FROM DEPARTMENT OF ORTHOPAEDICS AND TRAUMATOLOGY,
UNIVERSITY CENTRAL HOSPITAL, HELSINKI, FINLAND

USE OF FREE FAT TRANSPLANTS TO PREVENT EPIDURAL SCAR FORMATION

AN EXPERIMENTAL STUDY

BY

OLLI KIVILUOTO

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CONTENTS

		Page
1.	INTRODUCTION	7
1.1.	Observations leading to the investigation	7
1.2.	Purpose of the investigation	7
2.	EARLIER INVESTIGATIONS	8
2.1.	Fat transplants in experimental animals	8
2.1.1.	Autogenous transplant	8
2.1.2.	Homogenous transplant	10
2.2.	Fat transplants in man	13
2.2.1.	Clinical studies	13
2.2.2.	Histology	16
2.3.	Bone repair	17
2.3.1.	Healing of fractures	17
2.3.2.	Effect of cortisone	18
2.3.3.	Spongostan and its effects	19
3.	OWN STUDIES	21
3.1.	Material	21
3.2.	Methods	21
3.2.1.	Anaesthesia	21
3.2.2.	Operation	21
3.2.3.	Postoperative follow-up	23
3.2.4.	Sacrifice	24
3.2.5.	Decalcification and sections	25
3.3.	Results	25
3.3.1.	Pilot study	25
3.3.2.	The first series (fat application and control)	26
3.3.3.	The second series (fat and fat + cortisone)	34
3.3.4.	The third series (cortisone and control)	39
3.3.5.	The fourth series (fat + cortisone and control)	39
3.3.6.	The fifth series (fat + cortisone and control)	40
3.3.7.	The sixth series (fat and gelatin)	57
3.3.8.	Summary of the results	64
4.	DISCUSSION	66
4.1.	Free fat transplants	66
4.2.	Own studies and comparison with earlier investigations	67
4.3.	Intervertebral disc surgery	68
4.4.	Conclusions	68
5.	SUMMARY	69
6.	REFERENCES	70

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1. INTRODUCTION

1.1. Observations leading to the investigation

In connection with experimental work on rabbits and pigs to develop methods for the treatment of scoliosis, A. Langenskiöld and J.-E. Michelsson used free transplants of subcutaneous fat tissue to prevent excessive scar formation. The use of fat transplants was based on studies published by Erich Lexer (1919). It was found that free transplants of fat implanted in spaces which would otherwise have been filled with blood or serum were not replaced by scar tissue but remained as soft fat tissue for months or even years (Langenskiöld and Michelsson 1960).

On the basis of these findings, the use of free fat transplants placed on the spinal dura after removal of protruded discs in order to prevent scar formation on the dura was adopted in 1964. Since then, several of the patients who have had fat transplants placed on the dura in connection with disc operations have had new operations at which the area of the transplantation has been explored. At most of these explorations, several carried out many years after the first operation, the dura has been found to be without any overlying adherent scar and it has been easily exposed by blunt dissection (Langenskiöld and Kiviluoto 1976).

1.2. Purpose of the investigation

It is not possible in operations on patients to take material for histologic examination of the dura without causing damage to the patient. Re-operations on patients with disc protrusions who have had fat transplanted on the dura at the first operation are not common enough to form a large series covering a reasonable period of time. To obtain histologic evidence of the fate of free fat transplants placed on the dura and to compare the transplants with situations in which a haematoma or seroma has been left on the dura, it seemed necessary to produce the correspondig situations in experimental animals. It was especially interesting to ascertain whether the fat transplant could prevent the spinal dura from attaching to the scar tissue formed after the laminectomy.

2. EARLIER INVESTIGATIONS

2.1. Fat transplants in experimental animals

2.1.1. Autogenous transplant

The first studies on an autogenous graft were performed in the 19th century, when fat was transplanted into the gastrointestinal tract. The experimental animals were dogs and the transplants remained viable and adhered to the intestine (Jobert de Lamballe 1849 and Senn 1888). Tables 1 and 2 list the authors of articles on the subject, the years of publication, data concerning the site from which the graft was taken and the transplantation site, the principal observations and conclusions.

The purpose of these studies was usually to examine the fate of fat transplants. Furthermore, the haemostatic properties of fat were examined, and the value of fat in the treatment of ankylosis and dural defects, in the filling of osseous cavities and in the fixation of eye prosthesis was studied. Free fat grafts were also used to prevent adhesions around nerves and tendons. In the latest study (Österman 1972) fat was transplanted to prevent premature epiphyseal closure. Rabbits, dogs and rats were used as experimental animals, and free fat transplants were taken from different places of the body, usually from the inguinal region or the abdomen. Fat was transplanted to various sites in the animals. The graft was found to be preserved, and a small part of it was replaced by connective tissue. As an exception, the size of a fat piece was increased when testicular fat was transplanted subcutaneously into rats aged 4—6 days. If the diameter of the graft was 0.5 mm or smaller, the fat piece did not survive. The author (Eastlick 1947—1954) concluded that the number of cells involved was too small and the graft was absorbed before its circulation was restored. Fat tissue proved effective in stemming haemorrhages, and the graft was useful in repairing dural defects, and in preventing formation of adhesions around nerves and tendons. The observation time varied from some minutes to over one year.

Histologically, disintegration of fat cells and formation of fat-containing cavities were observed. Large host histiocytes were seen and some thougth that these became fat cells. Others thought that these cells removed the free fat and the original fat cells were preserved.

Almost all the investigations agreed that apparently normal fat tissue was seen 8 months or longer after the transplantation.

Table 1. *Previous publications on autogenous fat transplantations in animals 1888—1913.*

Author and publication year	Purpose of the experiment	Transplantation from	to	Main observations and conclusions
Senn 1888	To prove the value of fat in intestinal anastomosis	Omentum	Around the intestine	Fat was fixed to the intestine and prevented leakage of the anastamosis
Bartels 1908	To hold an eye prosthesis firmly	Abdomen or gluteal and femoral region	Orbita of the dog	Fat partially replaced by connective tissue, good results for the prosthesis
Franco 1909	To study the biology of the fat cell	Interscapular region of the rat	Subcutaneous pockets in the ear	No difference between auto- and homogenous transplants
Franco 1911	To study the fate of transplanted fat	Autogenous, homogenous and heterogenous	Subcutaneous tissue of the rabbit	At first fat proliferates and then degenerates
Marx 1910	"	Femoral region (autogenous and homogenous)	Scleral cavity of the rabbit	Graft separated by connective tissue
Röpke 1911	To prove the value of fat in the treatment of ankylosis	Inguinal region of the rabbit or the dog	Resected lateral condyle of the femur	Fat preserved as such and suitable for the treatment of ankylosis
Makkas 1912	To fill osseous cavities	Subcutaneous tissue of the hypogastrium	Distal femur of the dog	Fat partially replaced by connective tissue, successful in 7 out of 8
Rehn 1913	To prove the value of fat in treating dural defects	Inguinal region of the dog	On the pia mater	Fat preserved and a good substitute for the dura
Hilse 1913	To stop bleeding	Inguinal region of the rabbit or the dog	Wound in liver, spleen or kidney	Fat well preserved, and the bleeding stopped

2.1.2. Homogenous transplant

Table 3 lists the authors of the articles on the subject, the years of publication, date concerning the site from which the graft was taken and the transplantation site, the principal observations and conclusions.

