# EXPERIMENTAL STUDIES ON OESOPHAGEAL REPLACEMENT

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#### FOREWORD

Ι

In the summer of 1963 the author was assigned to the Laboratories of Experimental Surgery of The Montreal Children's Hospital, with the purpose of spending two years in investigative work as a part of post-graduate training program in surgery. The results of the investigation recorded in this thesis have been obtained during the sessions 1963 - 1965.

The subject of oesophageal replacement was of great interest to me, offering remarkable potential possibilities to elaborate new approaches to the problem of correction of congenital oesophageal anomalies.

Therefore I greeted with pleasure the suggestion of Dr. David R. Murphy, Surgeon-in-Chief and Director of the Department of Experimental Surgery at The Montreal Children's Hospital, that I select this problem as the subject of my work. I wish to express my gratitude to him for giving me the opportunity to spend these two years in his laboratory.

Dr. Herbert F. Owen, who has been the project director of this research program, was most helpful in the many difficulties and problems encountered in the course of the work. His energy and friendship stimulated my efforts to bring the work to a successful conclusion. To him go my most sincere thanks.

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### INTRODUCTION

The earliest description of oesophageal atresia as a pathological entity was given by William Durston (1) in 1670. The first typical case of oesophageal atresia with tracheo-oesophageal fistula was recognized by Thomas Gibson (2) in 1697. Since then an increasing number of reports appeared. In 1861 Hirschsprung (3) presented 10 cases of oesophageal atresia, in 1880 Mackenzie (4) collected 37 cases, in 1919 Plass (5) collected cases reported to that date numbering 136. Rosenthal (6) in 1931 reviewed the world literature pertaining to the subject and collected 255 cases. In the last 25 years the malformation has been recognized with increasing frequency and numerous large series have appeared in the literature. Attention has been centered not only on the correct diagnosis but also on the surgical treatment of this anomaly. Varied concepts of surgical approach and a large body of experimental work have found their way into the medical journals.

### ETIOLOGY

The etiology of the oesophageal atresia is still uncertain. A number of etiological factors have been implicated - among them epidemiologic and teratologic factors, systemic diseases of the mother, including vitamin deficiencies, as well as virus infections, diseases of uterus and placenta, and mechanical trauma. In spite of great effort spent on the investigation of the genetic, embryologic, and anatomical aspects of this anomaly, as well as extensive and detailed study of familial and environmental factors, the etiology of this condition remains unknown.

#### EMBRYOLOGY OF OESOPHAGEAL ATRESIA

The embryology of this anomaly is not completely understood. It is generally agreed that the disturbance leading to oesophageal atresia must take place between the third and the sixth week of gestation, in embryos between 3.5 mm and 8 mm. Presence of vascular anomalies, such as an anomalous right subclavian artery, right aortic arch, or vascular ring has been observed to exist in association with oesophageal atresia, tempting one to search for a vascular etiology. Haight (7) finds this association present in 10% of his 200 cases. Similar observations have been reported by Keith and Spicer (8), Saunders and Wright (9), Fluss and Poppen (10), Langman (11).

#### ANATOMY

The oesophagus is a muscular canal, about 25 cm. long in the adult, extending from the pharynx to the stomach. It begins in the neck at the lower border of the cricoid, cartilage, opposite the 6th cervical vertebra, where it is continuous with the lower end of the pharynx. It descends along the front of the vertebral column, through the superior and posterior parts of the mediastinum, pierces the diaphragm opposite the 10th thoracic vertebra and ends at the cardiac orifice of the stomach at the level of the 11th thoracic vertebra. The anterior wall of the cervical part of the oesophagus is attached to the posterior membranous wall of the trachea by loose connective tissue. Its posterior wall lies on the vertebral column. Laterally on each side of the oesophagus lie the corresponding carotid artery and the posterior part of the lateral lobe of the thyroid gland. The thoracic part of the oesophagus continuing its course between the vertebral column and the trachea

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passes behind and to the right of the aortic arch and descends in the posterior mediastinum.

The thoracic oesophagus is in relation anteriorly with the trachea, the right pulmonary artery, the left main bronchus, and the pericardium; behind it rests upon the vertebral column, the longus coli muscles, the right posterior intercostal artery, the thoracic duct, the azygous vein, and the aorta. On the left side it is in relation with the aortic arch, the left subclavian artery, the thoracic duct, and the left pleura, while on the right side the oesophagus is related to the right pleura, the azygous vein, and the thoracic duct. Below the root of the lung the vagus nerves descend in close contact with the oesophagus; the right nerve chiefly behind, and the left chiefly in front of it. The two nerves unite to form a plexus around the tube. The abdominal part of the oesophagus having passed through the right crus of the diaphragm lies in the oesophageal groove of the posterior surface of the left hepatic lobe, and ends in the stomach at the level of 11th thoracic vertebra.

The oesophagus, in common with the digestive tube in general, has four coats.

1) <u>The mucous membrane</u>, consists of a layer of stratified, squamous epithelium, lying on the loose connective tissue of the lamina propria, papillae from which project into the epithelium. In the deeper parts of the lamina propria, smooth muscle bundles of the muscularis mucosa are to be found. At the commencement of the oesophagus the muscularis mucosae is absent, lower down it forms

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a considerable stratum. At the gastro-oesophageal junction the stratified squamous epithelium is abruptly succeeded by the simple columnar epithelium of the stomach.

 <u>The submucosa</u>, loosely connects the mucosa and muscular coats and contains larger blood vessels, nerves, and mucous glands.

3) The muscularis, is composed of two layers: an external layer of longitudinal, and an internal layer of circular fibres; the longitudinal fibres form a complete investment for nearly the the whole of the oesophagus and their thickness exceeds that of the circular muscle coat; the circular fibres are continuous superiorly, on the posterior surface with the superior constrictor; anteriorly the uppermost are inserted into the lateral margins of the tendon of the two longitudinal fasciculi; interiorly the circular muscle fibres are continuous with the oblique fibres of the stomach. In the upper quarter both layers consist of striped muscle, in the second quarter bundles of smooth muscle appear and these gradually replace the striped muscle more caudally.

 <u>The external</u>, consists of a layer of areolar tissue containing elastic fibres.

The oesophageal glands are small. In the extreme upper and lower parts of the oesophagus the glands resemble those in the cardiac part of the stomach (cardiac glands), and are situated between the muscularis mucosae and the lumen of the gut. The arteries supplying the oesophagus are derived from the inferior thyroid branch of the thyro-cervical trunk, from the descending thoracic aorta, from the bronchial arteries, from the left gastric branch of the coeliac artery, and from the left inferior phrenic branch of the abdominal aorta. The veins from the cervical part of the oesophagus drain into the inferior thyroid veins. The abdominal part drains into the azygous and left gastric vein.

The nerves are derived from the vagus and sympathetic. The cervical part of the oesophagus receives branches from the recurrent laryngeal nerves and from the cervical sympathetic trunks. The thoracic part has branches from the vagal trunks and oesophageal plexus, and from the sympathetic trunks and greater splanchnic nerves. The abdominal part is supplied by the vagal trunks, the thoracic sympathetic trunks, the greater splanchnic nerves, and the plexus around the left gastric and inferior phrenic arteries. The nerve form a plexus containing groups of ganglion cells, between the two layers of the muscular coat, and a second plexus in the submucous tissue.

#### PHYSIOLOGY

The act of swallowing has been divided into three stages. The first stage takes place in the oral cavity, where the food already prepared by mastication collects at the base of the tongue. The second stage the food enters the pharynx as a result of a complex process of contraction of the glosso-palato-pharyngeal muscles and moved down into the upper part of the oesophagus. The third stage involves the passage of the food down the oesophagus. The bolus is squeezed by a peristaltic wave, which travelling along the oesophagus carries the material before

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it into the stomach. The rate of progress of the bolus along the human oesophagus is not the same at all levels. The upper (cervical) third of the oesophagus, which consists of striated muscle, propells the food in one second. The middle third consists of striated and smooth muscle, moves the bolus in 12 to 2 seconds. The movement of food through the lower part of the oesophagus takes approximately 3 seconds. Liquids are squirted forcibly from the mouth to the pharynx and down into the oesophagus and reach the lower end of the gullet in less than 1 second. The carriage of food through the upper two thirds of the oesophagus is dependent on extrinsic nerves and not initiated, or controlled by nerve plexuses in the wall of the oesophagus. Contraction of the lower oesophagus, like the intestines, is regulated by the intrinsic nervous mechanism. But also like the intestines, can be influenced by the central reflex. This reflex can not be initiated from the oesophagus itself. Reverse peristalsis in the oesophagus is rather uncommon and usually appears in presence of some obstruction. Introduction of acid, cold water, gastric contents into the lower third of the oesophagus may cause the spasm of the oesophageal wall and reverse peristalsis above. The so called lower oesophageal sphincter, or cardia, is supplied with fibres from the vagus and the sympathetic. The chief influence exerted by the vagal fibres is inhibitory, while the predominant function of the sympathetic is probably excitatory.

