.0	125.0	125.0	+	+	
6	o	R 3	10	r	2/4 -43	69.0	69.0	86.0	86.0	+	+	iron
	c	R 3	24	r	9/7 -43	92.0	89.0	112.0	113.0	+	+	

TABLE OF EXPERIMENTS (cont.)

No.		animal no.	age in weeks	Side	date	length in mm				technique		
						femur		tibia		site		material
						r	l	r	l	E	M	
7	o	R 4	10	r	2/4 -43	63.0	63.0	86.0	86.0		+	ivory
	c	R 4	24	r	9/7 -43	90.0	90.0	111.0	111.0		+	
8	o	R 6	9	r	6/8 -43	63.0	61.0	74.0	74.0	+	+	ivory
	c	R 6	18	r	14/10-43	87.0	86.0	99.0	99.0	+	+	
9	o	R 7	9	r	6/8 -43	69.0	68.5	77.0	76.0		+	ivory
	c	R 7	18	r	14/10-43	88.0	84.0	105.0	105.0		+	
10	o	R 8	9	r	6/8 -43	64.0	64.0	78.0	78.0		+	ivory
	c	R 8	18	r	14/10-43	87.0	87.0	105.0	104.0		+	
11	o	R 11	6	r	?/10-43	—	—	—	—		+	ivory
	c	R 11	18	r	28/1 -44	82.0	82.0	109.0	109.0		+	
12	o	R 12	6	r	30/1 -44	—	—	—	—		+	ivory
	c	R 12	19	r	29/4 -44	78.0	72.0	89.0	89.5		+	
13	o	R 13	6	r	30/1 -44	—	—	—	—		+	ivory
	c	R 13	19	r	29/4 -44	93.0	92.0	109.0	109.0		+	
14	o	R 14	6	r	30/1 -44	—	—	—	—		+	ivory
	c	R 14	19	r	29/4 -44	94.0	91.0	107.0	107.0		+	

Explanation of the abbreviations:

D: dog — o: operation — M: metaphysis
C: cavia — c: control — E: epiphysis
R: rabbit

growth region does not move from the place of the stimulus. When we deposit the stimulating pins in the metaphysis, the epiphyseal cartilage may get too far away from the place of reaction, and no longer experience sufficient stimulation. In the course of the experiments it appeared however that the deposit of the pins in the epiphysis remained without any success, so that we started placing the pins in the metaphysis.

Results of the experiments:

We give here a table, showing the results of the different experiments and shall confine ourselves to a summary of results.

With respect to the place of stimulation, we concluded that the pins put in the epiphysis did not cause a reaction in the

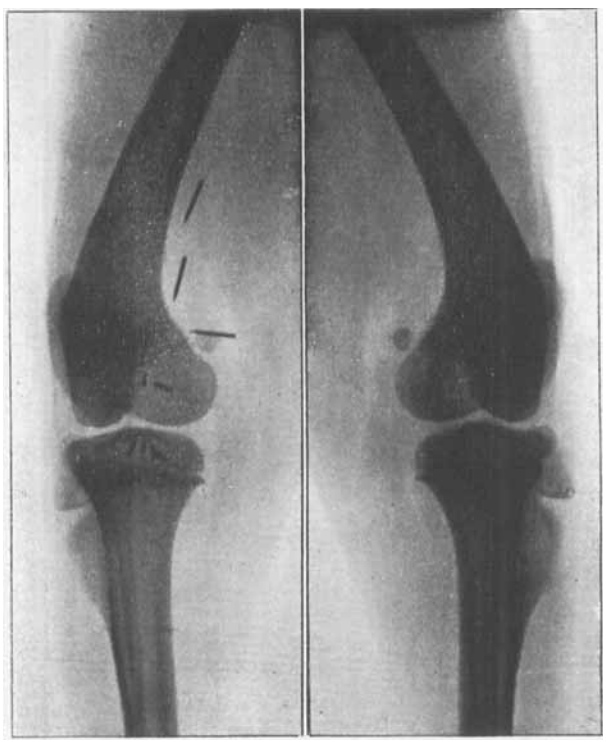

Fig. 2.
Dog D 1. Irritation by V2A-steel pins. No increase of growth 4 months after operation.

