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<td>Watanabe, Kousaku</td>
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<td>引用</td>
<td>日本外科宝函 (1955), 24(2): 132-153</td>
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<td>発行日</td>
<td>1955-03-01</td>
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EXPERIMENTAL STUDY ON CROSSED ANASTOMOSIS BETWEEN ANTAGONISTIC PERIPHERAL NERVES
by
Kousaku Watanabe

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(Director: Prof. Dr. Chisato Araki)
(Received for Publication: Jan. 10, 1955.)

INTRODUCTION

As early as in 1873, Letiévant attempted, for the purpose of restoration of the peripheral nerve function lost by injuries, anastomosis between that nerve and another spinal nerve with different innervation. Later, Rawa (1885), Gunn (1886), Sick and Sanger (1897), Menasse (1900), Kennedy (1910), Osborne and Kilvington (1911), Shibuya (1934), Norioka (1934), Barron (1934), Sperry (1940, '41 and '47) and Arizawa (1952) made anastomosis, both in patients and in animals, between heteronymous or heterogenous nerves.

But there were diverse opinions as to the possibility of reestablishment of physiological function of the anastomosed nerve; some were in the affirmative, and others of the opposite.

The literature concerned may conveniently be classified, from the viewpoint of functional recovery, into the following three categories:

A) theory which admits the recovery occurring rather early in the postoperative period,
B) theory of on-recovery, and
C) theory in which the recovery can take place by exercise after the nerve regeneration.

Menasse (1900) reported that in a patient anastomosis of the peripheral portion of the paralyzed facial nerve with the accessory nerve resulted in successful recovery of movements of the face after the operation. Since then, Cushing (1903), Ballance (1904) and Davidson (1907) did similar facial anastomosis with the accessory or a spinal nerve and recognized that in all the cases, improvement of tonus of facial muscles apparently occurred. However, they stated that complete recovery of delicate movement of the face, especially the facial expression, could not be attained.

Gunn (1886) and Sick and Sanger (1897) reported that improvement of paralysis was obtained by the implantation of the peripheral cut end of the ulnar nerve paralyzed or by that of the radial nerve paralyzed, respectively, into the normal median nerve.

Anastomosis between heteronymous nerves had been accomplished also experimentally by various authors. Some of them believed the reestablishment of function, but others came to the opposite conclusion.

Recovery to the normal function of the nerves shortly after the operation was reported by Rawa (1885) when the tibial and fibular nerves were crosswise anastomosed in rabbits, dogs, cats and pigs. This was true of Kennedy's experiment.
CROSSED ANASTOMOSIS OF PERIPHERAL NERVES

Osborne and Kilvington (1911) confirmed that normal function was regained ten months after crossed anastomosis between the middle cords of the brachial plexus on both sides, when they observed that both fore legs reacted to unilateral electrical stimulation of the cortical motor areas.

Norioka (1934) observed functional recovery after crossed anastomosis between the phrenicus and the vagus, and Shibuya (1934) between the tibial and the fibular nerve.

Barron (1934) performed anastomosis between the following nerves: peripheral end of the n. femoralis with central end of the n. medianus or n. ulnaris; peripheral end of the n. ulnaris with central end of the n. tibialis; peripheral end of the n. tibialis with central ends of the n. medianus and n. ulnaris. And of the 34 rats, a great majority showed recovery to normal functioning of the legs, but in 4 unusual movements were observed.

The experimental results obtained by these authors may conform to the theory (A) described above.

In 1940, Sperry carried out transposition between the flexor muscle (m. gastrocnemius) and the extensor muscles (m. tibialis anterior et m. extensor digitorum longus) in rats. He found that normal function of the leg did never recover postoperatively despite all possible exercises. However, he could confirm recovery to normal function when he made crossed anastomosis of the fibular nerve with the tibial in addition. Further, he observed in 1941 that crossed anastomosis between the fibular and the tibial nerve in rats gave rise to reversed movement of the leg after the operation. This reversed movement persisted despite every kind of training, and was recovered only by crossed transposition of the muscles concerned.

Sperry’s experimental results may justify the theory (B) abovestated.

In 1947, Sperry made anastomosis between the nerves innervating the muscles of the elbow-joint of the spider and macaques monkeys and observed, that reversed movements of the elbow-joint appeared, three years thereafter, when the nerve regeneration seemed to have been completed. With training with a special apparatus, however, the monkeys regained the ability to perform purposive movements voluntarily. He, therefore, laid claim to the case of monkey to the theory (C) as described.

Arizawa (1952) in our laboratory accomplished crossed anastomosis between the tibial and the fibular nerve in 33 rabbits and 3 dogs, all of which showed recovery of the function to the normal. He consequently assumed that the functional recovery of the peripheral nerves which had undergone crossed anastomosis might be due to the compensation either in the brain or in the spinal cord.

Subsequently, Ishii (1954) in our laboratory anastomosed a cervical spinal nerve with the vagal nerve crosswise at the level of the neck in cats; it was then confirmed that sufficient nerve regeneration could take place even in heterogenous nerve ana-
stomosis, although the function reestablished was not physiological in such a case.

Whether or not does physiological function once lost of the peripheral nerve recover after anastomosis between the two nerves with different functions, and, if the recovery does occur, in what part of the brain or the spinal cord does functional compensation actually take place? For studying these problems, I made crossed anastomosis at the level of the upper leg in dogs, between the tibial nerve, which innervates flexor muscles of the hind leg, and the fibular nerve innervating the extensors.

Further, the peripheral nerves were crosswise anastomosed after previous decortication of the motor areas or medullary pyramidotomy.

In the control animals, partially crossed anastomosis of the peripheral nerves was done and the animals were observed for the peripheral functions for 3 to 12 months postoperatively, during and after which period electrical stimulation, and macro- and microscopic examinations of the anastomosed nerves were carried out. The present report concerns with the results thus obtained.

MATERIALS AND METHOD OF EXPERIMENT

I) Experimental animals. Healthy adults dogs, weighing around 10 kg., were used, as they readily survive sufficiently long postoperatively until the nerve regeneration is completed and they have the well developed pyramidal tract. In 30 dogs, various operations described in the following were done successfully.

II) Experimental method.

Group 1: Completely crossed anastomosis of the peripheral nerves (C.C.A.). 20 dogs.