The main purpose of the studies was generally to examine the fate of the graft. In addition, haemostatic properties were examined, and homogenous and autogenous transplants were compared with each other. Fat tissue was taken from different sites in the laboratory animals, which were rabbits, rats, and dogs. The transplantation site varied. The observation period ranged from one day to half a year. The transplant was not preserved. One exception occurred in which testicular or ovarial fat was transplanted from 3—4-day old rats. In this study fat multiplied (Hausberger 1938). Homogenous fat transplants also had haemostatic properties (Ohkohchi 1914).

In histologic studies numerous polymorphonuclear cells were seen, and connective tissue divided the fat into small parts (Marx 1910). The middle part of the graft became gangrenous and there was cystic degeneration at the edges (Rehn 1912). Most authors found that the grafts were completely replaced by host connective tissue. Some research workers noted some adipose tissue growing from the host cells (Neuhof 1923).

Table 2. *Previous publications on autogenous fat transplantations in animals 1914—1975.*

Author and publication year	Purpose of the experiment	Transplantation from	to	Main observations and conclusions
Eden and Rehn 1914	To protect nerves and tendons against adhesions	Inguinal region of the rabbit	Around nerves and tendons	Fat is preserved and suitable. Observations over one year
Eisleb 1916	To study the fate of fat transplants	"	Knee joint	Fat is preserved and partly replaced by connective tissue
Lexer 1919	"	Inguinal region of the dog	To replace a dural or cerebral defect	Fat is preserved but shrinks a little
Hilse 1928	"	Inguinal region of the rabbit or abdominal wall of the dog	Liver, spleen, and kidney	At first degeneration, later regeneration to normal fat
Gurney 1937	"	Inguinal or testicular fat of the rat	Subcutaneous tissue of the thoracic wall	Graft vascularised within one week. Fat is preserved
Hausberger 1939, 1941	To study the fate of fat transplants in young animals	Testicular fat from a 3—6 day old rat	Subcutaneous tissue	Fat mass multiplied
Williams 1953	Do free fat transplants survive?	Abdominal fat, omentum and brown fat	Transparent chamber installed in the ear of the rabbit	Vascular system was preserved, and fat survived
Österman 1972	To prevent premature epiphyseal closure	Interscapular fat from rabbits	The epiphyseal plate of femur	Premature closure was prevented, and fat survived

Table 3. *Previous publications on homogenous fat transplantations in animals.*

Author and publication	Purpose of the experiment	Transplantation form	Transplantation to	Main observations and conclusions
Franco 1909	To study the biology of fat cells	Interscapular fat	Subcutaneous tissue of the rabbit ear	No difference between the autogenous and homogenous transplant.
Marx 1910	To study the fate of fat transplants	Not mentioned	Scleral cavity	Fat largely replaced by connective tissue
Rehn 1912	"	Inguinal region of the rabbit	Under the dorsal fascia	At first atrophy and then new fat lobules
Rehn 1913	To compare autogenous transplants with homogenous	" + that of the dog	To replace the dura	Autogenous fat without reaction. Homogenous with reaction or does not heal at all
Ohkohchi 1914	To demonstrate haemostatic properties of fat	Abdominal wall	Wounds in the kidney and the liver	The haemorrhage stopped
Bertocchi 1925	To study the fate of fat transplants	Different sites of the rabbit	Outer skin of the ear	Fat gradually replaced by connective tissue
Gurney 1937	"	Groin or peritoneal cavity of the rat	Anterior wall of the thorax	Fat disappeared
Hausberger 1938	To study the development of fat tissue	Testicular or ovarial fat from a 3—4 day old rat	Inner side of the abdominal wall	Fat cells are specific cells. The amount of fat multiplied 700 times
Hausberger 1941	To study the fate of fat transplants	Testicular or other fat from a 4—6 day old rat	Subcutaneous tissue	Fat replaced by connective tissue

2.2. Fat transplants in man

2.2.1. Clinical studies

2.2.1.1. Raising of facial depression

A patient had a scar below the eye. It was due to tuberculosis when the patient was young, resulting in adhesion of the skin to the bone. A free fat transplantation was performed for the first time on man and a cosmetic result was achieved (Neuber 1896). Similar reports were made by other authors (Silex 1896, Zoege-Manteuffel 1896, Axenfeld 1903). A large piece of fat (3 x 12 cm) from the abdominal coverings was transplanted to the face. Good results were achieved with the same technique for a receding chin, too (Lexer 1910). Fat from the thigh was transplanted to replace a removed frontal sinus. The result one year after the transplantation was excellent, though a small depression was visible at the transplantation site. Therefore, the use of a transplant larger than the estimated requirement is recommended (Marx 1910). A fat transplant was used for cosmetic correction of a frontal impression, saddle nose, sunken cheek and the submandibular area. The transplants shrank somewhat in volume and became more dense than they were originally (Lexer 1911). Fat from one cheek to another was transplanted and a satisfactory result was achieved (von Bramann 1911). Tissue defects in mandible and temple were successfully corrected by fat transplants. The results were good a few years after the operation (McArthur 1913, Stevenson 1949).