#### INCIDENCE

There are considerable variations in the incidence of atresia of oesophagus given by different authors. An average accepted figure is one per 3-4 thousand live births.

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### TYPES OF ANOMALY

The classification of oesophageal atresia suggested originally by Gibson (12) in 1703 has remained essentially unchanged up to the present time.

In 1929 Vogt (13), an American radiologist, divided cases of oesophageal atresia into 3 main categories: (Fig. 1)

1. Complete absence of oesophagus.

2. Atresia without tracheo-oesophageal fistula.

- 3. Atresia associated with tracheo-oesophageal fistula; this type has been further subdivided in to three variations:
  - a) Upper segment entering trachea, lower segment blind.
  - b) Lower segment entering trachea, upper segment blind.
  - c) Both segments entering trachea.

More popular on this continent is the classification suggested by Gross (14) in 1953. He divided cases of oesophageal atresia into 6 groups:

- 1. Complete or partial absence of oesophagus without fistula.
- Atresia with fistula, in which the upper segment enters the trachea.
- 3. Atresia with fistula, in which the lower segment enters the trachea.

4. Atresia with both segments entering the trachea.

- 5. Stenosis of the oesophagus with tracheo-oesophageal fistula.
- Stenosis of the oesophagus without tracheo-oesophageal fistula.

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Fig. 1. The most commonly used classifications of ocsophageal atresia.

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The most commonly occuring variety is oesophageal atresia with tracheo-oesophageal fistula, in which the lower segment enters the trachea and the upper segment remains blind. Haight (7) observed this type in 86.5% of the total of 200 cases. Other statistics indicate a slightly higher percentage, up to 93% . In this common variety, the distance between the oesophageal ends varies from few mm. to 3 cm. The fistula enters the trachea usually at the level of the carina, or slightly above it. The upper blind segment varies in length and usually extends to the level of the 3rd dorsal vertebra and only occasionally below it. In very rare instances it ends in the lower part of the neck and does not enter the thoracic cavity. The diagnosis of this type of anomaly is readily established radiologically by the demonstration of a blind proximal oesophageal pouch together with the presence of gas in the stomach. Those cases showing no air in the stomach belong to the type of oesophageal atresia without tracheo-oesophageal fistula. In this latter group, there is a longer gap between oesophageal segments, usually greater than 3 cms., the lower segment being represented by a short pouch which does not extend above the diaphragm more than 1 or 2 cms.

The other listed types of oesophageal anomalies are rare enough to be of little clinical significance.

#### HISTORICAL REVIEW

Pioneering efforts of many surgeons working in this field during the last 25 years have resulted in the development of a satisfactory method of correcting most oesophageal atresia i.e. those in which the gap between the oesophageal segment in not

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excessive. Although there were much earlier sporadic attempts to correct the anomalies, all of them were failures.

In 1938 Robert Shaw (15) was probably the first to perform a ligation of the fistula and a simultaneous direct anastomosis between the two ends of oesophagus in a way that is still in use. Lanman (16) in 1940 published his observations on 32 cases from which the earliest were operated upon in 1936 and 1937. The first successfull one stage direct anastomosis was performed in 1940 by Haight (17) and this method has certainly solved the problem of cases in which the distance between the two ends of oesophagus does not exceed 2<sup>1</sup>/<sub>2</sub> to 3 cms.

The management of cases in which the oesophageal deficiency is so great as to render impossible a direct anastomosis is, however, still subject to debate. As far back as in 1891 Hacher (18) successfully performed on dogs and humans a procedure identical to the one presently known as Wookey procedure. In 1894 Bircher (19) used a skin channel connecting the cervical oesophagus with the stomach and described this method in 1907. His method with different modifications persists to the present time. One of the modifications was that of Esser (20), who in 1917 described the use of Tiersch grafts placed on a stent in a subcutaneous tunnel. The use of intrathoracic skin tubes was accomplished by Bricker (21) and associates in 1949. Lilienthal (22) in 1925 formed a skin flap from the back in cases of cancer of the cervical oesophagus. Wookey (23), a Canadian surgeon, in 1942 used in similar circumstances a skin tube taken from the anterior chest wall. In the first successful case described by Ladd (24) in 1944 a skin lined tube was placed between the

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oesophagus and the stomach. In 1950 Owen and Negus (25) have performed the first successful reconstruction of the pharynx and cervical oesophagus as a one stage procedure using a free, split thickness skin graft held in place by a mold. Bruck (26), Salzer (27), Kunzen (28), Efros (29), Burford (30), and others have described several methods of reconstruction of the cervical oesophagus using full thickness pedicle skin grafts in multi stage procedures. Skolimof (31), Jusbasic (32), Szabo (33), Rubenstein (34) and others experimented with split thickness skin tubes as replacement of the thoracic oesophagus. They all concluded that an autogenous skin graft "takes" and bridges created defects of the oesophagus.

Antethoracic jejunal transplantation was suggested and described by Wullstein (35) in 1904. This method was used in France by Roux (36) and in Russia by Herzen (37) in 1907. There have been numerous modifications of this method by many surgeons since that time, either with or without a short skin tube connecting the cervical oesophagus with the proximal end of the transplant. The first successful antethoracic transplantation of jejunum was performed and described in 1947 by Swenson (38) and Leven and Varco (39).

Intrathoracic jejunal transplantation has been a more recent accomplishment as reported by Rienhoff (40) and later by Robertson (41), Harrison (42), and others.

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The stomach has been transplanted extrathoracically by Beck and Karrell (43) in 1905. In 1912 Jianu (44) proposed and described a method which makes use of a tube fashioned from the greater curvature of the stomach. This tube was used to replace the lower part of oesophagus. He also transplanted subcutaneously the entire stomach. A similar method was described by Fink (45) in 1913 and by Kirschner (46) in 1920. The intrathoracic transplantation of the stomach was described for the first time by Adams and Phemister (47) in 1938. Since then increasingly higher transplantations of the stomach have been accomplished so that Gralock and Sweet (48) in 1940 and 1946, respectively, were able to perform an anastomosis between the oesophagus and the stomach high in the neck. The method of elevation of the stomach antethoracically as well as intrathoracically became popular and was used by many surgeons not only in oesophageal atresia, but also in other lesion of the oesophagus, especially in malignant neoplasms.

In 1913 Torek (50) reported first successful case of resection of the thoracic oesophagus and replacement by transverse colon. In 1953 Fry (51) investigated the use of a segment of colon to replace the lower oesophagus. Similar methods were described in the same year by Buttersby (52) and Kergin (53). In 1954 very encouraging resultswere reported by Mahoney and Sherman (54) and Dale and Sherman (55). Since that time more and more reports appeared relating to increasing number of cases successfully treated both with ante- and intrathoracically placed colon. Some of the authors suggested the use of the transverse colon, others

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again preferred the ascending colon; others again propagated the use of descending colon. A detailed and exhaustive report was submitted by Waterstone (56) in 1964.

#### DISCUSSION OF METHODS

From all presently existing methods of oesophageal replacement the colon transplants are considered to be the most valuable. Skin transplants were finally abandoned because of their technical difficulties and necessity of multi stage procedures, often complicated by ulceration due to gastric reflux, or scar formation and stricture. These complications occurred most frequently with split thickness skin grafts. Jejunal transplants have been extensively utilized, but their blood supply is well recognized to be precarious, and this is especially so in infants. Elevation of the stomach into the chest was also considered to be imperfect. The presence of the stomach in the small thoracic cavity of an infant has adverse affects on the respiratory function and interferes with the venous return to the heart. Furthermore it has the disadvantages of a diaphragmatic hernia and the gastric reflux, which commonly occurrs, is liable to cause oesophageal ulceration. All these procedures require an absolutely perfect surgical technique, carry a great risk and all of them involve "borrowing" certain abdominal organs thereby disturbing the anatomical and physiological balance of the thorax and abdomen. Furthermore, the safety with which such major surgical procedures can be done does not reach a reasonable level until the child is about two years of age, or older.

### FACTORS AFFECTING SUCCESSFUL TREATMENT OF OESOPHAGEAL ATRESIA

<u>Prematurity</u>. A high percentage of newborns affected with oesophageal atresia are premature infants (25 - 40%). It is generally agreed that prematurity or low birth weight (less than 2500 Gm) significantly influence the results of the treatment of this anomaly. The mortality in premature infants with oesophageal atresia is markedly higher than in full term babies. It is also interesting that prematurity occurrs more often in the second group of cases, i.e. in infants with oesophageal atresia without tracheo-oesophageal fistula.

