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Experimental Intracranial Transplantation of the Omentum majus in Dogs : A Tentative New Treatment for Hydrocephalus and Cerebral Ischemia

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The omentum majus plays a role in the absorption of fluid¹⁰⁾²⁴⁾²⁵⁾²⁸⁾ vascularization of ischemic tissues⁷⁾¹⁸⁾²¹⁾²²⁾²⁶⁾ production of antibodies⁶⁾²⁷⁾ and protection against inflammation by adhesion or barricade formation²¹⁾²³⁾. These functions can be fully realized if the omentum can be mobilized to the appropriate area by transposition or transplantation. We have been investigating these related factors since 1972. The purpose of the present paper is to report our heretofore obtained results. The following is considered herein:

1. Establishment of the technique
2. A tentative new treatment for hydrocephalus—Absorptive ability of the omentum—Kaoline hydrocephalus and omentum transplantation
3. A tentative new treatment for cerebral ischemia
4. Conclusion

Establishment of the technique

The technique involved in omental transposition was first reported by GOLDSMITH in 1967¹⁰⁾ who succeeded in applying this method of transposition to the brain surface of the dog in 1973⁹⁾. We have investigated various techniques of omental transposition and transplantation in attempts to determine the most suitable and effective approach. At last microsurgical method (microdissection and microanastomosis of about 1mm diameter vessels) enabled us intracranial free graft transplantation of the omentum majus.

Materials and Methods

Thirty mongrel dogs weighing 20—30 kg were separated into three groups. The first group of nine dogs was used, in part, to assess the possibility of making the pedicled

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omental transposition, after the method of GOLDSMITH et al, into the intracranial cavity. Such was most difficult as a lengthy distance is involved. The vascular anastomosis of the free omentum to the lingual artery and external jugular vein was also carried out, but this procedure also proved to be difficult.

The second group of 12 dogs underwent acute experiments with transplantation completed within 3 days. The third group of nine dogs was used for chronic experiments that averaged 3 weeks.

All dogs were anesthetized with allylisopropylbarbiturate, 0.5mg/kg, and when necessary, maintained with thiopental. The animals were intubated, connected to an automatic ventilator, and surgery was carried out with the dogs in a supine position with head turned to the left. The anesthetic agent was changed from intravenous administration of barbiturates to fluothane inhalation as various postoperative problems occurred. Through a medial xyphoumbilical incision, the omentum was evulsed from the abdominal cavity. The parent gastroepiploic artery and vein, which give off and receive multiple vessels to the stomach, were electrocoagulated and cut with the assistance of the operating microscope set at 4 or 6 x magnification. On the omental side, a 4 to 5 cm length of the parent artery and vein usually gave off four or five branches to the arcade complex (Fig. 1). The sheet of the omentum was fashioned to include this arcade complex, and the omental segment to be transplanted was thus isolated. The gastroepiploic artery and vein were occluded first distally and then proximally. A small Silastic tube, 0.6mm in outer diameter, was placed in the artery and the isolated omentum was perfused through this tube with Collins³⁾ or Ringer's solution at 4°C. The perfusion pressure did not exceed 120 cm H₂O. All traces of blood disappeared and clear effluent was seen coming from the vein. The remainder of the omentum majus was repositioned inside the abdominal cavity and the abdominal wall was closed.

The method of craniotomy and the preparation of the superficial temporal artery and vein used in this experiment have previously been described³⁰⁾³¹⁾. We removed a large portion of the medial muscle so that a generous pouch could be provided for the omental transplant. An osteoplastic craniotomy was performed, and the dura and arachnoid were opened.

The adventitia of the four vessels was stripped in the transplant area. The gastroepiploic artery and vein are 0.8 to 1.0 mm in outer diameter; the superficial temporal artery is 1.0 mm and its concomitant vein is 1.2 to 1.5 mm in outer diameter. Operating

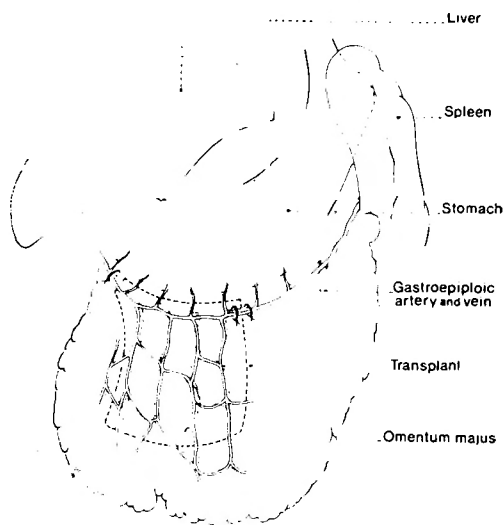


Fig. 1 Diagram showing preparation of a segment of the omentum for free transplant.