2.2.1.2. Repair of mammary gland defects

A lipoma from the lumbar region was transplanted into a breast excised for chronic cystic mastitis. A year after the operation this breast differed from the other only in its smaller size and darker colour (Czerny 1895, Lexer 1911). Two cases of transplantation of large grafts from the region of the trochanter major into the mammary gland to repair a defect caused by interstitial mastitis were reported. The amout of fat transplanted in one of them was the size of two fists (Klapp 1912). A case was reported in which a fist-sized fat transplant was used to replace a cyst in the breast. The result was excellent (Wrede 1927). When other tissues, such as fascia, were included with fat tissue in the graft, it decreased less than when there was no fascia (Figi 1931). A fat transplant from the exterior-posterior aspect of the thigh was taken and placed between the pectoralis fascia and the left breast. Another piece including fascia lata was transplanted to the right side. The first transplant diminished by two-thirds, the other one less (May 1941). Fat from the gluteal region was transplanted. It included skin from which the epidermis had been removed. The graft was placed on the pectoralis with the skin against the mammary tissue. Ninety per cent of the volume

of the transplant was preserved. The thinking behind his procedure was that this form of transplant includes a rich blood supply which promotes early and good circulation in the fat tissue (Bames 1953). A transplant for enlargement of the breasts lost one-fourth of its original size during the follow-up period of 6—9 months (Schörcher 1957).

2.2.1.3. Prevention of adhesions

Fat tissue was transplanted successfully to protect a nerve liberated from the callus, and another nerve sutured after the removal of a neurofibroma (McArthur 1913, Eden and Rehn 1914). Fat tissue was transplanted to the anterior and posterior surface of the quadriceps muscle to free it from the environment. The adhesions had been caused by suppurative myositis. The range of movement of the knee was restored (Mauclaire 1915). Fat tissue was sutured around the peroneal nerve. On growing in size, fat compressed the nerve. The consequence was weakening of the sense of feeling, corrected by removal of the transplant (Kölb 1916).

Fat was transplanted around the short and long flexor tendons of the thumb. The severed tendons had been repaired by suturing, after which adhesions had formed and the interphalangeal joint had become immobile. The fat transplant prevented re-formation of adhesions (Douglas 1920).

2.2.1.4. Articular surgery

A graft consisting of fascia lata and fat was transplanted into the shoulder joint, producing a painfree joint with normal mobility. A larger part of the graft was preserved when fascia was taken with the fat graft. The same technique was successfully used in other joints, too (Devine 1914). Normal mobility was restored to a stiffened elbow joint after transplantation of a fat graft (Wrede 1915). A study of 165 arthroplasties revealed good results in 128 cases (Lexer 1919).

2.2.1.5. Eye surgery

Fat tissue was successfully transplanted into the orbit after enucleation of the eye (Barraquer 1901). A fat transplantation was performed into the orbit after enucleation of the eye. The prosthesis survived well on the fat tissue and the cosmetic result was good three years postoperatively (Bartels 1908) Ten-year resluts from the Axenfeld clinic were reported. The transplants tended to shrink and the use of a larger graft than appeared to be indicated was recommended

(Verderame 1909).

2.2.1.6. Brain surgery

Fat from the upper arm was transplanted on the surface of the brain. A patient with cranial trauma suffering from neurologic symptoms made a good recovery (Rehn 1912). A successful transplantation of fat tissue to repair a meningeal defect was described (Smirnoff 1913). A patient with epilepsy was operated, revealing brain tissue attached to the skull. The scar was freed, a part of the dura was removed and a fascia-fat transplant from the thigh was inserted in its place with the fascia outwards. The patient's symptoms disappeared rapidly (Witzel 1915). A series of 49 patients was reported in whom large fat grafts had been transplanted at brain operations. The 5-year recovery rate was 40 per cent (Guleke 1933). All these studies possibly indicate that fat immediately replaced the scar and was preserved for several years.

2.2.1.7. Stemming haemorrhage

Omentum and subcutaneous fat were used successfully in gallstone and liver surgery to staunch bleeding (Hilse 1913). Perirenal fat was used to check haemorrhage in the hilar region of the kidney. A fat graft was successfully employed for the same purpose in liver and lung operations (Polenow 1913). The haemostatic quality of fat tissue is based on the fast attachment of fat to the bleeding site, preventing continuation of the bleeding (Lexer 1919).

2.2.1.8. Other surgery

Pieces of fat were successfully transplanted between the pleura and the ribs (Tuffier 1911). A good result was achieved in the treatment of tibial osteomyelitis with a fat graft (Hesse 1912). The umbilical hernia of an obese female patient was repaired by suturing a piece of fat measuring 3.5 x 12 x 15 cm to the edges of the hernial opening (Chaput 1913). A fat transplant was used to replace the mucosa of the urethra (Eden and Rehn 1914).

The fat transplant increased in size in the course of 48 hours and then decreased as its consistency became denser. A year postoperatively, connective tissue strands were seen in the fat tissue, which was either equally large or smaller than it had been at the initial operation (Julliard 1920). Small transplants were less successful than one large transplant. A fat transplant diminishes by two-thirds and it is advisable to use a sufficiently large transplant to achieve an optimal result (Lexer 1925). Successful use of fat tissue was made in operations for cleft palate (von

Gaza 1926). Fat tissue was also used for atrophy of the upper limb, lipodystrophy, congenital absence of the pectoralis muscle and in cases of underdevelopment of the mammary gland. The graft lost 50 per cent of its size. The importance of immediate transplantation to the desired site and an atraumatic technique was stressed because of the vulnerability of the graft (Peer 1950 and 1956).

2.2.2. Histology

The first histologic study was published in 1911 when Tuffier described sections of a fat graft transplanted four months earlier in the extrapleural space. He encountered fat cells which he considered were new and not present in the original graft. In an autogenous graft connective tissue strands with leucocytes in the middle of normal fat tissue were noted; the graft was encircled by a fibrotic capsule (Zipper 1912). Morestin's (1914) opinion was that nothing remains of a fat transplant. Pronounced leococyte infiltration into the transplant was observed 12 days after the operation (Eloesser 1915). A study was made of an autogenous fat transplant taken from the leg and grafted onto brain tissue. Part of the tissue had survived and part had disintegrated (Nieny 1917). A graft was removed from the brain 59 days after the transplantation. Normal fat tissue was seen in places and connective tissue proliferation and lymphocytic infiltration elsewhere (Martin 1919). Ten-week-old grafts from the brain were described which displayed destruction of fat cells, histiocytes and giant cells containing pieces of fat (Marchand 1919). The presence of normal fat tissue was reported in transplants around the nerves (Julliard 1920). Samples were taken at reoperations, the time interval from the initial operation being 5, 8 and 13 years. The size of the fat grafts in the brain had decreased, but microscopy disclosed normal fat tissue in addition to regeneration and degeneration (Gluleke 1933).