Associated anomalies. The number of co-existing congenital malformations is unusually high. Most statistics report the incidence at approximately 40% of cases, at least half of these being of life threatening significance. The most common are anomalies of cardiovascular system, alimentary tract, and of neurological and genitourinary origin.

<u>Pulmonary complications</u>. Another factor of great importance, influencing the results is the frequently (in almost 80% of cases) occurring extensive pneumonia, which appears in the first hours of life. It is due to aspiration of saliva or food and in some cases due to reflux of gastric secretions through the patent fistula into the tracheo-bronchial tree. This factor of course increases the surgical hazard and in many instances causes the death of the infant.

<u>Time of diagnosis</u>. Unfortunately there still exist a significant number of newborns with oesophageal atresia, who are not immediately referred to the surgical unit. It is obvious that surgery should be performed as soon as possible after birth.

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Anatomical and physiological factors. Location of the oesophagus deep in the chest close to the heart, great vessels, lungs and other important anatomical structures, creates serious technical difficulties. The usual transpleural approach, which facilitates surgical manipulation, creates the additional danger of pulmonary complications and, in case of insufficiency of the anastomosis and development of fistula, of empyema. In an attempt to avoid these complications, some surgeons are now advocating an extrapleural approach, but experience with this is still scanty. It is also commonly known that the blood supply of the oesophagus is unusually meagre, probably owing to the fact that it does not function in the absorption of food stuffs. The precarious state of circulation is further aggravated by the fact that during the operative procedure the necessarily extensive mobilization of both oesophageal segments impairs the already deficient blood supply, a fact that certainly interferes with the healing process. In addition the oesophagus is subject to constant movement, with both respiration and with swallowing resulting in stress at the suture line. This is particularly true if oesophageal length is at a premium with tension at the suture line. Furthermore the oesophagus lacks a serosa, which plays such an essential part in intestinal anastomoses sealing the suture line with exuded fibrin. The above circumstances create unfavourable conditions for oesophageal anastomosis increasing the frequency of dehiscence of sutures with resulting mediastinitis and/or empyema.

#### REVIEW OF EXPERIMENTAL DATA

Because of the shortcomings of the existing surgical procedures numerous scientists searched for years for an artificial prosthesis to replace the oesophageal defect. Innumerable different materials of organic and inorganic nature were tried (Fig.2). Berman (57) was the first to employ a polyethylene tube. Baronofsky and Hilgar (58) reported on the use of fascia lata graft applied over a tantalum mesh. Pickrell, Connor, and Campbell (59) have used split thickness free dermal grafts fashioned into a tube. Edgarton (60) has added to this procedure a supportive layer of tantalum mesh; Klopp, Alford, and Prespont (61) a polyethylene mold. Buttersby and King (62) reported some success with the use of polyethylene film over a dacron mesh. Braunwald and Hufnagel (63) used stainless steel mesh over tygon tubing. Pressman (64) has used a homograft of lyophilized aorta, the while Kothe (65) suggested employment of lyophilized mucosa over a teflon tube. Rubenstein (66) used oesophageal transplants of preserved and fresh homografts, as well as crimped nylon and tygon tubes which were implanted between the two layers of pleura for 6-8 weeks prior to the procedure. He reported that during this period a thin fibrous tissue tube has formed around the plastic tube. This connective tissue tube was then used to bridge the oesophageal defect.

The results of all these attempts were complicated by either leakage of the suture line and infection, or scar formation and resulting stenosis. The most promising results seem to be obtained with crimped teflon prosthesis, as used in vascular surgery. Studies in experimental application of this material in oesophageal replacement surgery were initiated by H. Owen and Ascoli (67) in 1960 at McGill University.

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Fig. 2. Different plastic materials used as oesophageal prosthesis: 1 - polyethylene

2 - tygon

3,-4 - crimped teflon vascular graft

5 - dacron

### REPORTS OF EXPERIMENTS WITH CRIMPED TEFLON GRAFT

Continuing the work initiated by Dr. Owen et al. we have used porous, crimped teflon tubes to replace a resected oesophageal segment in puppy dogs (Fig. 3). Our experiments relate to 37 puppy dogs divided into 3 groups. In the 20 dogs comprising group 1, we removed about 2 cm. of the oesophagus and replaced it by approximately double the length of teflon graft.

Operative Procedure. In order to obtain sufficiently deep and long lasting anaesthesia intravenous Sodium Nembutal was originally Soon we realized that puppies have poor tolerance to Nembutal. used. We substituted it with 5% intravenous Chloralose. An infusion of 5% Dextrose in water with Penicillin was routinely used during the operation. An endotracheal tube was introduced and connected to a Bird respirator. After a number of unsuccessful attempts of approaching the oesophagus extrapleurally, which is extremely difficult in puppies, we chose a transpleural approach. Through a thoracotomy at the level of the 5th intercostal space we opened the right pleural cavity. The lung was gently deflected with a wet sponge. The azygous vein was isolated and divided between two ligatures. The mediastinal pleura was then incised, the oesophagus separated and exposed. A 2 cm. long segment of oesophagus was then excised. A crimped teflon tube, approximately 4 cm. long and 0.6 or 0.8 cm. in diameter, was connected to both oesophageal ends by means of two layers of silk sutures. The inner layer between the teflon graft and the mucosa was continuous, while the outer layer formed by interrupted silk sutures connected the teflon with the muscular coat, which was brought over the teflon edges to a distance of 2 mm. The mediastinal pleura was tightly closed over



B - resection of oesophageal segment;

C - placement of the first layer of sutures;

D - placement of the second layer of sutures.

the anastomosed teflon tube. The lungs were re-expanded and the thorax closed in a typical way. No drainage was left in place.

Postoperative Treatment. All puppies received 500,000 U. of Penicillin daily during the first 5-7 post-operative days. Three different schedules of feeding have been tried. The first group received Dextrose in saline intravenously and/or by subcutaneous infusion for one week when the oral feeding was instituted. In the second group the feeding was carried out through a gastrostomy. In the third group water was given by mouth from the first post-operative day on. We have not observed any significant influence of different feeding managements on the healing process of the anastomosis.

Pleural punctures in the post-operative period were carried out routinely. Some of the puppies required high oxygen atmosphere in the immediate post-operative period. In 2 dogs a continuous suction drainage of the pleural cavity was attempted. In 3 puppies dilatation procedures of the oesophageal stenosis were performed every 2nd day beginning upon appearance of clinical signs of stenosis.

Post-mortem examination was performed on all dogs.

### REVIEW OF CASES - GROUP 1.

1. Dog No. 545 - Age: 5 weeks - Weight: 1375 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; left transpleural approach; resection of 2 cm. of oesophagus; teflon graft 4 cm. long 0.6 cm. in diameter; 500,000 U. I.M. Penicillin daily; water by mouth from the lst post-operative day.

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Vomiting appeared on the 3rd post-operative day. Therefore intravenous infusion was started of 5% Dextrose/Saline. On the 4th day the dog died. Autopsy showed leakage of both suture lines and empyema.

2. Dog No. 546 - Age: 5 weeks - Weight: 1380 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 1.5 cm. of oesophagus ; teflon graft 3 cm. and 0.6 cm. in diameter; 500,000 U. I.M. Penicillin daily for 7 days; water to drink from the 1st postoperative day; on 12th post-operative day began to vomit. Signs of occlusion. X-ray examination on the 13th day showed significant degree of stenosis. Died on the 14th day. Autopsy showed acute mediastinitis and pneumonia, stenosis of the site of anastomosis, leakage of the suture line.

3. Dog No. 548 - Age: 4 weeks - Weight: 1380 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 1.5 cm. of oesophagus; teflon graft 3 cm. long 0.6 cm. in diameter; 500,000 U. I.M. Penicillin daily; water by mouth from the 1st post-operative day on.

Vomiting appeared on the 2nd post-operative day. Died on the 3rd post-operative day. Autopsy examination shows leakage of sutures, empyema. 4. Dog No. 567 - Age: 4 weeks - Weight: 1600 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus ; teflon graft 4 cm. long 0.6 cm. in diameter; 500,000 U. I.M. Penicillin daily. No oral feeding. Subcutaneous and I.V. infusions. Died on 2nd post-operative day. Autopsy shows leakage of sutures and empyema.

5. Dog No. 503 - Age: 5 weeks - Weight: 1220 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 4 cm. long 0.6 cm. in diameter; 500,000 U. I.M. Penicillin daily. No oral feeding. Subcutaneous and I.V. infusions. Pleural taps. Died on 4th post-operative day. Autopsy shows leakage of sutures and empyema.