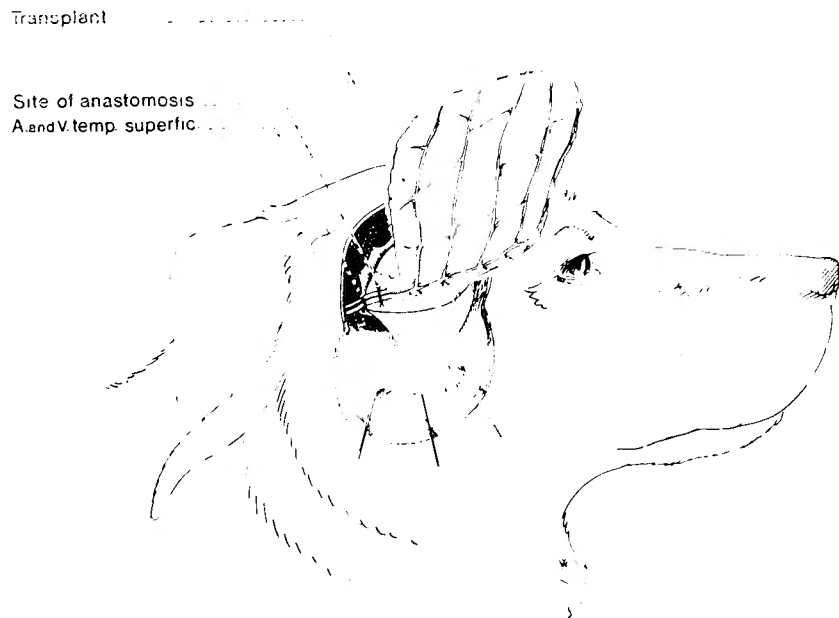


Fig. 2 Completed anastomosis between the transplant and superficial temporal artery and vein.

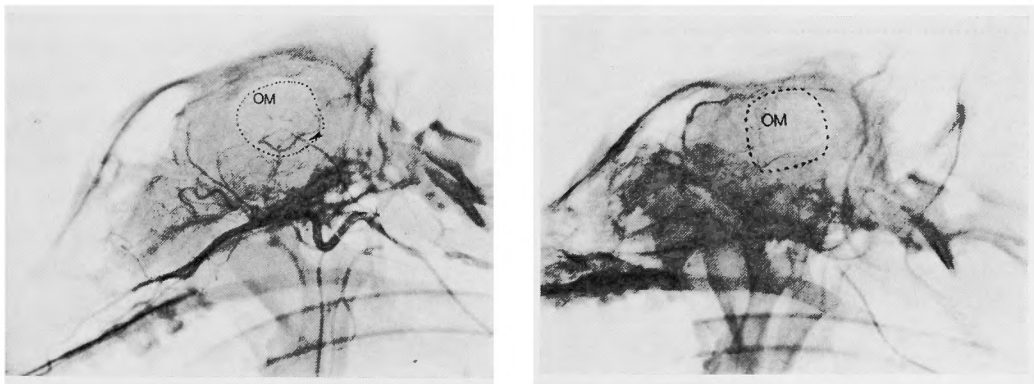


Fig. 3 Patent anastomosis. The arrow shows the site of anastomosis. Left: Three months after operation. Right : Four weeks after operation (late arterial phase). OM : dotted line reveals the transplanted omentum.

under 10 or 16 X magnification, we used either the end-to-end or end-to-side type of anastomosis with 10-0 supramid suture material. The veins were anastomosed first, while the piece of omentum was being perfused, and the arteries were anastomosed after removal of the perfusing catheter (Fig. 2). When the anastomosis was completed and the temporal vessels were opened, the omental arcades would flush red and the transplanted segment would pulsate. The omentum was then introduced directly against the cortex between the

dura and arachnoid and the skin closure completed.

Patency of the anastomosis was evaluated directly by microscopic inspection at autopsy or by angiography performed by injecting the contrast medium either into the external carotid artery or into the superficial temporal artery. A simultaneous patent arterial and venous anastomosis is required for the transplanted omentum to function (Fig. 3).

Results

There was a 30% patency rate for the anastomoses in both the acute experiment and chronic experiments; since these early experiments our patency rate has improved to 70%. The omentum without patent anastomosis underwent fatty degeneration and necrosis. A thin membrane consisting of connective tissue was always observed between the functioning transplant and neighboring tissue, even on the surface of the cortex in the chronic experiments (Fig. 4).

Partial removal of the omentum had no deleterious effect on the gastrointestinal tract of the nine dogs in the chronic experiments.