Peer (1950) and 1956) transplanted autogenous fat from the abdominal coverings to inside the sheath of the rectus. The transplant was cut into two equally large parts, one of which was divided into small pieces. Three such transplantations were made, and later six others in which a homograft was employed. The transplants were removed from three days to 14 months postoperatively. A connective tissue capsule was seen around the autograft with normal fat tissue inside it. No formation of new fat cells was seen. The graft transplanted in one piece lost only 45 per cent of its weight in a year or more. The graft divided into several parts lost a greater proportion of weight than the whole graft. Normal circulation between the organism and the graft was established four days after the transplantation. In homotransplantation the graft was replaced by fibrotic tissue.

2.3. Bone repair

2.3.1. Healing of fractures

A fracture is defined broadly as any break in the continuity of a bone (Lichtenstein 1970). Although the healing of a fracture is a continuous process (Ham 1969), it has been divided into three different stages (Bloom and Fawcett 1969):

(1) organization of hematoma at the fracture site (by granulation tissue and fibrous connective tissue), leading to procallus;

(2) conversion of procallus to fibrocartilaginous callus; and

(3) replacement by osseous callus, resulting in bony union.

2.3.1.1. Effects of the injury

When a fracture occurs there is both direct and indirect injury to tissue. The direct trauma breaks the bone and damages soft tissue associated with the bone. The blood vessels crossing the fracture line are torn and blood pours into the fracture area. This blood coagulates and forms a clot. The indirect injury depends on the fact that the ends of the torn blood vessels are sealed off, so that circulation stops. This causes death of tissue. The life of the osteocytes depends on the haversian vessels in which there are the central vessel and canaliculi. Circulation stops back to sites where the haversian vessels anastomose. These anastomoses are not abundant so that the osteocytes die for a considerable distance from each fragment. The same factors cause death of periosteal and marrow tissue. They do not die for a great distance because of better circulation. Dead bone is recognized as osteocytes undergo lysis ; hence the lacunae are empty. Before dissolving osteocytes may become pyknotic (Ham).

2.3.1.2. Callus and its origin

New tissue which forms a bridge between the fragments is termed callus. Many accounts describe the first step in the repair as depending on the invasion of the blood clot by new capillaries and fibroblasts (granulation tissue). The fate of this temporary callus is not certain. It may be replaced, or turns into permanent callus. In 48 hours after a fracture the cells responsible for the repair are actively dividing. These cells come from the deep layer of the periosteum, endosteum and the undifferentiated cells of bone marrow. As a result of this growth the fibrous layer of the periosteum is lifted away from the bone. When the osteogenic cells proliferate, the capillaries among them proliferate, but not so quickly as the cells. As a result the osteogenic cells more deeply

disposed (closest to the bone) differentiate in the presence of a good blood supply; consequently they become osteoblasts and form bony trabeculae. The osteogenic cells in the more superficial part do not have a good blood supply, so they differentiate into chondroblasts and chondrocytes. As a result, cartilage develops. The amount of cartilage probably depends on how quickly the callus grows. If it grows rapidly, capillaries cannot keep up with it, so much cartilage is formed. If callus tissue grows slowly, almost no cartilage is formed.

2.3.1.3. The fate of the cartilage and remodelling

Those cartilage cells that are closest to the newly formed bone begin to secrete phosphatase, which causes calcification of the intercellular substance and the death of the cells. The calcified cartilage is progressively replaced by bone, so finally the cartilage is completely replaced by cancellous bone. Between new bone trabeculae there are areas of dead bone which is dissolved. New bone occupies this area. The cancellous bone directly between the two fragments and around their immediate periphery is converted into compact bone. This makes the bone so strong that the trabeculae in the periphery are no longer necessary. They are gradually resorbed.

2.3.1.4. Non-union

When the fracture does not heal we speak of non-union. There are several causes of non-union: inadequate immobilisation, extensive loss of bone, poor apposition, interposition, inadequate blood supply, excessive resorption of fractured bone ends, old age, faulty nutrition, serious systemic disease, infection, etc. The gap between the fractured bone ends is filled by vascularized fibrous connective tissue. Although this tissue is rich in capillaries and sometimes contains small inactive foci of cartilage, there is little or no bone formation. Focal deposition of fibrinoid material, myxoid degeneration and cystic softening may be noted. They may lead to the formation of a sinuous cleft-like space referred to as a pseudoarthrosis. Its lining may resemble synovium (Lichtenstein).

2.3.2. Effect of cortisone

Several studies concerning the effect of cortisone have been made. In one study sixteen rabbits were subjected to fractures of the femur. Eight of these were under treatment with intramuscular injections of cortisone. Healing of the fracture and absorption of the hematoma were delayed in the animals receiving cortisone (Blunt et al. 1950). In another

investigation of the effects of cortisone on the healing of fractures in rabbits, all the histological processes of repair in bone were retarded (Sissons and Hadfield 1951—52). In rats the administration of from two to four milligrams of cortisone intramuscularly daily did not delay the healing of experimental fractures (Key et al. 1952). In a quantitative study on rats it was found out that the formation of new bone is late in starting, and poor when the rats were given cortisone, compared with the control group (Koskinen 1959). The callus also remained small in size throughout the repair process in the cortisone group, and fibrous tissue constituted the dominant component.

Both systemic and local use of corticosteroids is able to impair granulation tissue formation (Newcombe 1972). The effect of intramuscular cortisone was studied in rabbit ear chambers (Ashton and Cook 1952) and it was found to cause vascular constriction, which was thought to be an important factor in the inhibition of repair processes. Parenterally administered cortisone prevented the formation of granulation tissue and adhesions around traumatized tendons in rabbits and dogs (Carstam 1952, Wrenn et al. 1954). The local use of hydrocortisone did not improve the function of tendons in dogs (Gonzalez 1953).

2.3.3. Spongostan and its effects

Spongostan (Ferrosan) is a gelatine sponge which is sterilized, hardened, made porous by air bubbles and dried (Mayer 1952). Gelatin has been used in surgery for 30 years (Rauch 1958). There are various absorbable hemostatic agents (Corell et al. 1945) but gelatin was chosen because it is easily obtainable and non-antigenic.

Gelatin has been successful in correcting dural defects in neurosurgery (Pilcher and Meacham 1945, Light and Prentice 1945). Other indications in this field of surgery are the hemostasis of epidural veins, under the bony margins when closing a bone lambo, diffuse bleeding from a tumour cavity and epidural bleeding in the spinal canal. Other fields of surgery in which gelatin is useful are operations on parenchymatous organs (Jenkins and Janda 1946), blood vessels, anus and rectum, otorhinolaryngology (Senturia et al. 1950), stomatology and plastic surgery (Fabri 1971).