6. Dog No. 104 - Age: 4 weeks - Weight: 2080 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection 2 cm. of oesophagus; teflon graft 3.5 cm. long 0.6 cm. in diameter. Gastrostomy. Fed by gastrostomy from the 1st post-operative day on. X-ray examination on the 12th post-operative day with barium swallow showed marked stenosis. Died 2 weeks post-operative. At autopsy severe stricture at the site of anastomosis and no teflon was found. Pathological examination showed acute inflammation, ulceration, and muscle destruction; early healing at the edges. Prosthesis not present.

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7. Dog No. 300 - Age: 4 weeks - Weight: 1700 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 3.5 cm. long 0.6 cm. in diameter. Gastrostomy. Feeding through gastrostomy tube on the 1st post-operative day. Died on the 6th post-operative day. Autopsy shows leakage of sutures and empyema.

8. Dog No. 301 - Age: 4 weeks - Weight: 1650 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon 3.5 cm. long 0.6 cm. in diameter. Gastrostomy. Feeding by gastrostomy tube from the lst post-operative day on. X-ray examination with barium swallowing on the 12th postoperative day - complete obstruction. Died on the 13th day. Autopsy shows severe stenosis, leakage of the sutures, teflon graft found in the stomach.

Pathological examination - severe stenosis at the site of resection due to productive chronic inflammation with absence of mucosa and muscular coats.

9. Dog No. 326 - Age: 5 weeks - Weight: 2020 Gm.

Anaesthesia: Chloralose I.V. with infusion of 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus, teflon graft 4 cm. long, 0.8 cm. in diameter. Gastrostomy. Feeding by gastrostomy tube from the lst post-operative day on. Bloody diarrhea appearing on the 5th day. Died on the 8th day. Autopsy shows teflon in situ, normal lungs and mediastinum.

10. Dog No. 328 - Age: 4 weeks - Weight 1340 Gm.

Anaesthesia: I.V. Chloralose with infusion of 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 4.5 cm. long 0.8 cm. in diameter. Gastrostomy tube feeding from the 1st post-operative day on. Drainage under suction from the 3rd post-operative day. I.V. infusion. Died on the 5th day. Autopsy shows leakage and empyema.

11. Dog No. 340 - Age: 5 weeks - Weight 1750 Gm.

Anaesthesia: I.V. Chloralose and Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus, teflon graft 4 cm. 0.8 cm. in diameter. 500,000 U. I.M. Penicillin daily. Water by mouth from the 1st post-operative day. Milk and Pablum added on the 7th post-operative day. 11th day - teflon graft found in excrements. 16th day x-ray examination showed occlusion. On the 18th day attempts of dilatation every second day. After 4 weeks repeated x-ray examination showed a localized stricture of 0.5 cm. in diameter. Sacrificed 5 weeks post-op. At autopsy severe stricture, lungs normal.

Pathological examination showed complete loss of muscles with replacement fibrosis of central area of oesophagus with covering area of granulation tissue and acute inflammation and ulceration.

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12. Dog No. 341 - Age: 4 weeks - Weight: 1650 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection 2 cm. of oesophagus; teflon graft 4.5 cm. long 0.8 cm. in diameter. 500,000 U. I.M. Penicillin daily. Water by mouth from the 1st post-operative day on. Died on the 4th day. Autopsy shows leakage of suture and empyema.

13. Dog No. 342 - Age: 4 weeks - Weight: 1240 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 4.5 cm. long 0.6 cm. in diameter. Anaesthetic death.

14. Dog No. 343 - Age: 4 weeks - Weight: 1140 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 4.5 cm. long 0.6 cm. in diameter. 500,000 U. I.M. Penicillin daily. Water by mouth from the 1st post-operative day. Milk and Pablum added on the 8th day. Vomiting appeared on the 12th day. X-ray examination on the 20th day showed slight stricture. From the 22nd day on dilatation of the oesophagus every second day. Sacrificed after 4 weeks. Autopsy shows stricture.

Pathological examination - large ulcer of oesophagus extending to the adventitia with slight repair and minimal epithelization.

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15. Dog No. 344 - Age: 5 weeks - Weight: 1960 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 4.5 cm. long 0.6 cm. in diameter. 500,000 U. Penicillin I.M. daily. No oral feeding. I.V. and subcutaneous infusions. Died on the 3rd post-operative day. Autopsy shows leakage and empyema.

Due to the fact that in almost all cases leakage of suture line was observed, we decided to change our technique and use one single layer of interrupted fine silk suture instead. Other elements of surgical technique remained unchanged. In the postoperative treatment schedule we added I.M. Streptomycin to the previously used Penicillin.

16. Dog No. 372 - Age: 4 weeks - Weight: 1800 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2.5 cm. of oesophagus; teflon graft 5 cm. long and 0.6 cm. in diameter. 500,000 U. I.M. Penicillin and 0.2 Gm. of I.M. Streptomycin. Water by mouth from the 1st post-operative day on. Milk and Pablum added on the 8th day. Vomiting appeared on the 12th day. X-ray examination on the 20th day showed slight stricture. From the 22nd day on - dilatation performed every 2nd day. Died 4 weeks after surgery due to starvation. Autopsy shows teflon in situ, occlusion of oesophageal lumen due to collapse of anterior wall of teflon graft.

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17. Dog No. 373 - Age: 4 weeks - Weight: 1700 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 3.5 cm. long and 0.6 cm in diameter. Penicillin and Streptomycin I.M. daily. Water by mouth from the 1st day on. Milk and Pablum added on the 7th day. X-ray examination on the 14th day - no stenosis. Accidental death during the x-ray examination. Autopsy normal healing, teflon in situ.

18. Dog No. 374 - Age: 4 weeks - Weight: 1350 Gm.

Anaesthesia: I.V. Chloralose with 5% Dextrose infusion + 500,000 U. Penicillin; right pleural approach; resection of 2 cm. of oesophagus; teflon graft 3 cm. long and 0.6 cm. in diameter. Penicillin and Streptomycin I.M. daily. Water by mouth from the lst day on. Milk and Pablum from the 6th day on. On the 14th day signs of occlusion appeared. On the 19th day - death of starvation. Autopsy - normal healing, teflon in in situ, occlusion due to collapsed wall of the prosthesis.

19. Dog No. 375 - Age: 5 weeks - Weight: 1850 Gm.

Anaesthesia: I.V. Chloralose with 5% Dextrose infusion + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 3 cm. long and 0.6 cm. in diameter. Penicillin and Streptomycin I.M. daily. Water by mouth starting on the 1st day. Received solid food erronously

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on the 2nd day. 3rd day- fistula formation. 7th day x-ray examination confirms presence of fistula. 12th dayfistula closed. 14th day - vomiting appeared. 24th day death from starvation. Autopsy shows complete occlusion teflon not found.

20. Dog No. 376 - Age: 4 weeks - Weight: 1600 Gm.

Anaesthesia: I.V. Chloralose with 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus; teflon graft 3 cm. long and 0.6 cm. in diameter. Penicillin and Streptomycin I.M. daily. Water by mouth starting on the 1st day. Milk and Pablum added on the 5th day. On the 7th day - signs of occlusion. No further oral feeding. I.V. and subcutaneous infusions only. On the 13th day graft regurgitated. On the 24th day accidental death at attempts of dilatation. Autopsy shows severe stenosis, normal healing.

#### RESULTS OF GROUP 1

From the total number of 20 dogs:

1 dog died due to anaesthetic error.

9 dogs died during the first post-operative week due to empyema. From the remaining 10 dogs:

6 dogs died of starvation during the 2-4 weeks following surgery.
2 dogs died accidentally:

l during radiological examination carried out 2 weeks
post-operatively.

1 during oesophageal dilatation 24 days after surgery.

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2 last dogs were sacrificed in 28 and 35 days respectively. (Table 1)

In all the ten dogs we observed a significant stenosis or even an almost complete occlusion of the oesophageal lumen by a contracting scar (Fig. 4). These pathological changes appeared between 2-5 weeks following surgery. Grossly the site of constriction presented as a 2-4 mm. wide, circular scar (Fig. 5 & 6). Microscopically the site of anastomosis presented as an area of replacement fibrosis with loss of muscle and mucosa, as well as signs of granulation and epithelization. Acute or productive chronic inflammation with ulceration was usually found. It became evident that the original distance between the two oesophageal ends equal to the length of the prosthesis has been reduced during the process of scar contraction to a distance 2-4 mm. In other words the oesophagus has been correspondingly elongated.