Group 2: Completely crossed peripheral nerve anastomosis after recovery from the hemiplegia as the result of the preceding decortication of the contralateral motor areas (D.+C.C.A.). 3 dogs.

Group 3: Completely crossed peripheral nerve anastomosis after recovery from the hemiplegia resulting from previous contralateral pyramidotomy (P.+C.C.A.). 2 dogs.

Group 4: Partially crossed anastomosis of the peripheral nerves (P.C.A.). 5 dogs.

Postoperative impairments of the function were compared with each other among these four groups from variable points of view as were described later.

III) Operative procedures.

A) Anaesthesia. General narcosis with injection into the free peritoneal cavity of 10% Isomytal solution, 0.3c.c. per kg. body weight after preliminary basis narcosis with subcutaneous injection of 4% Narcopon scopolamine 1 c.c.

B) Completely crossed anastomosis of the peripheral nerves. With the right hind leg in extension, a skin incision, ca 5 cm. long, was made so that m. biceps femoris and m. semi-tendineus could easily be retracted when the tibial and fibular nerves were seen to bifurcate from the main trunk of the sciatic nerve.

After mobilization and cutting of these nerves, ARTZAWA made end-to-end anastomosis after the routine method of nerve anastomosis and tubulation with autogenous fascia. At autopsy,
it was found in his experiments that the sites of the anastomosis adhered to each other, showing conglomerated swelling, which histologically revealed comglomeration of nerve fibers, some of them passing into the homonymous peripheral nerve stump. For a successful crossed anastomosis, such comglomeration of nerve fibers must be avoided. Therefore, I devised a new technique, a combination of the autoarterial tubulation method of Weiss with TAKETOMO’s non-suture method using a tube of auto-fascia or vein. In my technique an arterial tube fixed in 70% alcohol was used for tubulation. This method was previously published in detail. It will be summarized in the following: each of the two nerves is doubly ligated, and then cut. At the middle of the arterial tube preserved in 70% alcohol, a small hole is made, through which the cut end of the one nerve inserted from one end of the tube is pulled out with a fine thread attached to that cut end. In this position, two or three sutures with fine silk thread were made between the arterial tube end on this side and the epineurium of the nerve without injuring the nerve parenchyma. Then the cut end of another nerve is likewise pulled out of the hole and the end of the arterial tube on this side is sutured with the epineurium. The two nerve ends appearing outside the hole of the tube are refreshed and then reposed within the tube so that the refreshed ends are exactly adjusted without direct suturing.

In this way, the central end of the tibial nerve and the peripheral end of the fibular nerve, or the central end of the fibular nerve and the peripheral end of the tibial nerve are crosswise anastomosed (Fig. 1, a).

C) Partially crossed anastomosis of the peripheral nerves: After exposing the two nerves, their epineuriums are incised longitudinally and each nerve is divided into one larger and one smaller bundle (6:1 to 8:1 in proportion). The smaller one is left unsevered while the larger one is severed and each end is crosswise anastomosed with that of another nerve in the same way as described in (B) (Fig. 1, b).

D) Unilateral decortication of the motor areas: Although exact location and extension of the cortical motor areas in dogs are not definitely established, gyri sigmoideus anterior et posterior are generally considered to be these areas. A part of gyri proreus and coronalis are also included in the motor areas: this fact was taken into consideration in my operation.

Nomenclature of the gyrus and sulci of the dog’s brain is given in Fig. 2.

The head of a dog in prone position is fixed, a median incision from the glabella to the occipital protuberance is made, the fascia of the left temporal muscle is cut at its attachment, and the temporal muscles are turned laterocaudally, resulting in sufficient exposure of the temporal and frontal bones. After the periosteum is detached at the upper margin of the temporal bone, is made a burr hole, which is enlarged, so as to expose the frontal sinus frontally and extend to the midline at the vertex. Then sulcus cruciatus and gyri sigmoideus are visualized through the transparent dura mater. The dura is then incised at the part...
overlying the sigmoid gyrus and, having sucked the cerebrospinal fluid, both the anterior and the posterior sigmoid gyrus are decorticated with a curette; in this procedure the cortex of the inner surface along the central sulcus should be removed. After haemostasis is secured, the dura, the fascia and the skin are sutured.

E) Transoral medullary pyramidotomy (unilateral): The pyramidal tract in dogs has been studied by various authors since VULPIAN in 1871 traced secondary degeneration in the spinal cord following unilateral removal of the sigmoid gyrus. According to KATO (1934), the pyramidal tract in dogs arises in the cortical motor areas and descends on the ipsilateral side passing through the medullary pyramid in the ventral part of the medulla, where most fibers decussate, though some remain on the same side. All these fibers terminate in the spinal cord, where they are arranged in four bundles, namely, fasciculus pyramidalis lateralis cruciatus et rectus and fasciculus pyramidalis anterior cruciatus et rectus; the fasciculus pyramidalis lateralis cruciatus is the most powerful bundle thereamong. For severing selectively the pyramidal tract, without impairing other nervous pathways, decortication of the motor areas is not appropriate, because not only the pyramidal tract but other projection fibers also arise from the cortical motor areas. As the pyramidal tract descends deep in the spinal cord, it is impossible selectively to sever the pyramidal tract at this level. Consequently, the most favorable part of the central nervous system where selective pyramidotomy can be done is the medullary pyramid, which occupy the most ventral part of the medulla down to the pyramidal decussation. Selective pyramidotomy may therefore be successfully carried out at this level.

Regarding medullary pyramidotomy, STARLINGER was the first who did the operation bilaterally in 1895 in dogs. He succeeded, by the approach from the ventral side of the neck, pushing aside the trachea and the oesophagus and reaching the basis cranii, in exposing the medullary pyramid, which was cut bilaterally, and studied the physiological and anatomical changes after the operation. Later, ROTHMANN (1900), SCHÜLLER (1904 and '06), SCHÜFER (1910), BARRON (1934), MARSCHALL (1934), TOWER (1935) and others contributed by making unilateral or bilateral pyramidotomy in dogs, cats, rats and monkeys, to the problem of anatomo-physiological changes after the operation. Their operative procedures were all analogous to those of STARLINGER's transcervical method. RANSON (1934) approached to the medulla in cats transorally, but all of the experimental animals succumbed within 24 hours to infections. Recently, THOMSON (1952) succeeded in hypophysectomy in dogs with transpalatal approach.
Kudo et al. (1952) was able to expose the ventral surface of the midbrain by a new transoral approach with previous luxation or fracture of the mandible. In modifying and improving the methods of Thomson and Kudo, I devised a transoral method, in which the ventral surface of the medulla was exposed pretty widely so that the pyramid could be cut exactly unilaterally.