Gelatin was used as vehicle for minerals, sulfonamides and penicillin to fill bone cavities (Schram and Fosdick 1943). Spongostan was placed into large cavities of bone left by the enucleation of cysts and tumours of the jaws. It acted as a space obliterator, and after absorption and replacement by fibrous tissue, it incorporated into bone (Thoma and Sleeper 1948. Rossi 1952).

The cellular reaction of Spongostan is slight (Bing 1947). At first there

is a moderate leucocytic reaction. Later on there will be macrophages and giant-cells. Then connective tissue migrates into the sponge, which will be absorbed at a velocity varying with the degree to which it has been hardened. Usually the sponge will be absorbed in about a month. In the event of a strong infection, absorption will be much quicker.

3. OWN STUDIES

3.1. Material

The experimental animals were 145 rabbits whose pre-operative weight ranged from 1,700 to 3,940 g. Their sex was not recorded. Their age varied from five to eight months.

3.2. Methods

3.2.1. Anaesthesia

The premedication for one-third of the rabbits was 0.3 mg of atropine-sulphate (Atropin, Orion) and 3 mg of pethidine chloride (Petidin mite, Star) intramuscularly. The rest of the animals were given only the former. The drug was administered 30 min. before the operation. Actual anaesthesia was started with Nembutal (Abbott) containing 50 mg/ml of mebumal sodium. Doses up fo 30 mg/kg were injected into the limbic vein of the ear lobe after depilation and sterilisation of the injection site with 0.1 per cen benzalkonium chloride.

In addition to general anaesthesia, local anaesthesia was used when the rabbit had been placed on the operating table. Approx. 5 ml of 0.5 per cent Xylocain-Exadrin (Astra) was infiltrated into the operative area. This substance contains lidocain chloride and adrenalin. The latter also improved haemostasis.

3.2.2. Operation

A median incision was made along the spinous processes to the lumbosacral region (Craigie 1969). After cutting through the skin and the subcutaneous tissue, the fascia of the muscle was opened from the left of the spinous processes. The muscles were pulled aside laterally to expose the spinous processes and vertebral arches. A small retractor was inserted into the wound and an oval defect of approx. 3 x 10 mm was drilled in the lamina with a dentist's drill. The size of the laminectomy varied. Small defects were made, especially at the beginning, and in some cases the spinous process was removed and a large laminectomy made. Bone wax was used only in a few cases to stop

bleeding from the bone. Gelatin sponge (Spongostan Standard, Ferrosan) was also used occasionally for haemostasis. A second similar laminectomy was made with one intact vertebra between the laminectomies (Fig. 1). This served as a "control site" (definition in Table 4. The drill bit was cooled occasionally with saline. Care was taken while drilling not to damage the spinal dura underneath

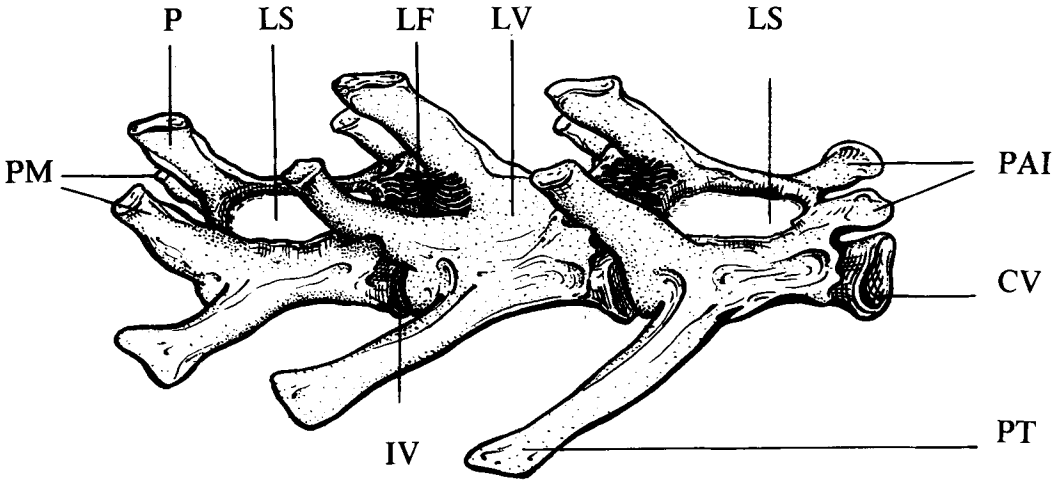

Fig. 1. A drawing of the laminectomy sites (LS) in the spinal column of a rabbit. CV = vertebral body, IV = intervertebral disc, LF = ligamentum flavum, LV = lamina of vertebral arch, PAI = inferior articular process, PM = mamillary process, P = spinous process, PT = transverse process.

the bone. The part of the arch drilled off was removed cautiously with a narrow dissector. A second incision was made in the median line between the scapulae. There was always subcutaneous fat tissue available in this region, but only a thin layer in the lumbar region. Pieces of fat tissue of different sizes were taken. They were weighed at the first two operations. The weights ranged from 260 to 1,054 mg, mean 620 mg. The fat tissue was transplanted onto the spinal dura. The wounds were then closed in the following way: The wound in the dorsal area was closed with a continuous suture of 3-0 mercelene (Ethicon) or supramide (SSC) of the same strength. In the lumbar region the wound was closed by placing a continuous 3-0 chromium catgut (Ethicon) suture in the muscular layer and closing the skin in the same way as the dorsal wound. For the sake of later orientation, a metal suture of 3-0 steel wire was placed in the muscle near the middle of the intact

vertebra between the hemilaminectomies. The skin was dried, cleansed and covered with Nobecutan (Bofors) of Scan film (Johanson & Johanson). No bandages were used.

This was the technique for the pilot series and the first series. The procedure was similar for the other five series, but now the elements in the two laminectomy sites were defined (Table 4). The examination and control sites in cranial and caudal laminectomies were changed in turns. The cortisone preparation used was Depo-Medrol (Upjohn), 0.1 ml of which was administered per laminectomy. 1 ml contains 40 mg of methylprednisolone acetate.