On the basis of autopsy examinations performed in different post-operative periods we concluded that the process of scar formation and progressive stenosis has a very typical course: in 8-10 days after the operation the introduced teflon graft is surrounded by an enveloping connective tissue cylinder, which bridges both oesophageal segments (Fig. 7). This connective tissue cylinder begins then to contract resulting in shortening of its original length and in progressive approximation of both oesophageal stumps (Fig. 8). The sutures anchoring the teflon graft to the oesophageal ends pull out and in about 2-4 weeks the prosthesis is rejected and regurgitated, or passed into the stomach. Sometimes the prosthesis remains in situ much longer, even for 7 weeks, probably due to incarceration of the crimped teflon by the tightening scar. After the prosthesis is

Group I - 2	0 Dogs
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Number	Time of Survival	Cause of Death	Anastomosis
1	during operation	anaesthetic error	
9	3 - 8 days	empyema	leakage
6	13 - 26 days	starvation	stenosis
2	14, 24 days	accidental	stenosis
2	28, 35 days	sacrificed	stenosis

Tab. 1. The results of group I.



Fig. 4. Barium filled oesophagus shows almost complete occlusion at the site of anastomosis.


Fig. 6 (below). Internal view of the same specimen.



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Fig. 7. Specimen taken 8 days after implantation of the teflon prosthesis.Note the connective tissue cylinder surrounding the teflon graft.



Fig. 8. Specimen taken 24 days after implantation of the teflon prosthesis. Significant shortening of the connective tissue cylinder present, originally of the same length as the prosthesis (see Fig. 7).

rejected the contraction of the connective tissue cylinder progresses not only in relation to its length, but also it its transverse diameter, leading to a severe stenosis of the oesophageal lumen. Occasionally symptoms of occlusion appeared before the rejection of the teflon graft and scar contraction. They were caused by collapsing wall of the proximal part of the teflon prosthesis.

# DISCUSSION AND CONCLUSION

The phenomenon of rejection of implanted prosthesis and progressive contraction of scar tissue formed around the prosthesis, observed by us in all cases, has been amply described and emphasized by all authors working on prosthetic oesophageal replacement. Disregarding other complications, such as leaking of sutures with resulting infection, or post-operative pulmonary complications, the process of scar contraction leading to a severe stricture of the oesophageal lumen was generally considered the most frequent and most serious complication discrediting in fact the method. Our experiments confirmed fully the results obtained by other authors. They permitted us, however, to observe another very important aspect of this process, namely the fact that the contracting scar does not only constrict the oesophageal lumen, but also, to a great extent, approximates both ends of the oesophagus so that the originally created gap, except for 2-4 mms. of constricted scar tissue, is bridged by normal oesophagus. Although dilatation of such a stricture might be possible in the human infants, our attempts in the dogs met with no success, and often with disaster. It was decided therefore to attempt to resect the stricture and reconstitute the oesophagus by end-to-end anastomosis.

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We proceeded to operate on the following 7 consecutive dogs (Group 2) with this plan in mind. Re-operation would be performed upon appearance of clinical signs of occlusion, but not earlier than is necessary for a sufficient contraction of the connective tissue cylinder. This corresponded to a time period of 3-4 weeks according to our observations obtained from the previous series.

### REVIEW OF CASES - GROUP 2

1. Dog No. 377 - Age: 4 weeks - Weight: 1600 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 3 cm. of oesophagus; teflon graft 3 cm. long 0.8 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily. Water by mouth starting on the 1st post-operative day. Milk and Pablum added on the 6th day. Difficulties in swallowing and vomiting on the 22nd day. Oral feedings were supplemented by I.V. infusions. Re-operated on the 53rd day. Right transpleural approach; resection of stricture and end-to-end anastomosis. Water by mouth starting on the 1st post-operative day; antibiotics I.M. through the post-operative period of 1 week. Milk and Pablum added on the 8th post-operative day. Sacrificed 200 days after the first operation and 147 days after the second. At autopsy complete linear healing was found with no sign of stricture of the lumen. 2. Dog No. 362A - Age: 3 weeks - Weight: 900 Gm.

Anaesthesia: I.V. Chloralose, I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 3 cm. of oesophagus; teflon graft 3 cm. long 0.8 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily. Water by mouth starting 1st post-operative day. Vomiting and dysphagia appeared on the 7th post-operative day. Oral feeding supplemented by I.V. and subcutaneous infusions. Died on the 10th post-operative day. At autopsy leakage of sutures and empyema was found.

3. Dog No. 378 - Age: 4 weeks - Weight: 1600 Gm.

Anaesthesia: I.V. Chloralose, I.V. infusion 5% Dextrose + 500,000 U. Penicillin; right transpleural approach. Resection of 2.5 cm. of oesophagus, teflon graft 4.5 cm. long 0.6 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily. Water-milk mixture by mouth starting the lst postoperative day. Pablum added on the 7th day. Vomiting began on the 15th day. 21st day oral feeding discontinued, except milk supplemented by I.V. and subcutaneous infusions. 27th day - re-operation. Excision of stricture, and direct anastomosis. Antibiotics given I.M. for 7 post-operative days. Water by mouth from the first post-operative day. Milk and Pablum added on the 9th day. Smooth post-operative course. The dog is alive and well 175 days after the first operation and 149 days after the second. No clinical signs of oesophageal stenosis.

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4. Dog No. 380 - Age: 4 weeks - Weight: 1500 Gm.

Anaesthesia: I.V. Chloralose; I.V. Dextrose 5% + 500,000 U. Penicillin; right transpleural approach; resection of 2 cm. of oesophagus, teflon graft 3 cm. long 0.6 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily. Water-milk mixture given orally from the 1st post-operative day. Pablum added on the 7th day. Vomiting and dysphagia started on the 36th day. Re-operated on the 45th day. Anaesthetic death.

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At autopsy - linear occlusion of the oesophageal lumen at the site of anastomosis. The distance between the two oesophageal ends about 2 mm. End-to-end anastomosis was easily performed.

5. Dog No. 381 - Age: 5 weeks - Weight: 1560 Gm.

Anaesthesia: I.V. Chloralose, I.V. 5% Dextrose + 500,000 U. Penicillin; right transpleural approach; resection of 2.5 cm. of oesophagus, teflon graft 3 cm. long 0.6 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily for 1 week. Milk feedings started on the 1st day. Pablum added on the 7th day. Vomiting and dysphagia starting on the 36th day. Re-operated on the 46th day. Teflon was found in situ. Resection of stricture and end-to-end anastomosis. I.M. antibiotics during the 1st post-operative week. Water-milk mixture starting the 1st day. Pablum added the 2nd day. Smooth post-operative course. The dog is alive and well 177 days after the first and 134 days after the second operation. No clinical signs of oesophageal stenosis. 6. Dog No. 384 - Age: 5 weeks - Weight: 1505 Gm.

Anaesthesia: I.V. Chloralose; I.V. 5% Dextrose + 500,000 U. Penicillinp right transpleural approach; resection of 3 cm. of oesophagus, teflon graft 3 cm. long and 0.8 cm. in diameter. 500,000 Penicillin and 0.2 Gm. Streptomycin I.M. daily. Milk-water mixture given orally 1st post-operative day. Pablum added on the 7th day. Vomiting and dysphagia started on the 21st day. Re-operated on the 30th day. Teflon graft was found in situ. Resection of the stricture and end-to-end anastomosis. I.M. antibiotics given for the 1st post-operative week. Watermilk mixture given by mouth from the 1st post-operative day on. Pablum added on the 6th day. Smooth post-operative course. The dog is alive and well 170 days after the first and 140 after the second operation. No clinical signs of oesophageal stenosis.

7. Dog No. 387 - Age: 5 weeks - Weight 1500 Gm.

Anaesthesia: I.V. Chloralose, I.V. Dextrose 5% + 500,000 U. Penicillin; right transpleural approach. Resection of 2 cm. of oesophagus, teflon graft 3 cm. long 0.6 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily. Milk-water mixture given orally on the 1st post-operative day. Pablum added on the 14th day. Vomiting and dysphagia started on the 22nd day. Re-operated on the 29th day. Resection of the stricture and end-to-end anastomosis. I.M. antibiotics given for 7 days. Milk by mouth from the 1st day on. Pablum added on the 7th day. Catarrhal infection, vomiting, anorexia. Sacrificed 47 days after the first and 18 days after

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the second operation.

At autopsy - complete linear healing of the anastomosis and no stenosis was found.