After the narcosis, the dog is laid in supine position and, prior to the operation, a canula is introduced through an incision into the trachea.

The maxilla is fixed, the mouth is opened maximally by a retractor and the tongue is pulled out and sutured to the skin over the mandible. The lips and the oral cavity are disinfected with 0.5% marsonin alcohol, draped, only exposing the soft palate and the pharynx, and the drape is sutured to the mucous membrane in order to avoid slipping. The soft palate is incised in the midline and the posterior nasal cavity and the posterior pharyngeal wall are exposed which are immediately disinfected.

The soft palate divided is turned aside and pulled laterally and the edges are sutured to the lips or to the gingiva, thus enabling good haemostasis and exact manipulation.

A schematic sketch of the posterior pharyngeal wall is illustrated in Fig. 3, in which spinose hamulus pterygoideus, spherical os temporale pars tympanica and foramen magnum are visible anteriorly, in the middle and posteriorly, respectively.

The midpoint of the line passing through the bilateral hamulus pterygoideus corresponds to the sella turcica, and that of the bullae tympani to the pons. The region extending from the level of the bullae to the foramen corresponds to the medulla.

Thus the pharyngeal wall is now incised in the midline deep enough to reach the bone from the level of the bullae down to the foramen and each of the edges is pulled laterally and sutured aside so that haemorrhage is easily controlled and the operation field is enlarged. Os sphenoidale posterior and os occipitale are then visible in the midline, and between these two bones is made with a chisel a hole 5–7 mm. in diameter which is enlarged by a bone forceps so carefully as not to damage the underlying dura to a length of about 2 cm. caudally to the foramen. In this procedure not much bleeding from the bone can be controlled with the bone wax. After complete haemostasis, the ventral part of the medulla is seen through the transparent dura; the basilar artery is seen in the midline to pulsate and run in a somewhat serpentine course, lateral to which is found on both sides the whitish medullary pyramid. The dura is then incised, taking care not to injure the basilar artery, the cerebrospinal fluid is sucked out and unilateral pyramidalotomy should be made under direct vision. For the cutting, instead of a knife, a dura-hook is used, which is inserted in the median sulcus, 2–3 mm. deep, of course avoiding any damage to the basilar artery, the tip of the hook being rotated for 90 degrees, and gradually pulled out so that the pyramid is cut unilaterally and bluntly. Such blunt incision seems to be superior to the sharp one, as with the former the cutting is complete and accompanied with less side damage. When the basilar...
artery is once injured, the resultant haemorrhage is uncontrollable owing to the narrow and deeply situated operation field. Furthermore, even a seemingly trivial haemorrhage is liable to form a clot to which the animal readily succumbs. When haemostasis is completed, place a small piece of gelatine sponge soaked with penicillin solution in the bony defect, leaving the dura unsutured, and then the pericstenum and the mucosa are sutured together. Antibiotics combined with haemostatica is systemically administered after the operation and the tracheal cannula is removed on the 2nd or 3rd postoperative day.

IV) Postoperative examinations.
The following items are examined postoperatively.

A) Functional examination (clinical signs).
   a) Unilateral decortication or medullary pyramidotomy:
      Paresis of the head and the four limbs were recognized by the changes in behavior at the time of movements, such as walking, running and standing with the hind legs. Paresis of the hind leg, in particular, was carefully analyzed by the state of both extension and flexion of the toes of that leg when the dog stood with the hind legs. In addition, abnormalities of tendon reflexes and of muscular tonus and the course of the recovery from the paresis were concurrently observed.
   b) Completely or partially crossed anastomosis of the peripheral nerves:
      i) Lameness (or crippling) appeared most frequently. State of crippling, particularly flexions of the toes, position and form of the ankle joint, state of standing with the hind legs, and coordination or non-coordination with the healthy legs at movements, were carefully examined.
      ii) Trophic disturbances. Loss of hair, deformation of nail, blush, bleeding, ulceration and necrosis of the leg were observed.
      iii) Resistance at passive flexion of the ankle joint. Immediately after the operation all the cases showed flaccidity, but along with the progress of nerve regeneration the resistance gradually increased.

B) Electrical stimulation by induced current.
Prior to killing the animal, both the tibial and fibular nerves on the healthy side and the tibio-fibular and fibulo-tibial nerves on the paralyzed side are exposed and, with DU BOIS-REYMOND’s apparatus (2 volt), electrical stimulation is given to the points shown in Fig. 4; i.e., points T and F on the healthy side and A and B (central), and a and b (peripheral) on the side operated on. The motor reactions elicited and the threshold values on both sides are compared with each other (Fig. 4).

C) Anatomical examination.
   a) Decortication of the motor areas or medullary pyramidotomy: When the animal is sacrificed, the brain and the spinal cord are removed and the medulla is fixed for 3 months in 10% formalin solution after the presence of adhesions in the previous operation field and extent of the decortication or of the pyramidotomy have been determined, stained with WEIGERT SCHNELL BEIZE for 2 weeks, dehydrated with alcohol, embedded in celloidin. Serial sections of 25 microns in thickness are made and stained with WEIGERT-PAL’s myelin sheath staining
Fig. 4. The points to which electrical stimulation is given.

Norm. : Normal side
C. C. A. : Completely crossed anastomosis
P. C. A. : Partially crossed anastomosis
Tib. : N. tibialis
Fib. : N. fibularis

Method. The specimens are examined by microscopy for the location of the pyramidotomy and for the damages to the neighboring nervous structures.

b) Completely or partially crossed anastomosis of the peripheral nerves: The nerves are cut at 5 cm. above and below the anastomosis, and then placed with tension on an object glass and after the intensity of adhesion and the formation of neuroma have been examined, fixed in 10% formalin solution for 3 months and the same staining as above are made. It should be noted that at the site of the anastomosis sectioning is to be made parallel to the course of the nerve and 25 microns thick, but distal to the anastomosis sections are more conveniently made transversely and 15 microns thick. The specimens are examined for regeneration of myelinated nerve fibers.