Table 4. *Examination and control elements in different series. The difference between the fourth and fifth series was in the observation time (1—2 and 4 months respectively). Empty means that the lamincetomy site was left to fill with blood and serum.*

Series number	Examination site	Control site
1	fat	empty
2	fat	fat and cortisone
3	cortisone	empty
4	fat and cortisone	empty
5	fat and cortisone	empty
6	fat	Spongostan

3.2.3. Postoperative follow-up

The animal was kept alone in its cage for a few days. Usually it soon began to move and to eat normally. However, some complications occurred (Table 5). Paralysis (4 cases) was observed, especially after the first operations, probably owing to poor operative technique. Infections were established in the wound areas and obviously also in the urinary tract of the animals affected with paresis. They were generally treated with sulphonamid or penicillin. If the wound infection was a deep one and reached the laminectomy site, the animal was excluded from the

final study (8 cases). The condition of some animals deteriorated so much that they were killed before the planned follow-up period ended. Some animals died from an unknown cause and some during the anesthesia, so that altogether 24 premature deaths occurred.

The follow-up was from one to two months in all series except the fifth, where it was about four months.

Table 5. *Complications of the 129 operated rabbits, on which two partial laminectomies each were perfomed.*

Number of series	Number of rabbits					
	Operated	Premature deaths	Wound infections	Paralysis	Sections taken from wrong site	Included in final study
1	20	3	1	2	1	13
2	24	5	1	2	0	16
3	23	6	1	0	0	16
4	20	3	2	0	0	15
5	20	6	2	0	0	12
6	22	1	1	0	0	20
Total	129	24	8	4	1	92

3.2.4. Sacrifice

Before the rabbits were sacrificed they were weighed and a note was made of their general condition, mobility, possible pareses and infections. The hair had grown almost completely in the operative area. The scar was usually neat, often almost unnoticeable.

Anaesthesia was conducted as at the operation, but sterility was disregarded and a greater quantity of barbiturate was administered to put the animal into deep sleep. Air was then injected through the same needle so that the rabbit died almost immediately. The operative area was denuded of hair and sutures. The skin incision was made at the same point as before in the lumbar region. The operative area was localised by the metal suture, which was generally easy to find. The spinal column was cut at both ends of the operative area so that at least the excised vertebrae were included in their entirety in the preparation. The cranial part of the specimen was marked with a pin and the entire spinal

column and part of the muscles were immersed in 10 per cent formaldehyde solution.

3.2.5. Decalcification and sections

After approx. 10 days in formaldehyde solution the specimens were transferred to a 32 per cent EDTA solution, pH 7.2—7.4. This procedure was used with the first specimens, which accounted for about one-fifth of the material. After that, formic acid and sodium formiate were used as they permit faster decalcification. The softening of the specimens was followed and a suitable state of decalcification was evaluated by bending the sample. It was generally easy to cut, once the preparation had become pliable. The former method required a couple of months, the latter approx. three weeks.

The specimen was then cut with a scalpel in the middle of the intact vertebra between the laminectomies. The metal thread marker was removed and the two tissue pieces produced in this way were reduced in size and left to decalcify for a few more days. The reduction was performed so that one side formed a surface from which the microscopical sections were cut later. The plane of the surface was cut in such a way that the microscopical section included the fat graft and the spinal cord.

About 20 sections were taken from each laminectomy site. One half of them were stained by hematoxylin-eosin and the other by van Gieson. In the microscopical study magnifications from 25 to 400 were used.

3.3. Results

They are first dealt with separately in each series and then in a summary. Results are documented as micrographs. They have been chosen so that the structures mentioned in the text are clearly seen and the sections taken from these animals are technically the most complete.

3.3.1. Pilot study

The technique has been described on pate 21. It was followed for all the animals, but it was not yet established in the first experimental animals. A chisel was used before adopting a dentist's drill. The chisel posed difficulties because the lamina was so thin. The holes in it were small at first, which made results difficult to assess. The first 16 rabbits were therefore placed in a separate pilot series. However, it was possible to see even in these specimens that the fat tissue had survived and prevented the formation of scar tissue.

3.3.2. The first series (fat and control)

This series comprised 13 rabbits. The comparison in this series was between two laminectomy defects, in one of which fat had been implanted and in the other not. The preoperative weight range of the animals was from 2,000 to 3,070 g, mean 2,450 g. At the time of sacrifice the weight was 1,420—3,330 g, mean 2,520 g. The follow-up period ranged from 31 to 84 days (Table 6).

Table 6. *Abbreviations used in the micrographs in alphabetic order.*

Abbreviation	Term in the text
B	bone
BM	bone marrow
BT	bone trabecle
BV	blood vessel
C	connective tissue capsule
CA	cartilage
CI	cellular infiltration
CV	vertebral body
D	dura
F	fat graft
FC	fat cyst
G	giant cell
IV	intervertebral disc
M	medulla
MU	muscle
P	spinous process
S	scar
SS	connective tissue septum

The height and width of the fat graft were measured from the sections on graph paper, making the measurement at a site which corresponded to the mean since the fat in the section often did not form a rectangle. The mean height was 6 mm, mean length 9 mm.

In microscopic sections the fat graft was seen as a light area (Fig. 2). Other structures could also be recognized surrouding the transplant: spinal dura as a thin line at the bottom edge, muscle at the top and spinal processes at the side edges. In Table 6 the abbreviations used in the micrographs are presented. With a bigger magnification it was easy to recognize typical fat cells in the lower micropraph of the same figure. In this micrograph it was possible to see how the fat tissue was lying closely on the dura.

When a greater magnification was used the junction between the fat graft and the dura could be studied in further detail (Fig. 3). A connective tissue capsule was surrounding the fat graft and the capsule was attached to the dura. Single fat cells were easy to recognize.