## RESULTS OF GROUP 2

From the total number of 7 dogs: (Table 2)

- 1 died 10 days after the first operation because of empyema.
- l died as a result of an anaesthetic error during the second operation performed 45 days after the first one.
- 1 dog was sacrificed 47 days after the first and 18 days after the second operation.
- 1 dog was sacrificed 200 days after the first and 147 days after the second operation.
- 3 remaining dogs are still living:

1 - 176 days after the 1st and 149 days after the 2nd operation
2 - 177 days after the 1st and 134 days after the 2nd operation
3 - 170 days after the 1st and 140 days after the 2nd operation

With exception of one dog that died during the first operation, all remaining six dogs were submitted to the second operation. In all cases a severe stenosis at the site of anastomosis was found during the second stage (Fig. 9). The width of the circular scar did not exceed 4 mm. (Fig. 10). It is worth emphasizing that group 2, in which we removed slightly longer segments of oesophagus (2-3 cm.) in comparison to group 1, the scar uniting both oesophageal ends had the same appearance of a 2-4 mm. wide ring. In other words, in spite of increase in oesophageal deficiency, the final result did not differ and a direct anastomosis was easily performed. The time interval between the two operations varied

	Number	Time of Survival		Cause of Death	Anastomosis	
Dead	1 1 1	10 days after 1st operation 45 days after 1st oper. — during 2nd oper. 50 days after 1st oper. — 13 days after 2nd			empyema anaesthetic error sacrificed	leakage stenosis no stenosis
Llive	1	163 days after 1st a	oper 119 day	s after 2nd	$\mathbf{X}$	no stenosis
	1	161 ••	133	• •		••
	1	154 • •	112	• •		• •
	1	147 • •	120	••		••

Group II - 7 Dogs

Tab. 2. The results of group II.

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Fig 10. Excised during the second stage operation stenosed segment of the oesophagus. The width of the circular scar does not exceed 4 mm.

from 4 to 7 weeks. The second operation presented in all cases significant technical difficulties, related to presence of dense, extensive adhesions between the oesophagus and the adjacent thoracic structures. In one dog sacrificed 47 days after the firs and 18 days after the second operation, linear healing and complete absence of narrowing was found (Fig. 11). In a second dog sacrificed 200 days after the first and 147 days after the second operation the oesophagus presented an identical appearance. The 3 surviving dogs do not show clinical evidence of oesophageal stenosis and their development and weight gain progress normally. Radiological examination carried out in two of them demonstrated slight degree of narrowing and no significant delay in peristaltic motility (Fig. 12). The results obtained in Group 2 seemed to confirm the validity of our hypothesis. They proved that the contracting scar formed in place of the introduced prosthesis is capable of sufficient elongation of the oesophageal ends to make a direct anastomosis possible.

Encouraged by the above results we attempted to remove a much longer segment of the oesophagus in order to observe the elongation process under these highly difficult conditions.

# REVIEW OF CASES - GROUP 3

In this group comprising 10 puppies, we removed a much longer segment of the oesophagus (5-8 cm.) and replaced it by an equal length, or a slightly shorter graft.

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Fig. 12. Radiological examination performed 3 mos. after the second stage operation shows minimal narrowing of the lumen at the site of anastomosis. 1. Dog No. 394 - Age: 4 weeks - Weight: 1400 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. Streptomycin. Right transpleural approach; resection of 6 cm. of oesophagus, teflon graft 6 cm. long and 0.6 cm. in diameter. Water-milk by mouth starting 1st post-operative day. Milk and Pablum starting 4th post-operative day. Vomiting began 2 weeks after surgery. Re-operated on the 18th post-operative day. Right transpleural approach; resection of stricture 2 cm. in length; end-to-end anastomosis. Anaesthetic death.

2. Dog No. 398 - Age: 4 weeks - Weight: 1300 Gm.

Anaesthesia: I.V. Chloralose and Nembutal; I.V. infusion 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. Streptomycin. Right transpleural approach; resection 6 cm. of oesophagus, teflon graft 6 cm. long and and 0.6 cm. in diameter. 500,000 U. of Penicillin and 0.2 Gm. of Streptomycin I.M. daily. Milk and water by mouth starting lst post-operative day. Milk and Pablum starting 7th day. Signs of occlusion after 2 weeks. 26th day died due to intestinal infestation with worms.

At autopsy examination prosthesis was found in situ surrounded by a thick connective tissue cylinder.

3. Dog No. 400 - Age: 4 weeks - Weight 1200 Gm.

Anaesthesia: I.V. Chloralose and Nembutal; I.V. infusion of 5%

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Dextrose + 500,000 U. Penicillin and 0.2 Gm. of Streptomycin. Right transpleural approach; resection 5 cm. of oesophagus, teflon graft 5 cm. long and 0.6 cm. in diameter. 500,000 U. Penicillin and 0.2 Gm. Streptomycin daily. Water and milk by mouth from the 1st post-operative day. Milk and Pablum starting on the 7th day. 14th day signs of peritonitis and intestinal obstruction. Died 15th post operative day because of intestinal infestation with worms.

At autopsy teflon prosthesis in situ surrounded by connective tissue cylinder.

4. Dog No. 401 - Age: 4 weeks - Weight: 1500 Gm.

Anaesthesia: I.V. Chloralose and Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. Streptomycin; resection of 6 cm. of oesophagus; teflon graft 5 cm. long and 0.6 cm. in diameter. Water and milk by mouth starting 1st post-operative day. Milk and Pablum starting 7th day. After 2 weeks signs of intestinal occlusion and peritonitis. Died 18th post-operative day because of intestinal infestation with worms.

At autopsy teflon graft in situ surrounded by thick connective tissue cylinder.

5. Dog No. 402 - Age: 4 weeks - Weight: 900 Gm.

Anaesthesia: I.V. Chloralose and Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. Streptomycin; right transpleural approach; resection 5 cm. of oesophagus; teflon graft 5 cm. long 0.6 cm. in diameter. Anaesthetic death. 6. Dog No. 403 - Age: 4 weeks - Weight: 1300 Gm.

Anaesthesia: I.V.Chloralose and Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. Streptomycin; right transpleural approach; resection of 5 cm. of oesophagus, teflon graft 5 cm. long 0.6 cm. in diameter. Gastrostomy. Penicillin and Streptomycin I.M. Milk by mouth and through gastrostomy tube starting 1st post-operative day. 7th post-operative day signs of empyema; repeated pleural punctures; died on 11th post-operative day because of empyema.

7. Dog No. 406 - Age: 5 weeks - Weight: 1250 Gm.

Anaesthesia: I.V. Chloralose and Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. of Streptomycin; right transpleural approach; resection of 7 cm. of oesophagus, teflon graft 5 cm. long, 0.6 cm. in diameter. Penicillin and Streptomycin I.M. Milk and water by mouth starting 1st postoperative day. Milk and Pablum starting 7th post-operative day. Signs of occlusion 2 weeks after operation; I.V. infusion. 16th post-operative day gastrostomy performed; fed through gastrostomy tube. Re-operated 4 weeks after the 1st operation. Resection of 1 cm. long scar and end-to-end anastomosis. Milk and Pablum by mouth 1 week after re-operation; smooth post-operative course. Sacrificed 70 days after the first and 42 days after the second operation.

At autopsy examination no stenosis was found and complete linear healing, in spite of the fact that radiological examination prior to death demonstrated a marked narrowing at the site of anastomosis.

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8. Dog No. 407 - Age: 5 weeks - Weight: 2100 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. Streptomycin. Right transpleural approach; resection of 6 cm. of oesophagus, teflon graft 5 cm. long 0.6 cm. in diameter. Penicillin and Streptomycin. Milk and water by mouth starting 1st post-operative day. Milk and Pablum starting 7th day. Signs of occlusion appeared 2 weeks post-operative; gastrostomy performed 3 weeks post-operative. Re-operated 4 weeks after the first operation; resection of scar. Pablum and milk by mouth 1 week after re-operation. Smooth post-operative course. Sacrificed 63 days after first and 35 days after the second operation.

At autopsy linear healing and no stenosis was found.

9. Dog No. 408 - Age: 4 weeks - Weight: 1300 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. of Streptomycin. Right transpleural approach; resection of 8 cm. of oesophagus, teflon graft 6 cm. long and 0.8 cm. in diameter. Penicillin and Streptomycin I.M. Milk and water by mouth starting 1st post-operative day. Died 2 days after the operation because of empyema.

10. Dog No. 409 - Age: 5 weeks - Weight - 2150 Gm.

Anaesthesia: I.V. Nembutal; I.V. infusion of 5% Dextrose + 500,000 U. Penicillin and 0.2 Gm. of Streptomycin. Right transpleural approach; resection of 6 cm. of oesophagus, teflon

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graft 4 cm. long and 0.8 cm. in diameter. Penicillin and Streptomycin I.M. Water and milk by mouth starting lst post-operative day; milk and Pablum starting 5th day. 1 week after the operation signs of occlusion. 11th post-operative day gastrostomy. Re-operated 3 weeks after the 1st operation; resection of a 2 cm. long scar and end-to-end anastomosis. Milk and Pablum by mouth starting 7th day after the re-operation. Smooth post-operative course. The dog is still alive and in excellent condition, at the time of submission of this paper 66 days after the first and 45 days after the second operation.