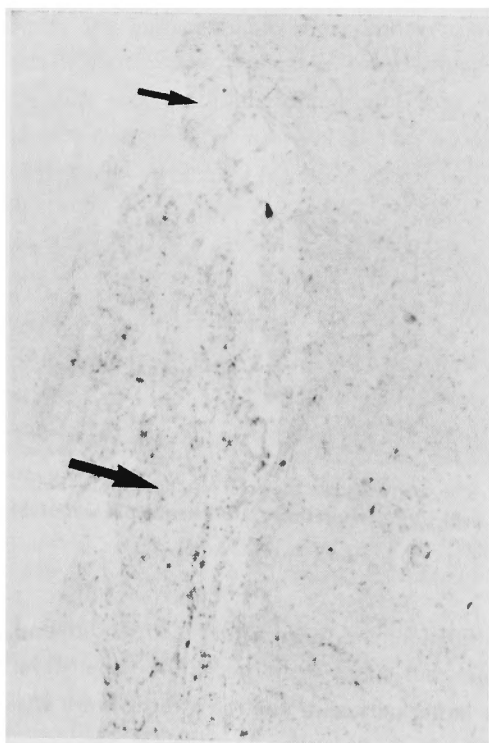


Fig. 4 Photomicrograph of membran formation covering the cortex (large arrow). Note residues of omentum at top (small arrow).

Discussion

Basic techniques of microvascular anastomosis have been reported elsewhere³⁰⁾³¹⁾³⁴⁾. The patency of an artery 0.8 to 1.0 mm in diameter following microanastomosis has been reported to be 70% to 80%³⁴⁾, and that of vein 18% (with no antithrombotic treatment) and 78% (topical application of heparin¹⁹⁾), a rate which we achieved with experience. However, in these cases, a simultaneous patent arterial and venous anastomosis was necessary. One percent heparin solution dripped at the suturing site during anastomosis is effective in maintaining the patency rate. Isotonic magnesium sulfate solution, which was reported to inhibit platelet aggregation, can also be used to improve the anastomosis patency rate of these small caliber vessels¹⁾.

Our work and that of McLEAN and BUNCKE¹⁷⁾, who succeeded in performing an autotransplantation of omentum in patient with a scalp defect, prove the technical feasibility of omental transplantation to the brain.

A tentative new treatment for hydrocephalus

The omentum and parietal peritoneum are considered to be main sites of fluid absorption. Currently there are two types of treatment for hydrocephalus; ventriculo-arterial shunt or ventriculo-peritoneal shunt, in which cerebrospinal fluid (CSF) is drained from the dilated ventricle into the atrium or the peritoneal cavity via a tube made of some synthetic material (silicone). Thus, the abdominal cavity is able to absorb fluid of more than 400–500 ml/day (volume of the daily produced CSF). The operation is simple and is easily facilitated, however, there are complications such as infections, occlusion of the shunt system, perforation of major organs etc¹⁴⁾. As these complications are often associated with a foreign invasion, an ideal approach would be to eliminate the use of any foreign material.

GOLDSMITH et al succeeded in 1967 in transposing omentum which could function as a new lymphatic drainage route¹⁰⁾; pedicled transposition of omentum was made into extremity of seven patients to treat lymphedema and subsequent clinical improvement was noted.

If omentum could be transplanted into the subarachnoid or ventricular systems, then hydrocephalus would be treatable without the occurrence of a foreign invasion.

—Absorptive Ability of the Omentum—

Materials and Methods

To investigate the absorbing ability of omentum majus the following procedure was performed. In three of six dogs in the chronic aforementioned experiments, 110 mg/ml of patent blue V was applied to the intact surface of the omentum, while in the other three, a 30% hydrogen peroxide solution was applied. Changes on the omentum were observed and photographed using a microscope. Additionally, in five dogs the transplanted omentum, which was connected to the systemic circulation only through its artery and vein, was

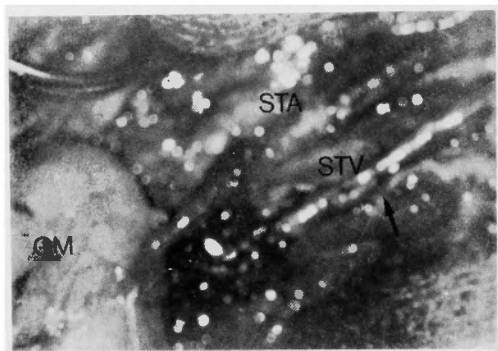


Fig. 5 Operative photograph (original in colour) showing staining of the superficial temporal vein (arrow) by Patent blue V which has been applied to the transplant.