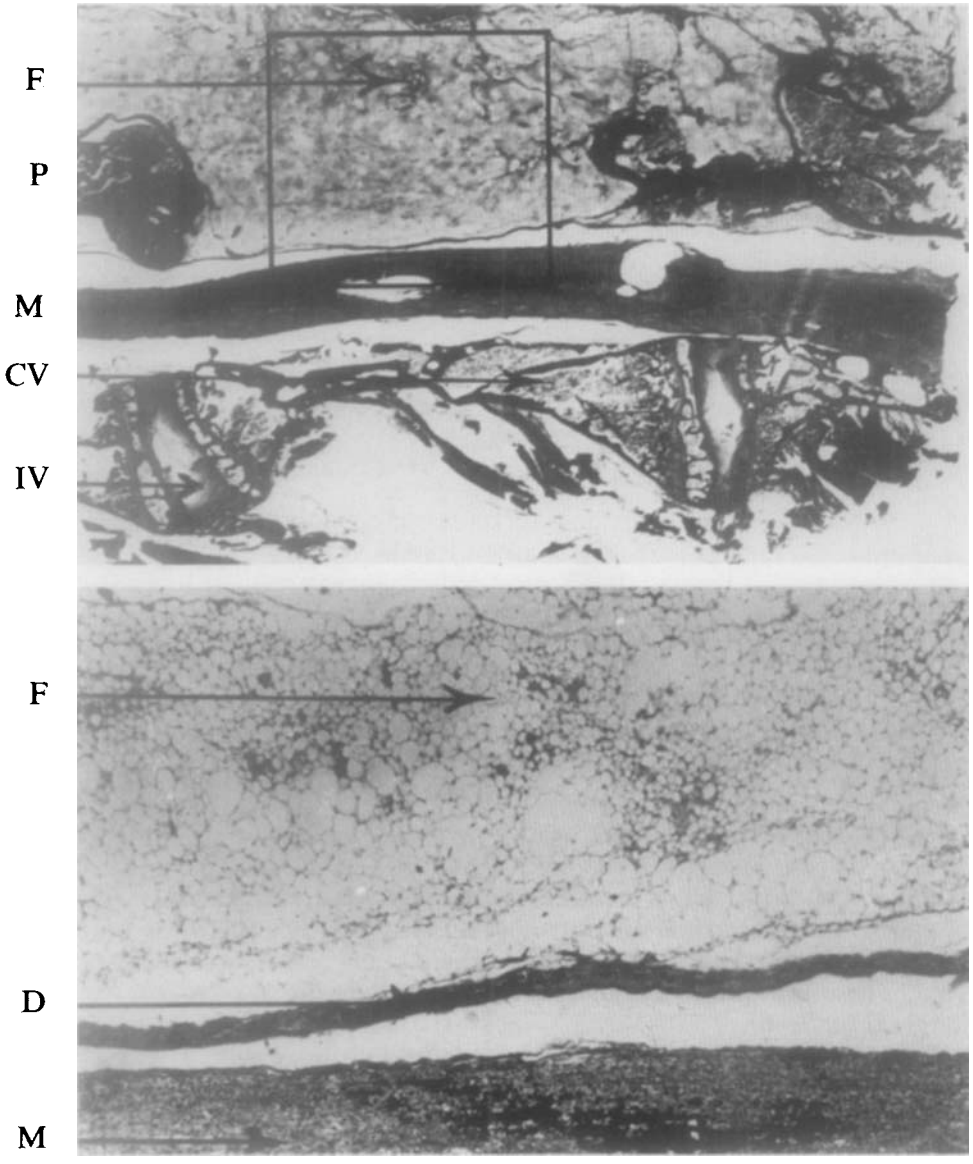

Fig. 2. Two photographs of a section from a rabbit in the first series (magnification x 4 and 40). A fat graft (F) was transplanted on the dura (D), observation time being 82 days. The close contact between the graft and the dura is seen. P = spinous process, M = medulla, CV = corpus vertebrae, IV = intervertebral disc.

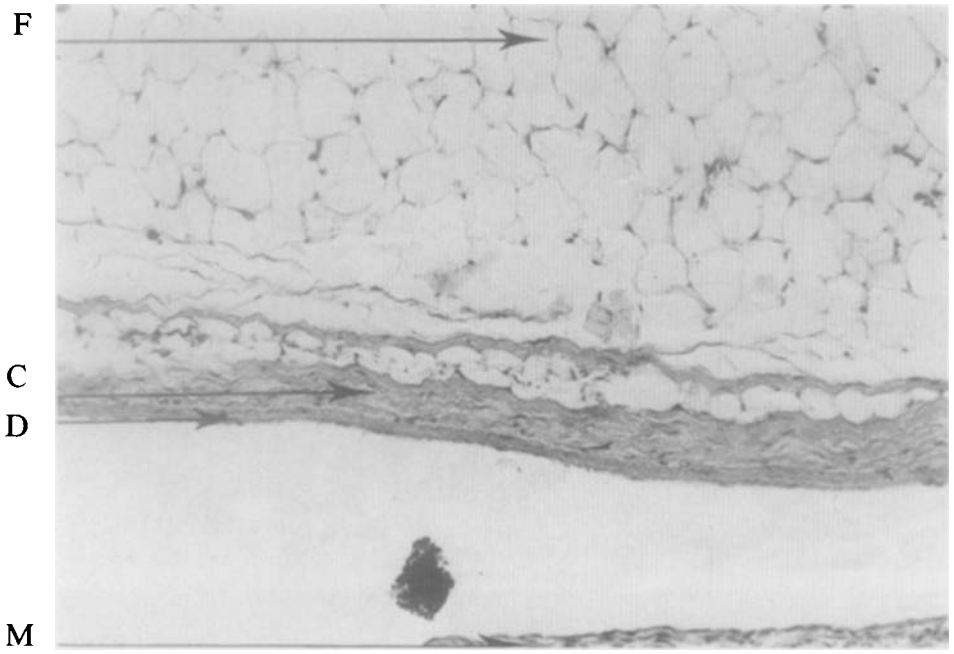

Fig. 3. A micrograph of a rabbit in the first series (x 100). A piece of fat tissue (F) was followed up 82 days. It is seen on the dura (D). Only a thin capsule (C) is separating fat cells from the dura. M=medulla.

In the marginal parts of the graft away from the dura (Fig. 4) plenty of fat cysts containing free fat could be seen. Many giant cells were also seen and cell infiltrations containing macrophages and white cells. The connective tissue capsule was surrounding the graft. The follow-up time was short (31 days) and especially then these kinds of elements could be seen. These inflammatory changes were less when the observation was longer (Fig. 5—6).

In the control laminectomy site (definition in Table 4 p. 23) connective tissue -like structures and bone could be seen (Fig. 7). With a microscope it was easier to be convinced about the scar tissue and bone. The dura seemed to be attached to the scar and bone. With a higher magnification it was possible to see the single cells and the intimate contact between the scar and the dura (Fig. 8). Cartilaginous cells were seen beside the bone cells joining them to fibrocytes. It was thus easy to understand how the scar tissue could be replaced by bone (Fig. 9).

Observation times and histologic findings are summarized in Table 7, where it can be seen that the transplanted fat tissue was preserved and prevented scar tissue

formation to the dura. In the control laminectomy site in which a haematoma or seroma was left on the dura there was scar and bone. In rabbits with longer observation times there seemed to be less reactive changes in the fat grafts than in rabbits with short observation times.