RESULTS OF THE EXPERIMENT

A) Functional changes (postoperative clinical signs).

a) Paresis appearing after unilateral decortication of the motor areas or medullary pyramidotomy.

1) Unilateral decortication of the motor areas.

Clinical signs and symptoms following decortication in 6 dogs (3 of them later underwent C. C. A.) are summarized as follows; Immediately after the operation, contralateral motor hemiparesis constantly occurred. The paresis was more pronounced in the fore leg than in the hind leg, and, in the former, the part distal to the elbow joint was more intensely paralyzed than that proximal, and at the hand joint the position in plantar flexion (posterior flexion) was always seen. In the hind leg, paresis was observed in the part distal to the ankle joint and the toes were usually flexed plantarly, or posteriorly. The head was turned to the side of the operation, tilting antero-ventrally, and unable to move upwards. The trunk was bent with the convexity towards the side of the operation. On standing, the animal was quite unstable and readily fell to the side of the operation when pushed or pulled. On walking, the animal rotated towards the same side, but with the lapse of time the rotating circle was gradually enlarged and he became finally capable of walking in a straight line. Every movement was generally unbalanced. On standing up, the limbs on the healthy side commenced the first movement, while, on assuming prone position, the limbs on the opposite side commenced it. Abnormal reflexes were absent, although the muscles lost the tonus and were flaccid. Recovery from the paresis was seen to develop earlier in the
hind leg than in the fore leg. The last to recover was the part distal to the hand joint. 2 to 3 weeks at most after the operation, the animals recovered from the paresis nearly to the normal, so that by usual examination the abnormality in the movements, if any remained, could not be found.

2) Unilateral medullary pyramidotomysis.
Clinical signs demonstrated in 3 dogs (2 of them later underwent C. C. A.) are summarized as follows; motor hemiparesis below the neck on the side contralateral to the operation constantly developed in more or less degree. The paresis was more severe in degree in the fore leg than in the hind leg, particularly in the part distal to the hand joint. Paresis of the hind leg was only slight. The movement of the head was not influenced by the operation. The trunk showed a slight arched bending towards the side contralateral to the operation. Standing up movements were unsteady, at which the contralateral hand joint was flexed plantarily. But once the animal stood up, the hand joint returned to the normal position and the animal could stand straight. The fore legs were usually in crossed positions on standing and, when pulled or pushed, the animal easily fell to the contralateral side. On walking, the animal at first rotated slightly toward the side of the operation, but soon was able to go straight, though liable to fall to the contralateral side. The hind leg recovered from the paresis earlier than the fore leg, of which the part distal to the hand joint was the last to recover. In 7 to 10 days postoperatively, recovery to nearly the normal took place without any permanent disturbance. Abnormal reflexes and increased tonic ity of the muscles were entirely absent both immediately after the operation and after the recovery of movements. Hemiparesis was of nearly the same nature in the case of pyramidotomy as in the case of decortication, but it was less in severity and recovered prompter in the former than in the latter.

b) Changes after completely or partially crossed peripheral nerve anastomosis.
1) Completely crossed anastomosis.
   i) Crippling: This was constantly seen after the operation. The part distal to the ankle joint on the side of the operation was maximally flaccid and lost active movements. During the period from the 3rd to the 14th postoperative day, the paralyzed hind leg was lifted up and the animal walked or ran with the remaining three limbs. This may be attributed to the pain arising from the operative wound. Thereafter, the toes became plantarily flexed and the animal walked with the dorsal surface of the toes dragging the ground. On running, however, the paralyzed leg was lifted up and the other three limbs were used. Such lameness was observed for 1½ to 4 months, averaging 2½ months postoperatively, which I should like to term 1st stadium of paralysis. Thereafter, the animal gradually recovered from this crippling state and became capable of walking and running normally at a glance. However, the ankle joint took a position of extreme dorsal flexion, although the toes were in the normal position. This stadium suggestive of recovery to normal function lasted for 4 to 9 months, 5½ months in average, which is termed 2nd stadium of compensation. During the period of compensation, the
position of the ankle joint returned from hyperflexion to the normal and the toes began to move actively. About the end of this stadium, peculiar movements, just opposite to the movements on the healthy side developed at meals, anger and astonishment. Such reversed movements became gradually more pronounced, especially in the ankle joint, and at the same time the toes and frequently the ankle also were again flexed plantarly. Consequently, due to such reversed movements, walking became unskillful and running was carried out with the other three limbs. In 7 to 10 months the reversed movements became the most manifest, and this stage is termed 3rd stadium of reversed movements. The position and form of the leg in the three different stadiums are shown in Fig. 5. Crippling by reversed movements never recovered later. As is shown in Fig. 6, postoperative crippling improved by the 4th month in nearly all dogs, when it again began to appear and fully developed in the 9th postoperative month, after which period crippling persisted for ever.

Of the 25 (20 C. C. A., 3 D. + C. C. A., and 2 P. + C. C. A.) dogs, 7 (28%) went into the second stadium soon after the initial stage of walking with three legs. In 2 of the 25 (8%) the crippling due to reversed movements (the 3rd stadium) developed in immediate succession to the first stadium without demonstrating compensatory normal walking (the 2nd stadium).

Crippling both in the first and the third stadium was more outstanding in D. + C. C. A. dogs than in C. C. A. dogs, although the period of walking with three legs was shorter in the former. Therefore D. + C. C. A. animals were seen more frequently to fall laterally. The reason is that the reduction in tonus and strength of muscles, which is still remaining latently after decortication although undetectable by usual

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Fig. 5. Postoperative state of the hind leg on walking (C. C. A.)

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Fig. 6. Frequency of crippling after the operation. Percentage of the number of the dogs showing crippling.
examination, is added to the paralysis due to C. C. A., so that D. + C. C. A. animals tend to cripple more severely and to fall laterally on walking. There was not much difference in the postoperative state between the P. + C. C. A. and the C. C. A. dogs.

ii) Trophic disturbances: Trophic disturbances were seen in the following number of cases, all appearing in the first stadium.

- No disturbance: 4 dogs
- Loss of hair and blush only: 2 dogs
- Bleeding and ulcer formation: 14 dogs
- Formation of deep ulcer reaching the tendon or bone: 3 dogs
- Necrosis and falling off of the distal end: 2 dogs

Formation of ulcer took place suddenly one week to one month after the operation and the ulcers were one to three or four in number, 0.5 to 1.0 cm. in diameter, round in shape and located mostly in the dorsum of the foot or on the tip of a toe. The ulcers were gradually covered with granulation tissue and healed in the 4th postoperative month (Fig. 7).