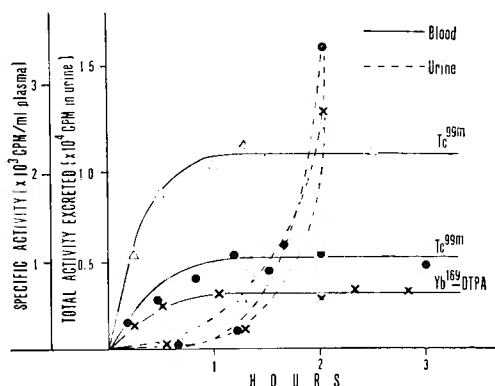


Fig. 6 Graph of radioactivity absorbed in the blood and urine. Cr^{51} -albumin and I^{131} -RIHSA failed to enter into the systemic circulation via the omentum.

immersed in 50cc of Ringer's solution maintained at body temperature. Radioactive isotopes were added to the solution as follows: 250 μCi of Yb^{169} -DTPA in one dog, 1 mCi of $\text{Tc}^{99\text{m}}$ -pertechnetate in two dogs, 100 μCi of Cr^{51} -albumin in one dog, and 200 μCi of I^{131} -RIHSA in one dog. Serial blood samples were taken from the femoral vein, and serial urine samples were obtained from an indwelling catheter. The radioactivity of the blood and urine was measured with a standard well-type scintillation counter.

Results

Upon application of patent blue V to the intact in situ omentum, rapid staining of the segmental vein and the parent gastroepiploic vein was observed; this phenomenon also was observed on the transplanted omentum. The dye was transported rapidly via the segmental vein into the systemic circulation (Fig. 5). Staining of lymphatic vessels also was observed; however, such occurred much more slowly, and it was difficult to follow the lymphatic vessels. Hydrogen peroxide also was absorbed from the intact surface of both the in situ and transplanted omentum. It reacted with catalase of the blood to make observable bubbles in the segmental and parent veins.

The time course of the activity of the blood and urine in the absorption study with isotope is shown in Fig. 6. Small particled substances such as Yb^{169} -DTPA or $\text{Tc}^{99\text{m}}$ -pertechnetate were absorbed from the intact surface of the omentum and caused an activity plateau in the blood within one hour. In contrast, substances of a larger molecular size such as Cr^{51} -albumin or I^{131} -RIHSA failed to enter the systemic circulation via the intact surface of the omentum.

—Kaoline Hydrocephalus and Transplantation of the Omentum—

Materials and Method

Hydrocephalus was produced after the method of DIXON and HELLER³; kaoline injection

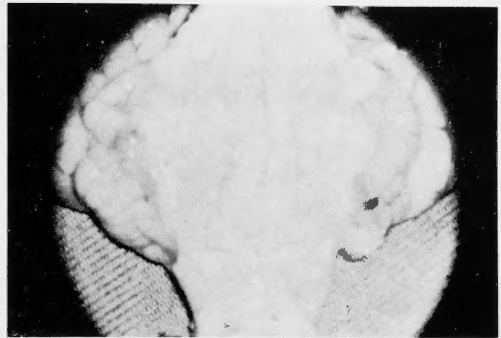
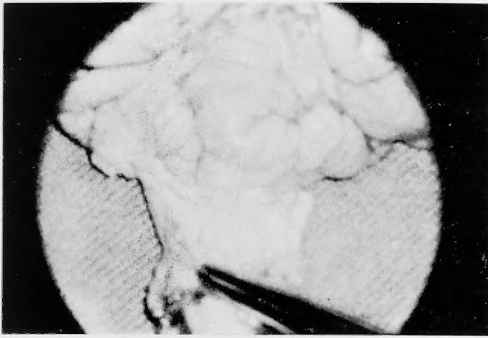


Fig. 7 Kaoline-hydrocephalus; kaoline injected intracisternally occludes completely outlets of CFS and basal cisterns.

(kaoline 1 gr. and CSF 1cc) into the cisterna magna. This method enables production of a hydrocephalus in 2-3 weeks in almost 100% (Fig. 7). This time (2-3 weeks) was critical because all dogs lost their appetite and became apathetic and emaciated. The time between 2 and 3 weeks after kaoline injection was considered suitable for the omentum transplantation. Ventriculography with Dimer-X was performed just before the operation through a Nelaton catheter or a Rickham's reservoir with the tip inserted into the lateral ventricle, to provide information concerning the degree of the preoperative hydrocephalus.

In 5 dogs, the omentum was transplanted into the cavity which had been produced with a temporal lobectomy on the right side with opening of the temporal horn. In 2 dogs, the omentum was transplanted into the lateral ventricle (Fig. 8). These procedures enable direct contact of the surface of the transplanted omentum with the CSF. When the dog was sacrificed by dosing with TI 61, 5ml, follow-up ventriculography was performed as already described and indigo-carmin was injected into the ventricle to determine leakage of the dye from the ventricular system.