#### RESULTS OF GROUP 3

From this last group comprising 10 puppies - 2 dogs died because of empyema (Table 3) (Fig. 13).

- 3 died due to intestinal obstruction caused by heavy infestation with worms.
- 2 others died due to an anaesthetic error, one during the first and another during the second operation. This last dog was re-operated 2½ weeks after removal of 6 cm. long segment and replacement by equal length graft. During the re-operation we observed the approximation of both oesophageal stumps to a distance of 2 cm. (Fig.14). Thus during the period of time of 2½ weeks the distance of 6 cm. was reduced to 2 cm. In other works the oesophagus has been elongated by 4 cm. Two dogs were sacrificed 70 days after the first, 42 days after the second and 63 days after the first, 35 days after the second operation, respectivelly. In these two dogs 7 and 6 cm. long segments were removed. Both dogs were re-operated 4 weeks later and scars of 1 and 1.5 cm. in length were found. In these two cases

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Number	Time of Survival	Post Operative Course	Anastomosis
• 1		death due to anaesthetic error during 1st oper.	
1	18 days	2nd oper.	stenosis
2	3, 11 days	· · empyema	leakage
3	15, 18, 26 days	intestinal obstruction	-
1	43 days, 20 days	doing well	slight sten.
1	41 days, 11 days	· • • •	• •
1	23 days, 7 days	• •	••

Group III - 10 Dogs

Tab. III. Results of group III.

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Fig. 13. Specimen taken 11 days after the first stage operation. Notice satisfactory growth of connective tissue cylinder in spite of wide spread empyema, which was the cause of death of the dog.



Fig. 14. Case # 394 (see text). 18 days after excision of 6 cm. long oesophageal segment. Notice the shortening of the connective tissue cylinder to the length of 2 cm.

the oesophagus has been elongated by 6 cm. and 4.5 cm., respectively. The last dog was re-operated 3 weeks after removal of 6 cm. long segment. the scar bridging both oesophageal ends was 2 cm. long. In this case in a period of time of 3 weeks the oesophagus was elongated by 4 cm. In all four re-operated dogs a direct anastomosis was easily performed, in spite of presence of dense and extensive adhesions (Fig. 15). (Fig. 15A).

### CONCLUDING REMARKS

These four examples manifest the plasticity of the oesophagus and the rapidity of its elongation. Considering the fact that the total oesophageal length of the puppies in question 10 - 12 cm., and that the excision of 6-7 cm. represents a loss of over 50% of its length, the elongation of the remaining oesophagus and return to almost its original length occurrs remarkably rapidly.

The results obtained are not offered as an ultimate proof of the validity of our method. They represent, however, an interesting body of evidence for the feasibility of mechanical stretching of the oesophagus. As a matter of fact the teflon prosthesis serves as a skeleton only for the formation of scar tissue. This scar in its further evolution accomplishes the mechanical approximation of the distant oesophageal ends by steady and effective traction.

Recently, several authors (81 - 85) have observed and studied an analogous phenomenon of wound contraction. Artifically created skin defects healed by contraction and progressive approximation of wound edges leaving in result almost linear scars. According to histological examinations the factor responsible for the wound contraction is the



Fig. 15. End-to-end anstomosis after excision of the stenosed part.



Fig. 15a. Appearance of the oesophagus 6 wks. after the second stage operation ( resection of the scar and end-to-end anastomosis).

newly formed connective tissue, particularly the fibroblasts. Our experiments and observations seem to present a certain analogy to the cited studies on wound contraction. It is difficult to determine at the present time if, and to what extent our observations of contracting of the connective tissue cylinder bridging the gap between the two oesophageal stumps can be explained by wound contraction or scar contraction phenomena. The answer can only come forth from detailed histological studies, which were beyond the scope of our work. It seems, however, that the phenomena have many common characteristics and biologically they represent the old and well known organism's tendency to "restitutio ad integrum".

We are aware of the shortcomings of the presented method. First of all it requires two thoracotomies and, of these, the second one is fraught with technical difficulties. There is a good chance, however, to avoid the necessity of the second thoracotomy in human surgery by early initiation of dilatation procedures. Secondly, there is the ever present danger of leakage and fistula formation. This danger, however, exists in all other methods as well.

In summary it seems that the presented results are encouraging and should stimulate interest in continuing further studies on the use of teflon prosthesis. If our observations are confirmed, the proposed method could be applied in cases of substantial oesophageal deficiency and, in selected cases avoid much more involved and prolonged surgical procedures.

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# REPORT OF EXPERIMENTS WITH FULL THICKNESS PEDICLE

#### SKIN GRAFT

### INTRODUCTION

Independently of the experiments with the artificial prosthesis we carried out simultaneously studies concerning the usefulness of full thickness autogenous skin graft in oesophageal replacement. Our previous experience with full thickness skin grafts brought to our mind the idea of using this material in oesophageal replacement. In contrast to the free skin grafts, which are predisposed to scar formation and ulceration, the full thickness pedicle skin should have much better chances to "take" under new conditions retaining all its original properties such as elasticity, good blood supply, and resistance to the digestive juices. We were faced with the technical difficulty of developing a method of safe introduction of the skin into the posterior mediastinum through the pleural cavity. A possible solution to this problem was found with satisfactory results.

### DESCRIPTION OF THE FIRST METHOD

A skin flap including subcutaneous tissue was mobilized from the right lateral chest wall at the level of the fourth to sixth rib with its base directed toward the back of the animal and parallel to the direction of the regional blood vessels. It is important that certain proportions are preserved, namely that the base of the flap should not be less than half of its length. The end part of the flap was then cut into a rectangular shape and rolled into a transverse tube, which serves later as the oesophageal graft. In order to create more favourable conditions for the union of the margin with the base a narrow strip of epidermis was removed from the surface of the base. Two layers of interrupted silk sutures were used for the union. The proximal part of the pedicle was then rolled into a longitudinal tube, again with the epidermis inside, by application of two layers of interrupted fine silk sutures. The flap formed in this fashion was then introduced into the posterior mediastinum through a thoracotomy at the level of the fifth intercostal space and united with the oesophageal stumps by two layers of interrupted silk sutures. A partial rib resection at the site of entry of the skin pedicle, formed a window for the base of the pedicle. This point is of importance in relation to the pedicle blood supply, which could be compromised by the pressure of the adjacent rib. The thoracic wall was then closed routinely; particular attention was paid to careful closure of the parietal pleura around the base of the pedicle.

# COMPLICATIONS

Basic, serious difficulty was observed already at the very beginning, namely the presence of hair covering the skin of all experimental animals. All attempts to use non-epilated but only shaved skin ended in dehiscence of the pedicle sutures due to rapid re-growth of hair in the first few post-operative days. This lead to a fatal outcome because of severe infection. It became obvious that only permanently epilated skin could be used. After considering several possibilities we chose x-ray radiation, as probably the most effective method. Soon we noticed that puppies poorly tolerate the irradiation even in very small doses of 300 r per cutaneous field.

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Out of 36 puppies submitted to irradiation 24 died in the following two weeks with evidence of anemia and pulmonary disease. Only 12 survived; 8 of those had signs of radiation sickness. The epilative effect of irradiation appeared in approximately 3-4 weeks, but complete epilation could never be obtained. On the other hand we have observed pathological changes in the skin in the form of peeling and thinning. We have presumed that these changes were not without influence on the healing of the graft. Out of 12 dogs operated upon (Table 4) 8 died within the first post-operative days with signs of wound infection. We have attempted to prevent it by repeated sterilization of the skin for 48 hours prior to surgery and by covering of the entire operative field with sterile dressing without much success. The use of Penicillin in all cases did not influence the course of infection. In 4 dogs a fistula between the lumen of oesophagus and the pedicle developed, beginning respectivelly on the 3rd, 4th, 7th and 10th post-operative days. In the dog sacrificed on the 4th day (Dog No.555) a communication between the transverse and the longitudinal tube was found due to dehiscence of sutures resulting from re-growth of hair.

In the second dog (Dog No. 553) sacrificed on the 14th day a similar condition was observed.

In the third dog (Dog No. 562) sacrificed after 19 days a wide fistula between the transverse and the longitudinal tube was present. The skin forming the anastomosis looked grossly unchanged; it was of the original dimensions and united with the oesophageal stumps by a linear scar.

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н н	Group	IV - 12 Dogs		
Number	Time of Survival	Cause of Death	Skin Transplant	
9 3	2 – 8 days 14, 15, 19 days	empyema sacrificed	leakage good healing	

Tab. IV. Results of group IV.

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Histological examination revealed a viable, well vascularized skin without significant pathological changes. The epidermis showed moderate acanthosis and slight parakeratosis. These changes were similar to those observed after irradiation.