In the third stadium, when crippling reappeared, loss of hair, deformation of nails and bleeding were occasionally seen, but there was no ulcer formation. Of the 25 dogs, 4 (16%) did not show a slightest dystrophy and 2 (8%) manifested loss of hair and blush only. The dogs, in which the crippling in the first stadium was not remarkable, were usually devoid of trophic disturbances.

In all the D. + C. C. A. dogs, ulcer formation was severe and in some of them the phalangeal bones were exposed for a certain period. The ulcers, however, healed in the 4th postoperative month. There was no difference in ulceration between the P. + C. C. A. and the C. C. A. dogs.

In 2 (Nos. 7 and 10, C. C. A.) dogs, there developed 4 and 45 days, respectively, after the operation at the distal end of the foot an ulcer, which was quickly widened and deepened and in the course of 15 days the distal half of the phalanx became necrotic and fell off. The cause of this ulcer was not evident, but it seemed that a neurotrophic factor might play a role, although infection by some specific microorganisms could not entirely be excluded.

iii) Resistance to passive flexion of the ankle joint: The normal resistance disappeared after the operation in all the cases. The hind limb distal to the ankle joint was completely flaccid and no longer actively movable. However, this resistance reappeared at the end of the 1st stadium, i.e. in 2 to 3 months postoperatively, improved gradually and at the end of the 2nd stadium, i.e. in 4 to 6 months after the operation, returned to the normal.
2) Partially crossed anastomosis of the peripheral nerves.

In all the 5 dogs no neurological changes appeared after the operation and they were capable of walking and running without crippling, despite that the unsevered part of both the tibial and the fibular nerve was only \( \frac{1}{6} \) to \( \frac{1}{4} \) in thickness of the whole nerve. On standing with the hind legs, the dogs sometimes stood with the dorsal surface of the toes touching the ground, but they soon turned actively the toes to the normal position. Postoperative trophic disturbances were also slight in these dogs. In only 2 dogs were found small subcutaneous haemorrhages or ulcers on the plantar surface of the foot, which healed in 3 to 4 months postoperatively. These dogs, however, began to cripple 6 to 7 months after the operation in the same way as in C. C. A. dogs, showing reversed movements of increasing severity, from which they never recovered.

B) Reactive movements to electrical stimulation by induction current.

The experiment was carried out 6 to 12 months after the operation. Both in C. C. A. and in P. C. A. dogs, the stimulation given to the portions of nerves central to the anastomoses (point A and B) gave rise to the reactions contrary to those on the healthy side: at the time of stimulation of the tibio-fibular nerve (point A), a weak current gave rise to spreading of the toes and a strong current dorsal flexion of the ankle besides. On stimulation of the fibulo-tibial nerve (point B), a weak current gave rise to plantar flexion of the toes only and a strong current to that of the ankle besides. In P. C. A. dogs, some of the toes showed, at times, normal reaction on weak stimulation, but, on somewhat stronger stimulation, all the toes demonstrated reversed reactive movements. Threshold values, when measured at point A and B (central to the anastomosis), and more than 7 to 8 months after the operation, returned in most cases to the normal and did rarely show a rising (the coil distance being less)—5 at maximum, if compared with those on the healthy side (Fig. 8). In a few cases (No. 1, 1 year; No. 15, 10

a) C. C. A.

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b) P. C. A.

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Fig. 8. Threshold values of electrical stimulation by induced current (cm.) using Du Bois-Reymond's apparatus. Voltage: 2 volt.

months; No. 20, 11 months; and No. 41, 1 year after the operation) even a decrease
(the coil distance being greater) in the values was noted.

On stimulation at points a and b (distal to the anastomosis), on the other hand, a greater majority showed a slight increase (less than 20%) in the threshold values, although some showed nearly the same values as those obtained by the stimulation of the central portions. This may be accounted for that the stimulation given to the distal portion is weakened by the massive connective tissue proliferated in between the nerve fibers. In one case (No. 14, 5½ months after the operation), the reactive movements were analogous to those described above, but the threshold values were markedly increased (the coil distance being less) even when the central portion was stimulated. Return of the threshold values to nearly the normal 7 to 8 months after the operation suggested that the nerve regeneration was almost completed after crossed anastomosis.

C) Anatomical Findings.

a) Decortication of the motor areas or medullary pyramidotomy.

i) Extent of the decortication (Fig. 9).

![Fig. 9. Extent and location of the decortication.](image)

In No. 41 dog (1 year after the operation), anterior and posterior sigmoid gyri (total) and also proreus and coronary gyri (partial) were decorticated on the left side: complete decortication of the so-called motor areas (Fig. 10). In No. 42 dog (3½ months after the operation), whole anterior sigmoid gyrus, most of posterior sigmoid gyrus and a part of coronary gyrus, all on the left side, were decorticated: in other words, decortication of nearly all the motor areas. In No. 46 dog (11 months after the operation), left anterior and posterior sigmoid gyri were removed: almost complete decortication.

In the dogs with a rather long postoperative period of survival (Nos. 41 and 46), the medullary pyramid on the side of the operation was seen evidently smaller in size than on the healthy side.
ii) Location of the medullary pyramidalotomy and damages to the neighboring nervous pathways.

In No. 59 dog (6 months postoperatively), the pyramidalotomy part of the medulla was seen to be slightly adhered to the dura mater, although the adhesion could be separated bluntly. In this case, the left medullary pyramid was cut across at the level 5 mm. below the pons and the pyramidal bundles both above and below the cut line reduced its size grossly to 1/2 of the normal. Histologically, the pyramid was found to be completely cut through at the level of the inferior olivary nucleus. The longitudinal fasciculus dorsal to the pyramid was seen severed and the myelin sheaths were faintly stained (Fig. 11 and 12).

In No. 60 dog (8 months postoperatively), the medullary pyramid on the left side was cut through at the level of the transition between the pons and the medulla. The pyramid distal to the cut line was 1/2 in size of the pyramid on the healthy side. Histological examination disclosed that the pyramid was cut across at the level of the fila rediculare of the vagal nerve and the cut reached in the depth of stratum interolive.

b) Completely crossed anastomosis or partially crossed anastomosis.