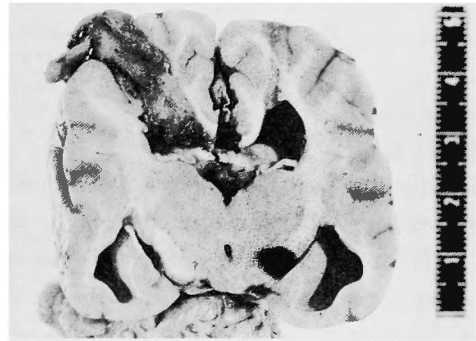


Fig. 8 Coronal section shows a intraventricular transplantation of the omentum.

Results

Four dogs died within 3 days after the operation and the three dogs survived more than one week. In two out of these three dogs (one; lobectomy, the other; ventriculostomy), ventriculography was performed within one week and the animals were sacrificed. Reduction of the ventricular size was evident but there was no leakage of the indigocarmine (Fig. 9). The remaining animal survived up to the time of sacrifice at one month. The preoperative hydrocephalus of moderate degree remained unchanged in size on the follow-up ventriculography. At autopsy indigocarmine study revealed no leakage of the dye, and membrane

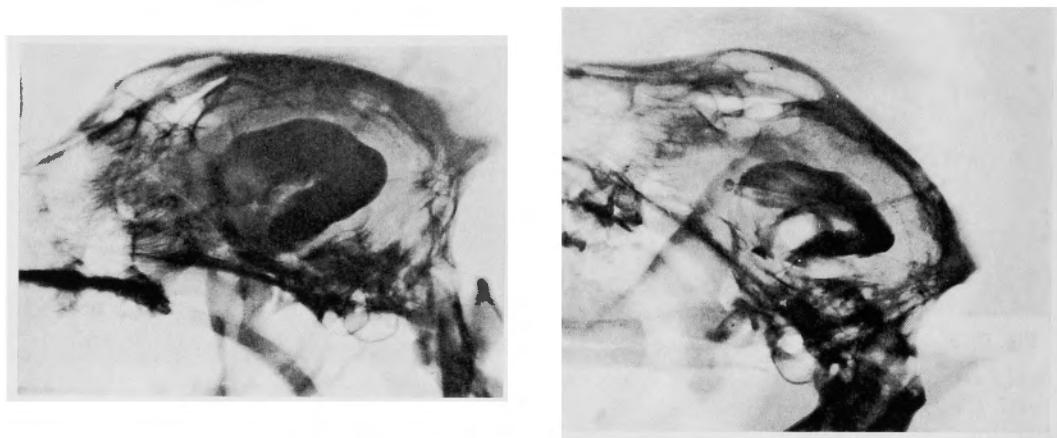


Fig. 9 Reduction of ventricular size one week after the transplantation.

a.) Preoperative hydrocephalus

b.) Reduction of the ventricular size in the same dog

formation between the lobectomy cavity and the omentum was observed. Such may have disturbed the absorptive function of the omentum.

Hydrocephalus was produced in several dogs, in which the skull was removed and kaoline was injected intracisternally in order to alleviate the intracranial hypertension associated with occlusive hydrocephalus. However the result was poor. The preoperative and postoperative state was not long enough in duration to evaluate the function of the transplanted omentum. All dogs died within three days.

Discussion

On the basis of dye injection experiments, it has been inferred that fluid in the abdominal cavity is absorbed mainly from the peritoneum that covers the diaphragma and from the omentum majus²⁴⁾. NYLANDER and TJERBERG investigated the lymphatic system of omentum majus in dogs and found that the flow of the patent blue V and thorium dioxide through the omental lymphatic seemed to be very slow²⁰⁾. They suggested that the absorptive capacity of the omentum by way of the lymphatic was rather insignificant. They questioned the theoretical basis for the transposition of the omentum majus in cases of lymphedema. However, our findings illustrate that substances consisting of small particles such as patent blue V, Yb¹⁶⁹-DTPA and TC^{99m}-pertechnetate are rapidly absorbed from the intact surface of the in situ as well as the transplanted omentum. These molecules pass directly into the systemic blood circulation, while large particles such as albumin are apparently not absorbed from the intact surface of transplanted omentum.

The results of experimental kaoline hydrocephalus and omental transplantation cannot validly be determined as the following factors remain unsolved; 1. a suitable method of producing hydrocephalus which enables further operative intervention without genera

emaciation of animals, 2. membrane formation at the surface of the omentum, which will block its function as an absorptive organ. LEVANDER et al successfully applied their transposition method to an actual clinical application treating hydrocephalus¹⁶⁾. Their theoretical background of the experiment was based on findings in the rat²⁸⁾. They found no membrane formation on the surface of the omentum and such added support for the clinical application.