growth in length (Fig. 2). In particular this holds good of V2A-steel as expected. V2A never causes a reaction, and quickly surrounds itself with a capsule, so that no further reaction can be expected, which might stimulate growth. By combination of copper and zinc, where a reaction was expected from the resulting galvanic current, only a rarefaction appeared around the pins on the X-ray (Fig. 3). This local reaction was not able either to exercise any influence on the longitudinal growth. With iron varying results were attained. On the one hand we found a slight increase in growth, on the other hand the growth of the bone was retarded. The visible reaction in the bone was very moderate, so that we quickly gave up this material and did not continue these experiments. The fluctuations were minimal, and might fall within the limits of possible error. The strongly toxic copper caused a distinct reaction in the bone in the experiment, so that deformities appeared, and the X-ray films showed a distinct rarefaction round the metal. As to the longitudinal growth we perceived here a lagging behind of femur and tibia, presumably on a toxic basis, so that this material did not appear to be fit for our further experiments.

As to the dimensions of the pins we must mention that small pins were encapsuled without further reaction, so that we had to choose thick pins both of metal and of ivory. So whilst the

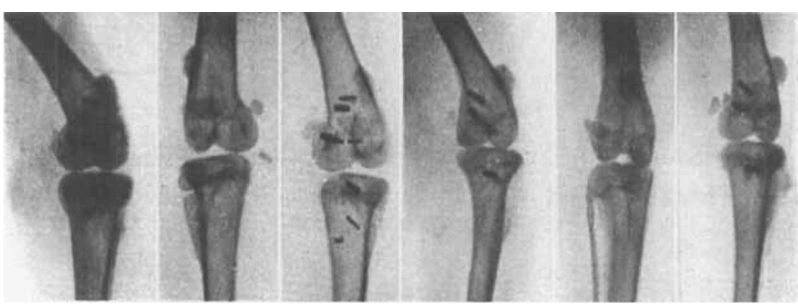

Fig. 3.

Rabbit R 2: irritation by copper and zinc. Postoperative control. Experimental result.

Rabbit R 3: irritation by iron pins. Postoperative control. Experimental result.

experiments with metal pins did not give satisfaction, we could show more reaction with ivory ones, and have exclusively continued the experiments with ivory.

Already with the first rabbit which we had stimulated with ivory pins three months after the operation a typical valgus

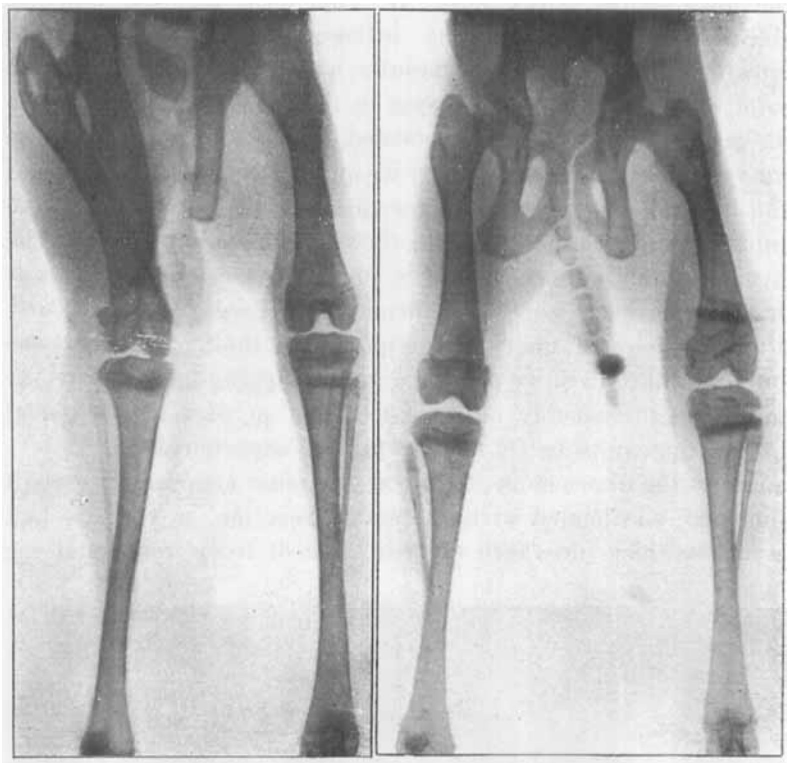

Fig. 4 a. Rabbit R 4. *Fig. 5 a.* Rabbit R 6.
Postoperative control.