The fourth and last dog (Dog No. 336) was sacrificed 15 days after the operation. At autopsy we grossly observed satisfactory linear healing of the graft and presence of a wide fistula between it and the pedicle. Microscopically the graft was entirely intact and viable with the mucosal surface showing granulation. No scar formation or other pathological changes were found. The failures and complications discussed above forced us to find a different approach.

### DESCRIPTION OF THE SECOND METHOD

In this procedure a skin flap from the region of the middle and lower abdomen was mobilized (Fig. 16). By two parallel incisions extending from the costal margins to the inguinal folds a skin flap of suitable width containing the subcutaneous tissue was carefully prepared. This flap was then rolled into a tube with the epidermis on the outside. A silicone tubing of suitable length and calibre was inserted into the tubed graft to retain its lumen. The posterior extremity of the tube was then"trained". This "training" consisted of daily, gradually lengthened periods of occlusion of the blood vessels by compression with an elastic, in order to stimulate the blood circulation supplied from the proximal pedicle base. After 3 weeks of "training" the second stage operation was performed. The pedicle was divided at its distal base and the silicone tubing removed. Through a thoracotomy at the level of the 5th right intercostal space a tunnel connecting the posterior

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excised esophagus

invagination of the pedicle

 First stage operation - formation of the skin pedicle.

2. Second stage operation - partial resection of the esophagus, invagination of the skin pedicle.



3. Second stage operation - anastomosis between the invaginated skin pedicle and the proximal esophageal segment. Closure of the distal esophageal segment.

- implanted skin graft
- 4. Third stage operation division of the proximal pedicle base and anastomosis with the distal esophageal segment.

mediastinal cavity with the lumen of the skin pedicle was created. Through this tunnel the free end of the pedicle was then invaginated, like a glove finger, with the epidermis on the inside, and introduced into the mediastinal space. A segment of the oesophagus, a few centimeters in length, was then removed. The invaginated distal end of the pedicle was anastomosed with the proximal oesophageal stump by means of a single layer of interrupted silk sutures. The lower stump, of the oesophagus was tightly closed and released. The skin pedicle introduced in this way formed a long salivary fistula with the opening in the upper abdomen. A gastrostomy was created at the same operative procedure. During the following 3-4 weeks the dogs were fed by gastrostomy tube with simultaneous oral feeding to retain the proper reflex mechanism of swallowing. During this period an adequate blood supply to the skin pedicle developed from the proximal oesophageal stump and the surrounding tissue. Then the third and final stage was performed. Through a second thoracotomy at the level of the 7th right intercostal space the previously introduced skin pedicle was exposed and divided at the level of its entry into the thorax. This end of the pedicle was then anastomosed with the distal oesophageal stump. In this way the middle segment of the oesophagus was replaced by a skin graft.

# REVIEW OF CASES

Dog No. 379 - Age: 5 weeks - Weight: 1640 Gm.

Anaesthesia: I.V. Chloralose with infusion of 5% Dextrose, 500,000 U. Penicillin and 0.2 Gm. Streptomycin I.M. daily.

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lst stage operation: skin flap formation. Gradually prolonged "training" of the pedicle starting the 5th post-operative day. After three weeks 2nd stage operation: dividing of the distal base of the pedicle, invagination and connection of the pedicle with the proximal stump of oesophagus; gastrostomy at the same time. After four weeks 3rd stage operation: dividing of the proximal base of the pedicle and anastomosis with the distal oesophageal stump. Milk by mouth starting lst post-operative day. Smooth post-operative course. The dog is still alive and well, eating semi-solid food and gaining weight 110 days after last stage operation.

2. Dog No. 382 - Age: 5 weeks - Weight: 1450 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin. 1st stage operation: skin flap formation. After three weeks 2nd stage operation: dividing of the distal base of the pedicle. Anaesthetic death.

3. Dog No. 383 - Age: 4 weeks - Weight: 1300 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin. Daily Penicillin and Streptomycin I.M. for 7 days. 1st stage operation: skin flap formation. After 3 weeks - 2nd stage operation: dividing of the distal base of the pedicle and connection of the pedicle with the proximal stump of the oesophagus; gastrostomy. After 7 days - death because of empyema.

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Dog No. 392 - Age: 4 weeks - Weight: 1350 Gm. 4.

Anaesthesia: I.V. Chloralose, I.V. infusion 5% Dextrose + 500,000 U. Penicillin. Daily Penicillin and Streptomycin I.M. for 7 days. 1st stage operation: skin flap formation. After 5 weeks - 2nd stage operation: division of the distal base of the pedicle and connection of the pedicle with the proximal stump of the oesophagus; gastrostomy. After 4 weeks - 3rd stage operation: division of the proximal pedicle base and connection with the distal oesophageal stump. Food by mouth starting 6th post-operative day. Smooth post-operative course. The dog is still alive and well, eating semi-solid food and gaining weight 130 days after last stage operation.

5. Dog No. 399 - Age: 6 weeks - Weight: 2150 Gm.

Anaesthesia: I.V. Chloralose; I.V. infusion 5% Dextrose + 500,000 U. Penicillin. Daily Penicillin and Streptomycin I.M. for 7 days. let stage operation: skin flap formation. After 29 days - 2nd stage operation: Division of the distal end of the pedicle and connection of the pedicle with the proximal stump of the oesophagus; gastrostomy. Death after 7 days due to empyema.

# DISCUSSION OF RESULTS

Five puppies were used in this experiment (Table 5). From this number:

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Group V - 5 Dogs

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Number	Time of Survival	Cause of Death	Skin Transplant
1	28 days after 1st oper 7 days after 2nd	empyema	good healing
1	36 7	empyema	••
1	23 + during 2nd oper.	anaesthetic error	
1	110 days after last stage		no stenosis
1	55.130		

Tab. V. Results of group V.

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- 1 died 28 days after 1st operation, 7 days after 2nd operation, due to empyema.
- l died 36 days after 1st operation, 7 days after 2nd operation, due to empyema.
- l died 23 days after 1st operation, during 2nd operation because of anaesthetic error.

1 alive 110 days after last stage.

1 alive 130 days after last stage.

The post-mortem examination of the first three dogs showed viable, well vascularized skin grafts with no fistula formation in spite of presence of wide spread emypema and mediastinitis in two of them. The two surviving dogs are in good condition, gaining weight and are taking semi-solid food with no obvious signs of stenosis. Radiological examination demonstrates a wide lumen in both transplants (Fig.17,18) with moderate stemosis at the site of distal anastomosis in one of them. One of the dogs shows marked oesophageal dilatation above the skin graft. It is probably caused by the fact that the lumen of the skin pedicle was originally smaller than that of the oesophagus. Furthermore the pedicle devoid of peristaltic function creates an added resistance to the propulsion of food. We did not observe any degree of gastric reflux and the function of the cardia was normal.

## CONCLUDING REMARKS.

The purpose of the presented work was to explore the usefulness of long full thickness autogenous pedicle skin grafts and observe their





healing process under the most difficult conditions existing in the posterior mediastinum. They demonstrated that the skin used in this fashion has a remarkable tendency to "take" due to adequate blood supply from the base of the pedicle and rapid revascularization from the site of the anastomosis. Furthermore the epidermis shows a noticeable resistance to digestive juices, even in presence of wide spread infection involving the surrounding structures, the healing process of the graft continues unimpaired.

The novelty of the proposed method rests on the fact that the skin pedicle prepared, trained, and finally turned "inside out" can be of desired length to bridge even very long gaps. The stability and adequacy of its blood supply makes it superior to the already known similar methods, e.g. the Wookey procedure.

The disadvantages, reducing the value of the presented method, are the following: Firstly - its many stages, which include two thoracotomies. Secondly - the rather long time of its duration, approximately 3 months. Thirdly - the transplanted skin graft, devoid of peristaltic function, behaves as a passive segment of the digestive tract creating a certain resistance to the propulsion of food.

It seems, however, that the described method of invaginating a tubed pedicle skin graft may find an application in several other surgical conditions requiring reconstruction of defective body channels, such as external auditory canal, nasal passages, uretheroplasty, anoplasty, etc.

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## SUMMARY

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- 1. Etiology and Embryology of oesophageal atresia, as well as Anatomy and Physiology of the oesophagus have been described.
- 2. Historical review of clinical and experimental data is quoted in detail and different methods of treatment discussed.
- 3. Detailed report of experiments with crimped teflon grafts is given. It was observed that the crimped teflon prosthesis is quickly replaced by connective tissue, which by subsequent contraction approximates the oesophageal stumps to a distance permitting direct anastomosis. This occurs even in cases, in which half of the total oesophageal length was resected.
- 4. A series of experiments with full thickness pedicle skin grafts to replace the oesophageal defects were done. An original method of inverted skin pedicle is described and the results reported in detail.

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