A tentative new treatment for cerebral ischemia

Cerebrovascular occlusive disease is universally one of the major cause of death. To prevent a stroke from developing in the presence of TIA (transient ischemic attack) or to prevent recurrence of stroke, various revascularization procedures have been performed; conventional technique of vascular surgery or the microsurgical procedure³¹⁾³³⁾. However there are still cases, in which these procedures cannot be applied, for example inaccessible occlusive lesion, diffuse occlusive disease, high risk, acute stroke etc..

It has been well demonstrated that vascularization of an extremity, the heart, the brain, and the spinal cord can be achieved with omentum⁷⁾⁹⁾¹¹⁾¹²⁾²²⁾²⁶⁾. The purpose of the next section is to explore the possibility of treating cerebral ischemia using this method.

Materials and Methods

Mongrel dogs weighing 20-30kg were divided into two groups. Group A consisted of seven dogs, in which the omentum was transplanted to the right brain surface and the patency of the anastomosed vessels was confirmed by angiography. Two to three months later, the right middle cerebral artery (MCA) was clipped through a transzygomatic approach to induce experimental ischemia. Group B included seven dogs in which the right MCA was clipped without previous omental transplantation.

The method employed has been already described³²⁾.

The MCA was exposed at the skull base by a transzygomatic approach and was clipped at the level of the lateral lenticulostriate artery, medial to the anterior temporal artery, using a microsurgical method. The site of the omental transplantation was not disturbed (Fig. 10).

After clinical observation for an average of 48 hours following occlusion of the MCA, each of the dogs was given an intracarotid injection of 5ml of TI 61 followed by 95 ml of 10% formalin. In dogs in Group A, 25ml of India ink was injected into the superficial

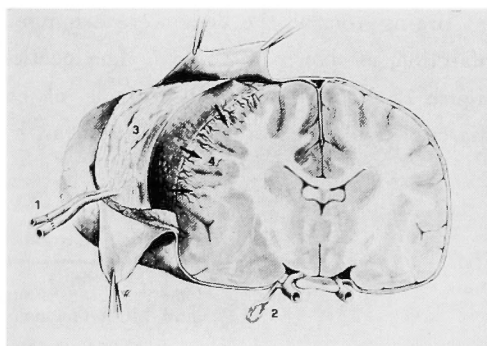


Fig. 10 Diagram illustrating the experimental model of the omentum transplantation and the occlusion of the middle cerebral artery.

1. Afferent and efferent vessels of the transplanted omentum.
2. Occlusion of the MCA.
3. Transplanted omentum.
4. Vascularization of the brain.

temporal artery (STA), which was in continuity with the transplanted omentum majus. The brain of each dog was carefully removed (together with the omentum if the animal was in Group A) and was fixed in 10 % formalin for three weeks. The brains were then cut into coronal slices and embedded in paraffin. Sections 10 μ thick were cut and stained with hematoxylin and Luxol fast cresyl violet.

The degree of infarction was classified according to the 4 grade scale of CROWELL and OLSSON⁴⁾:

Grade 0 = no infarction.

Grade 1 = infarction not exceeding 3 mm in diameter.

Grade 2 = medium sized infarction usually confined to the basal ganglia and internal capsule.

Grade 3 = a large infarction in the central territory of the MCA including the surface of the brain.

Results

Clinical observations

Epileptic seizures were not observed in any dog in Group A (before clipping of the MCA) during two to three months of observation following the transplantation

Three dogs (C-148, C-279, C-373) in Group A had no signs of neurological deficit after the MCA occlusion. The other four dogs in Group A revealed slight to moderate deficits such as a circling gait and a left homonymous hemianopsia. One dog (C-111) of Group B died of severe infarction. Only one dog (C-93) demonstrated a very slight deficit, the other five dogs in Group B had moderate to severe neurological deficits.

Size and location of infarction

Brains from all the dogs were examined and scored according to the 4-grade scale of infarction, as shown in Table 1. The locations of the infarctions are illustrated in Fig. 11. Figure 12 displays a typical example of each group, namely, C-148 of Group A with no infarction and C-83 of Group B with an extensive infarction. Infarction in the animal of

Table 1 Size of Infarction in Treated and Control Animals

Grade	Group A (Omental Transplantation and MCA Occlusion)	Group B (MCA Occlusion)
0	2 (C-373, C-148)	0
1	4 (C-448, C-576, C-545, C-279)	1 (C-93)
2	1 (C-129)	2 (C-171, C-141)
3	0	4 (C-95, C-111) C-83, C-63)
Total	7	7

Group A was usually small if it occurred and was located in the basal ganglia area with one exception (C-129) in which the lesion was near the cortex. On the contrary, the group B dogs usually displayed extensive infarction within the territory of the MCA. The difference in degree of infarction between the two groups was statistically significant ($p < 0.05$).