position of the tibia and of the fibula appeared, however without lengthening of the leg (Fig. 4). The valgus deviation took place in the metaphysis on the place of the ivory pin. The femur did not show any lengthening, nor any change of structure or position. Here the stimulating pins were, in contrast to the tibia, placed in the epiphysis. Looking for an explanation of the appearance of this deformity, we thought it might be assumed,

Fig. 4 b.
Rabbit R 4 — experimental result.

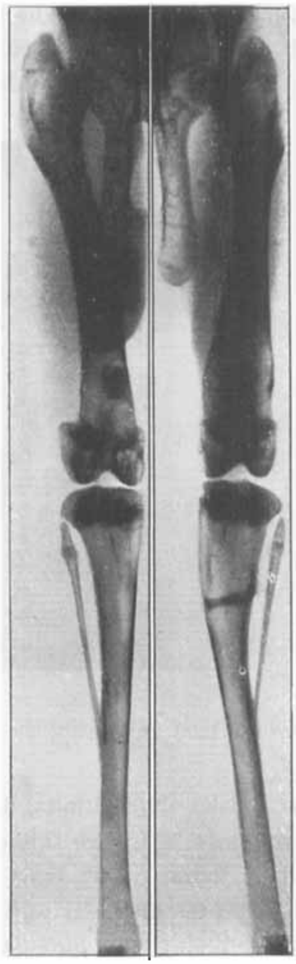

Fig. 5 b.
Rabbit R 6 — experimental result.

that one side had apparently grown harder than the other, through a one-sided stimulus of the growth region. It was however not impossible either that here some checking influence had proceeded from the unstimulated fibula which grew normally, and checked the accelerated growth of the tibia laterally, so that a valgus position was the result. This supposition seemed less probable to us, as the fibula was likewise curved in valgus, and moreover we supposed that with a more intense growth of the tibia the fibula would follow the traction, and likewise

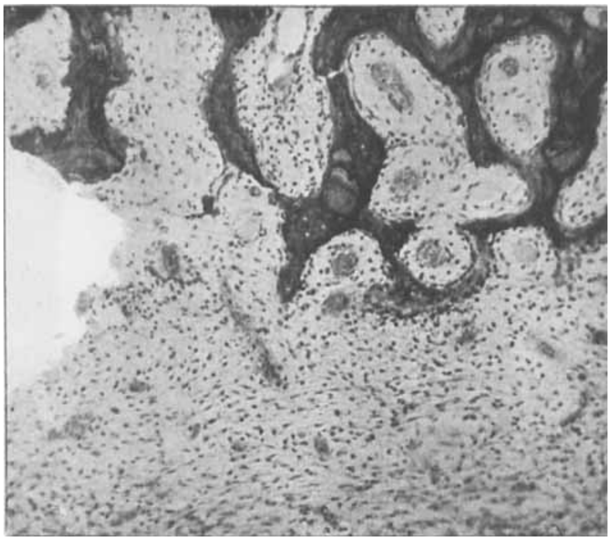

Fig. 6 a
Showing a part of the fibrous capsule, which enclosed the pin. (100 ×).

grow harder. Notwithstanding these considerations we decided to eliminate in future this checking factor. In future we always cut the fibula. Apart from this we introduced in certain cases the ivory pins medially and expected by this a valgus deformity. In introducing the pins laterally a varus deformity could be expected to appear. A bilateral introduction of the pins would result in a lengthening of the extremity.