1) Macroscopical findings:

In the case of C.C.A., the arterial piece used for tubulation remained and appeared as a white membrane even 1 year after the operation. At the site of the anastomosis, adhesion to the surrounding tissue was found in few cases only. The two arterial pieces were seen embedded together in the connective tissue, although they could be readily and bluntly shelled out. The two nerves appeared white and glistening. The periphery of the fibular nerve anastomosed to the central end of the tibial nerve doubled its preoperative size so that it became as large as the latter nerve, which remained unchanged. Insufficiency of the anastomosis, dense adhesion and formation of neuroma were not observed. In short, crossed nerve anastomosis healed

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Fig. 11. Medullary pyramidalotomy.
No. 59 dog (6 months after the operation). The left pyramid has been cut across at the point marked with an arrow (√). The pyramid, both above and below the cut line, is seen to have reduced the size to 1/2 of that of the right pyramid.

Fig. 12. Photomicrograph of the medullary pyramidalotomy.
No. 59 dog. The left pyramid is entirely absent. The longitudinal fasciculus on that side shows an obvious demyelinization (compare with the contralateral side). Weigert-Pal's staining method for myelin sheath. (×4)
completely (Fig. 13).

![Image](image-url)

**Fig. 13.** Gross appearance of the nerves which have undergone C. C. A.

No.13 dog, 10 months after the operation (enlargement ×2).

The arterial tubes used for tubulation remain and appear as white membranes. The two nerves (n. fibulo-tibialis is seen above and n. tibio-fibularis below) appear white and glistening. They are seen embedded together in the connective tissue, although they can be readily and bluntly shelled out. Crossed nerve anastomosis is complete. Proximo-distal direction from left to right.

well arranged course towards the peripheral piece used for tubulation and those of the

The mass of regenerated nerve fibers in the arterial tube was as a whole fusiform, because the interfibrar spaces were loose, but each fiber was seen to regenerate parallel to each other and has a straight course. Intercrossing of the nerve fibers of the two nerves were absent. In other words, there were no fibers which regenerated towards the peripheral end of the homonymous nerve, so that no tibial (or fibular) nerve fibers were seen to proceed towards the distal portion of the n. tibialis (or fibularis). As has been described, the individual fibers as a rule regenerate and proceed straightly (Fig. 15), but some may take slightly tortuous coursed (Fig. 16) and some others such irregular course as to intercross each other (Fig. 17). In the cross sections of the peripheral part of the anastomosed nerve, at the 6th postoperative month, the number of the regenerated nerve fibers was found already large enough, but the size was smaller than the normal, revealing qualitatively insufficient regeneration. In 8 to 12 months postoperatively, the number was nearly equal to that at the 6th month, but the size increased, becoming the same as that of the nerve on the healthy side, a fact indicating sufficient regeneration both qualitatively and quanti-

In P. C. A. dogs, the nerves which had undergone crossed anastomosis were seen to arrange in 2 parallel rows, white and glistening, on which were seen X-form nerve fiber bundles which had not been severed and anastomosed at the operation. In general, adhesion around and between the two nerves was more prominent in these cases than in the C. C. A. cases. Yet, the partially crossed anastomosis seemed to have healed successfully.

2) Histological findings:

In more than 6 months after the operation, the nerve fibers anastomosed showed sufficient regeneration. The regenerated fibers of the tibialis proceeded with a portion of the fibularis inside the arterial piece used for tubulation and those of the

![Image](image-url)

**Fig. 14.** Longitudinal section through the anastomosis.

No. 9 dog. (7 months after the operation).

The fibulo-tibial nerve is seen above and the tibio-fibular below. All the nerve fibers have regenerated, being arranged in a regular course, except for the part of the anastomosis where the fibers are not compact and appear fusiform as a whole. Intercrossing of the fibers is not seen. Thus the crossed anastomosis has healed completely. Ehrlich's myelin sheath stain. (× 8)
CROSSED ANASTOMOSIS OF PERIPHERAL NERVES

Fig. 15. Longitudinal section through the site of anastomosis.
No. 17 dog (7 months after the operation).
The regenerated nerve fibers are arranged in parallel and straight rows. WEIGERT-PAL's staining method for myelin sheath. (×80)

Fig. 16. Longitudinal section through the site of anastomosis.
No. 60 dog (8 months after the operation).
The tibio-fibular nerve. The regenerated fibers are arranged in nearly parallel rows, although some show finely tortuous courses. WEIGERT-PAL's stain. (×80)

Fig. 17. Longitudinal section through the site of anastomosis.
No. 14 dog (6 months after the operation).
The fibulo-tibial nerve. Some of the regenerated nerve fibers show intercrossing and irregular courses. WEIGERT-PAL's stain. (×40)

Fig. 18. Cross section of the healthy nerve.
Each fiber is of nearly the same size. WEIGERT-PAL's stain. (×400)

Fig. 19. Cross section of the nerve peripheral to anastomosis.
No. 20 dog (12 months after the operation).
The tibio-fibular nerve. The part corresponding to the fibular nerve. The size of the regenerated nerve fibers is somewhat smaller than that on the healthy side, but the number is nearly the same. WEIGERT-PAL's stain. (×400)

Thus from the findings not only of macroscopic but also of microscopic observations, the crossed anastomosis was considered to have healed successfully.

COMMENT

In dogs, I have performed crossed anastomosis, at the level of the upper leg, between the tibial nerve innervating flexor muscles, and the fibular nerve innervating extensors. After the operation, impaired walking once recovered nearly to the normal in the
period of 2 ½ to 5 ½ postoperative months. After this period, or subsequent to complete nerve regeneration, impaired gait gradually reappeared, demonstrating such contra-purposive reversed movements as to flex the toes plantarly when dorsal flexion should occur, and vice versa. From the impaired gait of this kind, the animals were seen never to recover.

In the case of P. C. A., the uncrossed, or unsevered nerve fibers, ⅓ to ⅘ of the original thickness of the nerve, seemed at first to be enough to rule normal walking. With the lapse of time, however, the nerve fibers which had undergone crossed anastomosis, regenerated and finally they became predominant to the uncrossed fibers in the effect of innervation, when reversed movements of the toes developed in the same way as in the case of C. C. A., thus resulting in crippling on walking.