India ink studies

On injecting ink through the STA into the omentum, vascularization could be traced through the omentum and leptomeninges into

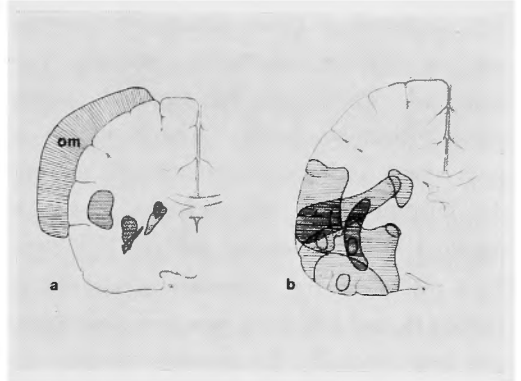


Fig. 11 Diagram showing the distribution and extent of the cerebral infarcts in *a*, animals of group A and *b*, animals of Group B.

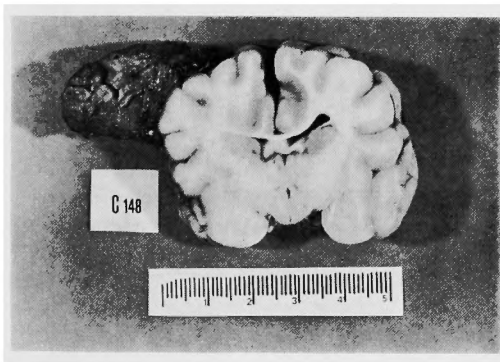


Fig. 12 A, Dog C-148. Coronal section of the brain showing no infarction (an example from Group A). B, Dog C-83. Similar section showing extensive infarction (an example from Group B).

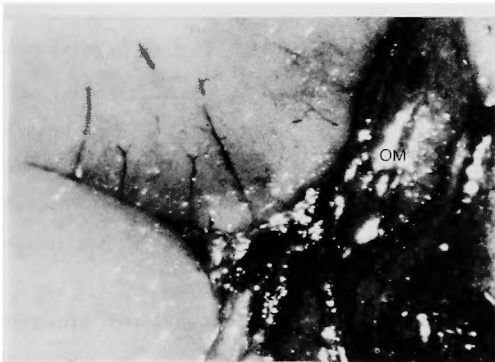
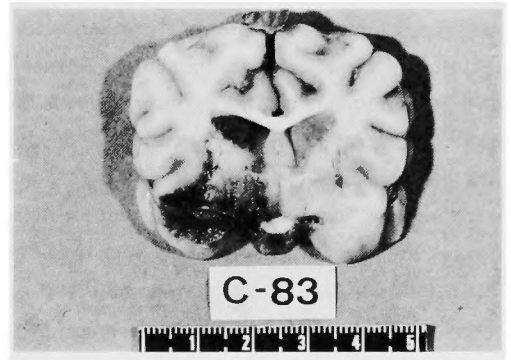


Fig. 13 Photograph showing penetration of india ink into the brain substance through the transplanted omentum (left).

the cerebral cortex (Fig. 13 and 14).

The India ink was observed not only within the ipsilateral hemisphere but also on the contralateral side (after passage through the circle of Willis). It was apparent that vascularization is favored when the arachnoid is opened extensively and such promoted direct contact of the omentum with the pia mater and pial vessels.

Discussion

The phenomenon of tissue vascularization by the omentum is now well known^{7,18)}

²¹⁾²²⁾. Ischemia of tissue is reported to stimulate the adjacent omentum to produce capillary buds which will be opposed to the tissue within six hours. The formation of such a connecting capillary network between the omentum and the ischemic tissue is reported to be completed within 24 hours. This ability of the omentum to vascularize various tissues has been reported experimentally and clinically, for example, to treat thromboangiitis obliterans of the extremities⁷⁾ and to treat ischemic cardiac disease in combination with or without internal mammary artery implantation²²⁾²⁶⁾. Vascularization of the brain and of the spinal cord by mobilized omentum using a transposition technique has also been reported⁹⁾¹¹⁾. Muscle and subcutaneous tissue apparently has the ability to vascularize neural tissue, and such has been applied in clinical use with some encouraging results¹³⁾¹⁵⁾, but neither of these tissues seems to function as well as does the omentum. GOLDSMITH et al reported the effectiveness of the method of transposition for a cerebral ischemia¹²⁾.