The rabbit R6= (Fig. 5) showed under stimulation with ivory in the metaphysis, a remarkable change of the femur, which became thick in the stimulated area and looked puffed up. A lengthening of 1 mm. appeared. The tibia which was stimulated from the lateral side, showed again a valgus position, but no lengthening, whereas the rabbit R7 = No. 9 stimulated medially in the tibia metaphysis showed practically no valgus and no lengthening. The corresponding femur, when stimulated medially, showed no deformity but a prolongation of its length of about 4 mms (about 5 % of the length of the other leg). In

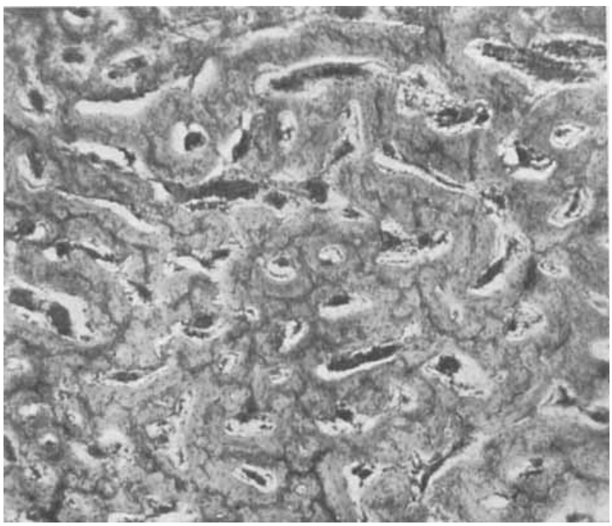

Fig. 6 b.
Local increased density of bone tissue in the vicinity of the pin. (50 ×).

case No. 10 rabbit R8, where the femur was stimulated centrally and the tibia medially after resection of the fibula, the femur showed some thickening of the metaphysis without lengthening, whilst the tibia as expected showed valgus position. The fibula had regenerated itself here. A lengthening of 1 mm. of the tibia appeared. Remarkable is the case No. 11 rabbit R11. Here the femur and the tibia were stimulated bilaterally, after resection of the fibula. The fibula could not regenerate. Some thickening of both bones occurred, but no lengthening, neither of the tibia nor of the femur. The case No. 12 rabbit R12 which is difficult to judge with regard to the gaining of length on account of faulty projection, is however further practically analogous to the preceding. Contrary to our expectations no lengthening with a bilateral stimulation of the bone was observed.

In the cases No. 13 and 14 rabbits R13 and R14, where the stimulus has taken place laterally and medially after resection of the fibula, we see no distinct valgus or varus deformity appear, but a thickening of the bone which we have observed before. As to the lengthening, both experiments are favorable, as in both cases the femora have shown some lengthening, though the tibiae have not shared in this process.

TABLE II

No.	Increase in growth			
	mms.		percentage	
	femur	tibia	femur	tibia
1	0.0	—	0.0	—
2	— 3.0	0.0	— 2.4	0.0
3	— 2.0	— 0.5	— 5.7	— 1.7
4	— 3.5	0.0	— 3.91	0.0
5	+ 1.0	0.0	+ 0.94	0.0
6	+ 3.0	— 1.0	+ 3.37	— 1.12
7	0.0	0.0	0.0	0.0
8	+ 1.0	0.0	+ 1.16	0.0
9	+ 4.0	0.0	+ 4.76	0.0
10	0.0	+ 1.0	0.0	+ 1.15
11	0.0	0.0	0.0	0.0
12	+ 6.0[1]	— 0.5	+ 8.34	— 0.69
13	+ 1.0	0.0	+ 1.09	0.0
14	+ 3.0	0.0	+ 3.3	0.0

Increase in length in mms. and percentage of the sound leg indicated by: +. Lagging in growth indicated by: —.

The measurements have been performed on X-ray photographs.

For absolute length see table I.

[1] unequal projection!