After the C. C. A. crippling due to immediate paralysis naturally appeared, from which the animal recovered in 1 ½ to 4, averaging 2 ½ months, when the nerve regeneration was probably still going on and seemed to have advanced only so far as to allow the muscles under innervation to maintain the tonus and to hold the normal position of the leg. In such a stadium of incomplete nerve regeneration, one is apt to assume that complete recovery to normal function has already taken place. But such an assumption is not correct, because, in P. C. A. cases, only ⅔~⅗ of the original nerve fibers was enough to control nearly normal walking.

As the regeneration went on and was finally completed, the disturbance in walking reappeared, due to the occurrence of the contra-purposive reversed movements. This seems to be the result of the establishment of the complete innervation of the nerves which had been crosswise anastomosed.

The efferent impulse of plantar flexion from the anterior horn cells of the spinal cord was conveyed through the crosswise anastomosed tibio-fibular nerve to the extensor muscles, and vice versa, resulting in contra-purposive reversed movements of the limb and, consequently, in walking disturbances.

Regarding the theory which admits the recovery occurring rather early in the postoperative period, I presume that the nerve regeneration might have occurred only incompletely owing to some failure in the technique of the nerve anastomosis, i.e. the process of the nerve regeneration advanced no further than the 2nd stadium of compensation. Also it is possible that even in C. C. A., if performed with insufficient technique, some per cent of the regenerated nerve fibers should proceed towards the homonymous nerve. In such imperfect operations, formation of a neuroma and adhesion are constantly present, hindering the regeneration of the nerve fibers, so that reversed movements hardly ensue. A rise in the threshold values (10~25%), or reduction in nervous excitability, as reported by many authors, would likewise justify this view. More than 7 to 8 months after the anastomosis, the threshold values measured at the central portion of the nerve anastomosed did actually differ not much in my experiment from those measured on the healthy side (the difference being 5% at the maximum). In a great majority of the cases, the threshold values were equal on both sides, but in some cases, they were even lower on the side of the anastomosis than on the healthy side. This fact is contrary
to the report of KIRIHARA et al, that the threshold values of one and the same nerve are always greater after the anastomosis than before.

The mere fact that reversed reactive movements do appear with electrical stimulation, does not necessarily mean that all the fibers Anastomosed have regenerated in the crosswise direction, because, in P.C.A. dogs, reactive movements on stimulation were always reversed, presumably as the result of the predominance of regenerated crossed fibers. Thus, it is possible that a reversed reaction takes place in those dogs of C.C.A. in which a part of the fibers crosswise Anastomosed has regenerated towards the homonymous nerve.

On the contrary, recovery of the threshold values to the normal indicates the completeness of the nerve regeneration. Whether or not the crossed anastomosis has been completed must be proved not only by the macroscopic and histologic findings, but also by the threshold values which are capable of giving rise to reversed movements. On this account, the reports made so far by various authors are quite unsatisfactory.

In 1940, SPERRY transplanted crosswise at the lower leg in rats the flexor, m. gastrocnemius lateralis, and the extensors, mm. extensor digitorum longus and tibialis anterior, at their distal ends of insertion. The muscles which move the ankle joint in rats are only these three muscles; the tibial nerve innervates the m. gastrocnemius lateralis and the fibular nerve the mm. extensor digitorum longus and tibialis anterior. After the crossed transplantation, excitement of the nerve was represented by dorsal flexion and that of the fibular nerve by plantar flexion of the ankle joint. This is quite analogous with the result obtained when crossed anastomosis between the tibial and the fibular nerve was completed.

SPERRY had not succeeded in bringing about recovery to the normal of the postoperative reversed movements in spite of long-term training. According to SPERRY, this reversed movement did, however, recover to the normal following the crossed anastomosis of the tibial and the fibular nerve at the level of the thigh performed after the methods of WEISS's auto-arterial (or venous) tubulation without suturing.

In 1941, SPERRY again made crossed anastomosis in rat, between the tibial and the fibular nerve, and observed the same reversed movements, as those in the rat which had undergone transplantation of the muscles, occurring along with the progress of postoperative nerve regeneration.

This time, the reversed movements recovered to the normal only when crossed transplantation of the muscles were accomplished, but not by every kind of training.

From my own experimental results, I agree with SPERRY's theory that recovery to the normal function can not be expected, if crossed anastomosis of a nerve with its antagonistic nerve is made. The inborn activity of the anterior horn cells to rule over the peripheral muscles remains always constant and never changes even when the muscles under innervation are replaced by the antagonistic muscles. In such states of changed peripheral innervation, also the nervous system higher in order than the anterior horn cells, for example, the motor cortex, does not seem
in dogs to play some role in bringing about an adequate functional adjustment to the new situation in the periphery, as was shown in my experiment.

However, SPERRY in 1947 reported that the reversed movements developing in monkeys after the crossed nerve anastomosis could be changed to the normal purposive movements by training. Thus, it might be possible that the motor neurons of the anterior horn directly connected with the peripheral muscles are purposively reorganized under the control of the higher centers. That is to say, an animal, which has the well developed higher center controlling the spinal motor system, may be able to reorganize the latter so as to change the reversed movements developing after the crossed anastomosis to purposive movements.

It is needless to say that, for reacquisition of purposive movements, an enormous amount of training under renewed situation is required.

Normally, the dog uses the four limbs on walking, but he may be able to walk with three of the four limbs. After the crossed anastomosis, the gait is impaired due to reversed movements of the hind leg, but the dog can still walk with the remaining three legs, the leg operated on being lifted up and not used. Therefore, practice and training for using this leg can hardly be carried out, and, consequently, there is little chance for the reorganization of the motor centers in the spinal cord. For this reason, it is easily recognized that in dogs the reversed movements once established remain permanently and the functional recovery does not take place. Whether the reorganization of the function by training is in dogs in some way possible, or not, will be made clear by a further study.

In the practice of clinical surgery, nerve anastomosis should be done as far as possible between the central and the peripheral end of one and the same nerve. It is rather unusual that anastomosis between the two nerves of different function is to be done. But when heteronymous nerve anastomosis is unavoidable, repeated practice and training for the reorganization should be carried out early in the postoperative period, since it seems not impossible that in man the normal function may return even after completely crossed anastomosis.