Our efforts were directed to the following points : 1. Does vascularization of the brain take place if transplanted omentum is used? 2. Is such vascularization effective in treating cerebral ischemic disease? 3. Is intractable epilepsy a complication of this procedure? It is now clear from the India ink study that brain vascularization by transplanted omentum actually does take place. It should be noted that transplantation was performed two to three months prior to MCA occlusion, in order to obtain sufficient stable vascularization to reinforce the leptomeningeal anastomoses. Our results indicate that this method of vascularization can prevent, or at least minimize, cerebral infarction. There were no infarcts in the cortex under the transplanted omentum and only small distant infarcts in the basal ganglia. The development of infarction probably depends upon the degree of vascularization which varies according to other factors such as hematoma formation, infection, the quality of the transplantation, etc.

Postoperative epilepsy was not a problem. No dog in Group A developed epilepsy during the postoperative interval of two to three months. HENSCHEN found that epileptic seizures decreased in frequency after muscle transposition to the surface of the brain performed to treat ischemia due to bilateral carotid stenosis¹³⁾. Furthermore, we know that

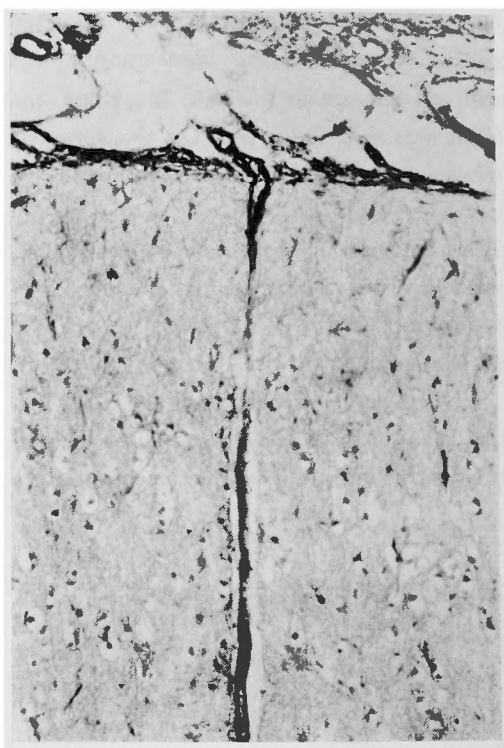


Fig. 14 Photomicrogram (100 x) showing penetration of india ink from the omental side (upper) through the leptomeninges and into the brain (lower).

there is no serious problem of epilepsy in patients, in whom part of the postoperative skull is removed surgically and the dura is not completely closed to provide decompression.

Thus omental transplantation can be considered as a potential treatment for cerebral ischemia, to substitute for, or to complement STA-cortical MCA anastomosis³¹⁾³³⁾ and conventional vascular procedures. It may be especially suitable for the treatment of Moya-Moya disease, multiple diffuse thrombosis of intracranial arteries, or localized deep ischemic lesions. The effectiveness of this type of operation in treating acute cerebral ischemia remains to be investigated. The slow revascularization accomplished by reinforcing leptomeningeal anastomoses may avoid the hemorrhagic infarction sometimes associated with acute revascularization²⁹⁾.

The omentum has also been used also to fill large skin defects¹⁷⁾, to protect carotid artery against rupture in patients requiring radiotherapy after radical neck operations⁸⁾, and to fill out dead space, for example after extirpation of rectosigmoid cancer²³⁾. In experimental therapy for brain tumors a transplanted omentum would provide contact with the tumor and such may be quite beneficial as the omentum is considered to be a site of antibody formation⁶⁾²⁷⁾. Furthermore, high concentrations of anticancer agents could be given through the transplanted omentum to be utilized selectively for the tumor treatment.

Conclusion

The technical feasibility of intracranial autogenous transplantation of the omentum majus using microsurgical techniques has been clarified. Clinical application of this method for hydrocephalus and cerebral ischemia has been explored, and such reveals a promising future. Other possible clinical applications have also been discussed.

TI 61 manufactured by F. Hoffmann-La Roche & Co. AG. Basel Switzerland. Dimer-X manufactured by Laboratoires André Guérbet F 93-Aulnay-sous-Bois France.

The entire experiment was performed in the microsurgical laboratory of the Neurochirurgische Universitätsklinik Kantonsspital Zürich, Switzerland. The work on the cerebral ischemia was submitted to the Fifth European Congress of Neurosurgery, Oxford England, September 1975.

The greater part of this report has been already published in *J. Neurosurg* 40 213-217, 1974 and *Neurosurg.* 1 : 256-259, 1977.

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和文抄録

実験的頭蓋内自家大網移植：水頭症及び 脳虚血性疾患の新しい外科的治療の試み

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雑種犬を用いマイクロサージャリーにより、頭蓋内に自家大網を移植する事が可能である事を示した。併せて、移植した大網の機能を利用して、水頭症及び脳

虚血症の新しい外科的治療となりうるか否かを検討した。その結果、これらの治療として臨床的に充分用いられ得る可能性のある事が判明した。