Histological examination:

After the animals had been killed the bones, in which the pins had been put, were removed and preserved in formalin 5 %. Then they were placed for a time in nitric acid, till they had become sufficiently soft to be cut into sections or to be sawn with a fret-saw. The cutting and sawing surfaces of these sections were chosen so that the seat of the pins was shown. With a view to the cutting of the sections enclosed in celloidine the metal pins had to be removed. This was done before the decalcified bone was cut into sections. They ivory pins could be left, because it was found that these became soft owing to the decalcification by the nitric acid. The difference in consistency between the decalcified bone- tissue and these softened ivory pins was however such, that in cutting the sections these pins fell out, and a cavity remained. In the histologic picture of the bone sections obtained like this, which had been coloured with haematoxylin and according to *van Gieson*, the growth region showed first of all a normal appearance. The cartilaginous zone had the same width in each section, and showed a very regular and normal structure. The zone of ossification likewise showed a normal and regular aspect. Slightly lower, where the pins had lain, a zone of fibrous tissue was found, the width of which differed in various cases. The fibrous tissue of this encapsulation was comparatively poor in cells and sometimes partly hyalinised. With the exception of a few cases, no cellular infiltrates were found. The adjacent bone-tissue showed a marked trabecular structure; the medullary tissue had an ordinary cellular aspect, as is to be expected with young animals. Round the pins there was unequal fibrous thickening of the periost. The underlying bone-tissue sometimes showed strong bone-lamellae lying close together. An exception to this description holding good nearly everywhere was formed by a rabbit whose leg had adopted a very slanting position, evidently owing to one-sided growth. (Fig. 6 a and b). Histologically it appeared first that on the convex side, i.e. on the side where the strongest growth occurred, the periost showed a strong fibrous thickening. A substitution of the bone-tissue had also taken place in the area, where the ivory pins had lain, just under the corticalis, by fibrous tissue already partly hyalinised. In its centre was a conglomeration of leucocytes and lymphocytes without there being any pus formation. The adjacent bone tissue showed increased density locally, both in the spongiosa and in the corticalis owing to the broadening of the bone lamellae, full of swollen osteoblasts. There was in this area of one-sided stronger growth a local disappearance of bone with substitution by inflammatory fibrous tissue, from which at the same time a stimulus to strong bone formation must have proceeded. The local character as well as the incidental appearance makes it acceptable, that we have here to do with an unusual growth tissue, owing to an inflammatory reaction, the cause of which was not clear. Bacterial staining yielded no result, so that the possibility of infection could not be confirmed. In general it can be said, that the histologic examination confirms the clinical results of the experiments.

SUMMARY

In summing up our results we must conclude, that it is indeed possible to cause some reaction which leads to a stimulation of growth by introducing metal or ivory pins into the metaphysis of growing bone. Frequently however the local reaction is not sufficient to influence longitudinal growth. Metal pins produce a strong reaction in so far as the metal acts toxically on the tissue, which may even result in damage to the growth. Mostly however the metal pins are surrounded by a membrane of fibrous tissue, so that reaction is eliminated. This also happens when various metals are deposited in bone tissue to produce a galvanic current. More positive results are obtained with absorbable material, which maintains a reaction in the bone during the time of absorption, e.g. ivory. After the introduction of ivory pins the reactive processes result in a thickening of the bone. The actual influence on the growth of the bone becomes of secondary importance. Some lengthening of the bone is indeed attained, but the results are very various and uncertain. Moreover the reaction often causes deformity of the extremity,

which can not be influenced at will by modification of the technique of the experiment. The lengthening moreover is minimal and many results are certainly still within the bounds of possible error. Our investigations show that a certain influence on the growth is possible by the introduction of ivory pins into the metaphysis of growing bone, but that this method is not suitable for human practice on account of its uncertainty, and because of the appearance of deformities.

Unilateral shortening of extremities should preferably be treated by *Phemister's* epiphyseodesis. By this method we obtained favorable results apart from those mentioned in the extensive literature. As an alternative the checking of growth by means of a wire-loop as indicated in 1945 by *S. L. Haas,* San Francisco, is open to discussion.