SUMMARY

1) I performed in 20 dogs completely crossed anastomosis between the tibial and the fibular nerve at the level of the thigh. The same anastomosis was made in three additional dogs after previous unilateral decortication of the cerebral motor areas and in two other dogs after medullary pyramidotomy. In all these dogs, comparative observations with regard to the postoperative functional state were carried out during the postoperative period ranging from 3 to 12 months. Further, partially crossed anastomosis of the peripheral nerves was done in other 5 dogs, which constituted the control group.

2) In the group of completely crossed anastomosis, the dogs recovered from the resultant crippling due to paralysis in 1½ to 4, averaging 2½, months after the operation and were able to walk seemingly normally in 3 months. As the nerve regeneration went on, non-purposive reversed movements of the toes developed from
the 4th to 9th, averaging 5 1/2 th, postoperative month so that the animals again showed pronounced crippling on walking, which never improved even after a fairly long time.

3) In the case of partially crossed anastomosis, the animals were seen capable of normal walking, if some 1/4 to 1/4 in thickness of the original nerves were left unsevered. However, when the nerve fibers, which had undergone crossed anastomosis, fully regenerated, the reversed movements of the toes, as seen in the case of completely crossed anastomosis, appeared, resulting in the walking disturbances which did hardly improve later.

4) Electrical stimulation applied to the point central to the anastomosis gave rise to reactive movements reverse to those on the healthy side in the cases of both C. C. A. and P. C. A. But the threshold values were not much different from those on the healthy side; a fact which indicated that the nerve regeneration in the crossed direction was completed.

5) Both the macroscopic and the histologic examinations of the anastomosed sites of the nerves confirmed that the crossed anastomosis healed successfully. In other words, the nerve fibers were found to have regenerated well and to have proceeded into the periphery of the heteronymous nerve.

6) Decortication of the cerebral motor areas or medullary pyramidotomy did not essentially influence on the functional changes after the crossed anastomosis of the peripheral nerves.

7) However, it is presumed from the literature that the animals which have the well developed brain may have an ability of reorganization of the peripheral motor system so as to change the reversed movements to the normal purposive movements if adequately trained at the time when the nerve regeneration has been completed.

8) It is my belief that, in the cases, where the recovery of function took place rather early after the crossed anastomosis of the peripheral nerves, the nerve regeneration was not complete and remained in the 2nd stadium of compensation probably due to some failure in the technique of the nerve anastomosis.

9) In the present experiment a new method of anastomosis has been adopted in which an arterial tube fixed and preserved in 70% alcohol is used for tubulation and the nerve ends within it are not sutured with each other. This method is simple and enables an ideal regeneration of the nerve fibers. It should be widely useful in clinical practice.

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異名末梢神経交叉縫合に関する実験的研究
京都大学医学部外科学教室第1講座（指導 荒木千里教授）
大学院学生 渡辺浩策

1) 私は犬（20頭）の脛骨、腓骨両神経を大腿部にて完全交叉縫合を行ない、更に一侧大腿運動筋皮質切除（3頭）及び延髄一側束体束切除（2頭）の後に対側の同様な末梢神経完全交叉縫合を行って、術後の機能状態を3ヶ月~1ヶ年に亘り、比較観察と共に、対照群としては、部分的交叉縫合（5頭）を行った。

2) 完全交叉縫合では、術後約2ヶ月半~4ヶ月、平均4ヶ月半で当初の麻痹性挙筋より脱し、約3ヶ月間略正常歩行を営むが、神経再生の完成と共に、術後4~9ヶ月、平均5ヶ月半頃より足筋の反作用の逆運動を呈して再び萎縮に陥りし、其後長時間の経過の後も再び機能の恢復は認めない。

3) 部分的交叉縫合により、神経の1/4~1/5程度が残されてあれば、それによって徒歩機能は著し完全に営む事は出来るのが、残余の交叉された残りの神経線維が再生を完成して来れば、完全交叉縫合と同様に、足筋の逆運動を呈して、機能は障害され、これはその後に至っても恢復しない。

4) 電気刺激により、縫合中枢側の刺検では、完全交叉、部分的交叉と共に健側に対逆の反応運動を呈するが、刺検値は健側に比して差異のない程度に恢復し、神経再生が完全に営まれた事を示している。

5) 縫合部の肉眼的、組織学的所見より、交叉縫合が成績している事を確かめ、再生神経線維は異名神経間にて、略し完全に再生延長する事が証された。

6) かえる末梢神経の変化に対して、大腿運動筋皮質切除、延髄束体束切除等は営むべく影響を及ぼさない。

7) 大脳発育の良好なる動物にては、逆運動発現後に、即ち神経再生が完成された時に訓練練習により合目的運動へと再編成、再統一が可能であるかを知らなかった。

8) 諸家の報告に於て、術後早期に機能恢復を認める論説に対し、神経再生の不全により、私のいう第二期、代償期の状態にて神経再生が求めたものと信じる。

9) 神経縫合に際し70％アルコール固定の浸みも用い、断端に全く余を残さない縫合術式を考案しえ用し、本術式は簡便であり、神経再生も完全に営まれる事を実験したから、臨床的応用もよいものと考える。

Pancreatitida.
R. M. Zollinger

膵炎の診断は病状に際し疑問を置き、更に血中アミラーゼ検査を行うことにより、以前よりも速かに診断に於て確定を下す得るに至った。

両治療法に就てとは急性膵炎の場合は相当標準的な治療法があるが、慢性膵炎では今日はその治療法に就て意見の一致をみていない現状である。著者の経験によれば急性膵炎の診断に当っては、本症の特徴である腹痛に関連した発熱を発症、血中アミラーゼ値の測定値、更にレ線所見を念頭に置いて診断を下すべきである。又その治療法はあくまで膵機能の休息にあらず、鎮痛、膵分泌抑制、血流量の復元に努め、抗生物質の投与を行うべきで、急性症状の持時期の手術は危険であるから、敢て手術を施行するならば急性症状の去った後に更に休むべきであると信じる。

慢性膵炎に就ては再発性結石性のものを特に挙げ、手術以外にその適切な治療法はなく、その術式として、Cholecystectomy, Transduodenal Sphincterotomy, Gastrectomy, Vagotomy, Biliaryshunt等を上げている。而して患者の病因、病理、条件等を良く熟者の上、これら術の何れかを決定すべきとしている。

(藤原恒和抄訳)