ZUSAMMENFASSUNG

Wenn wir unsere Ergebnisse zusammenfassen, müssen wir den Schluss ziehen, dass es wirklich möglich ist, eine Reaktion auszulösen, die durch Einführung von Metall- oder Elfenbeinstiften in die die Metaphyse von wachsenden Knochen das Wachstum fördert. Häufig reicht jedoch die lokale Reaktion nicht aus, um das Längenwachstum zu beeinflussen. Metallstifte rufen insoweit eine starke Reaktion hervor, als das Metall toxisch auf das Gewebe wirkt, was auch einen schädlichen Einfluss auf das Wachstum haben kann. Meist sind jedoch die Metallstifte von einer Membran von fibrösem Gewebe umgeben, so dass eine Reaktion unmöglich gemacht wird. Dies geschieht auch dann, wenn mehrere Metalle im Knochengewebe deponiert werden, um einen galvanischen Strom hervorzurufen. Mehr positive Ergebnisse wurden mit absorbierbarem Material erzielt, das während der Dauer der Absorption eine Reaktion im Knochen unterhält, z. B. Elfenbein. Nach der Einführung von Elfenbeinstiften führen die reaktiven Prozesse zu einer Verdickung des Knochens. Der tatsächliche Einfluss auf das Wachstum des Knochens bekommt sekundäre Bedeutung. Eine gewisse Verlängerung des Knochens wird wirklich erzielt; die Ergebnisse sind

aber sehr variierend und unsicher. Überdies verursacht die Reaktion oft eine Deformierung der Extremität, die sich durch eine Modifizierung der Technik des Experiments nicht willkürlich beeinflussen lässt. Ausserdem ist die Verlängerung minimal, und viele Ergebnisse liegen sicher innerhalb normaler Fehlergrenzen. Unsere Untersuchungen zeigen, dass durch die Einführung von Elfenbeinstiften in die Metaphyse eines wachsenden Knochens sich ein gewisser Einfluss auf das Wachstum erzielen lässt, dass diese Methode aber wegen ihrer Unsicherheit, und weil dabei Deformitäten auftreten können, sich für die Praxis am Menschen nicht eignet.

Eine unilaterale Verkürzung von Extremitäten sollte vorzugsweise mit der *Phemister*'schen Epiphyseodese behandelt werden. Mit dieser Methode haben wir günstige Erfolge erzielt, abgesehen von denen, die in der umfassenden Literatur angegeben sind. Eine diskutable Alternative ist die Hemmung des Wachstums mit Hilfe einer Drahtschlinge, wie *S. L. Haas*, San Francisco, sie 1945 angegeben hat.

RÉSUMÉ

Il est possible d'obtenir une stimulation de la croissance des os par unplantation dans les épiphyses osseuses d'une pointe métallique ou d'ivoire, néaumoins la réaction locale n'est souvent pas assez forte pour favoriser la croissance en longueur. Les pointes métalliques produisent une forte réaction à cause de l'action toxique sur les tissus du métal, cette réaction peut même gêner la croissance ; le plus souvent il se forme autour de la pointe une membrane fibreuse protectrice. Le même fait se produit quand on introduit dans les tissus osseux differents métaux pour obtenir un courant galvanique.

Les résultats sont meilleurs avec des pointes en matière résorbable, comme de l'ivoire, qui entretients une réaction osseuse jusqu'à resorption complète, cette réaction se traduits pur un épaississement osseux.

L'influence sur la croissance en longueur est variable et incertaine, et il se produit souvent une déformation de l'extré-

mité osseuse, déformation qu'on ne peut pas influencer même en modifiant la technique de l'expérience.

La croissance en longueur n'est que minimale et beaucoup de nos résultats se trouvent dans les limites d'une erreur possible.

Nos recherches montrent qu'il est possible jusqu'à un certain point d'agir sur la croissance en longueur des os par l'implantation de pointes d'ivoire dans la métaphyse, mais la méthode n'est pas applicable à l'homme à cause de son incertitude et des déformations qu'elle provoque.

Il est préférable de traiter un racouncissement unilateral des extrèmités par l'épiphyseodèse de *Phemister*. Cette technique nous a donné des résultats favorables en dehors de ceux mentionnés dans la littérature.

Quant à la possibilité d'arrêter la croissance moyennant un ruban d'acier méthode indiquée en 1945 par S. L. Haas de San Francisco, la question reste ouverte.

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