Table 7. *Results of the first series (fat application and control). On each rabbit partial laminectomy was carried out on two vertebrae. In one of the laminectomy sites a piece of fat tissue was placed on the dura, the other site was left to fill with blood or serum.*

Observation time (days)	Histologic findings at laminectomy site		No of rabbit
	fat	control	
31	fat + reaction	scar + bone	25
31	fat + reaction	scar + bone	26
31	fat + reaction	scar + bone	29
31	fat + reaction	scar + bone	30
31	fat + reaction	scar + bone	31
31	fat + reaction	scar	32
44	fat + reaction	bone + scar	81
55	fat	bone + scar	100
63	fat + reaction	scar + bone	28
64	fat	bone	18
68	fat	scar	22
82	fat	scar + bone	19
84	fat	bone + scar	17

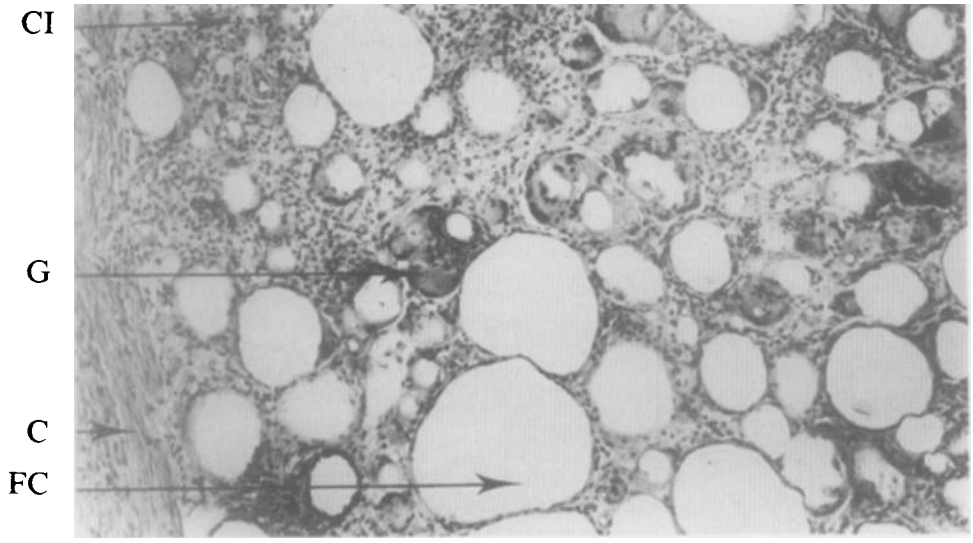

Fig. 4. The marginal part of a fat graft (x 100) 31 days after the transplantation (the first series). Cell infiltrations (CI) containing macrophages and leucocytes are seen. There are also plenty of giant cells (G) and fat cysts (FC). A capsule (C) surrounds the graft.

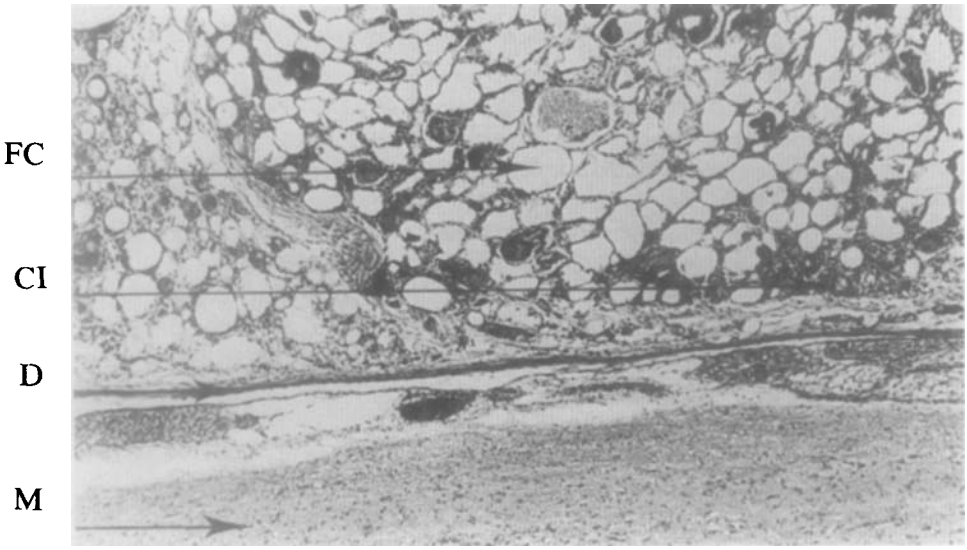

Fig. 5. A micrograph of a rabbit in the first series (x 40). A fat graft was followed up 31 days. Plenty of reactive changes are seen, such as cellular infiltration (CI) and fat cysts (FC). D=dura, M=medulla.

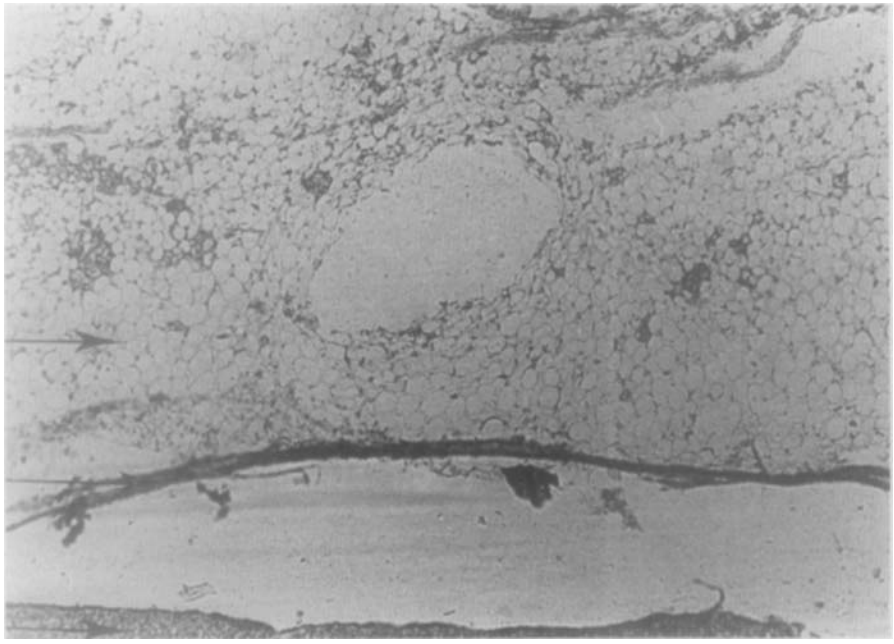

Fig. 6. A micrograph of a rabbit in the first series (x 40). A fat graft (F) was followed up 84 days. There are considerably less reactive changes in this section compared with Fig. 5, in which the observation time was shorter (31 days). D=dura, M=medulla.

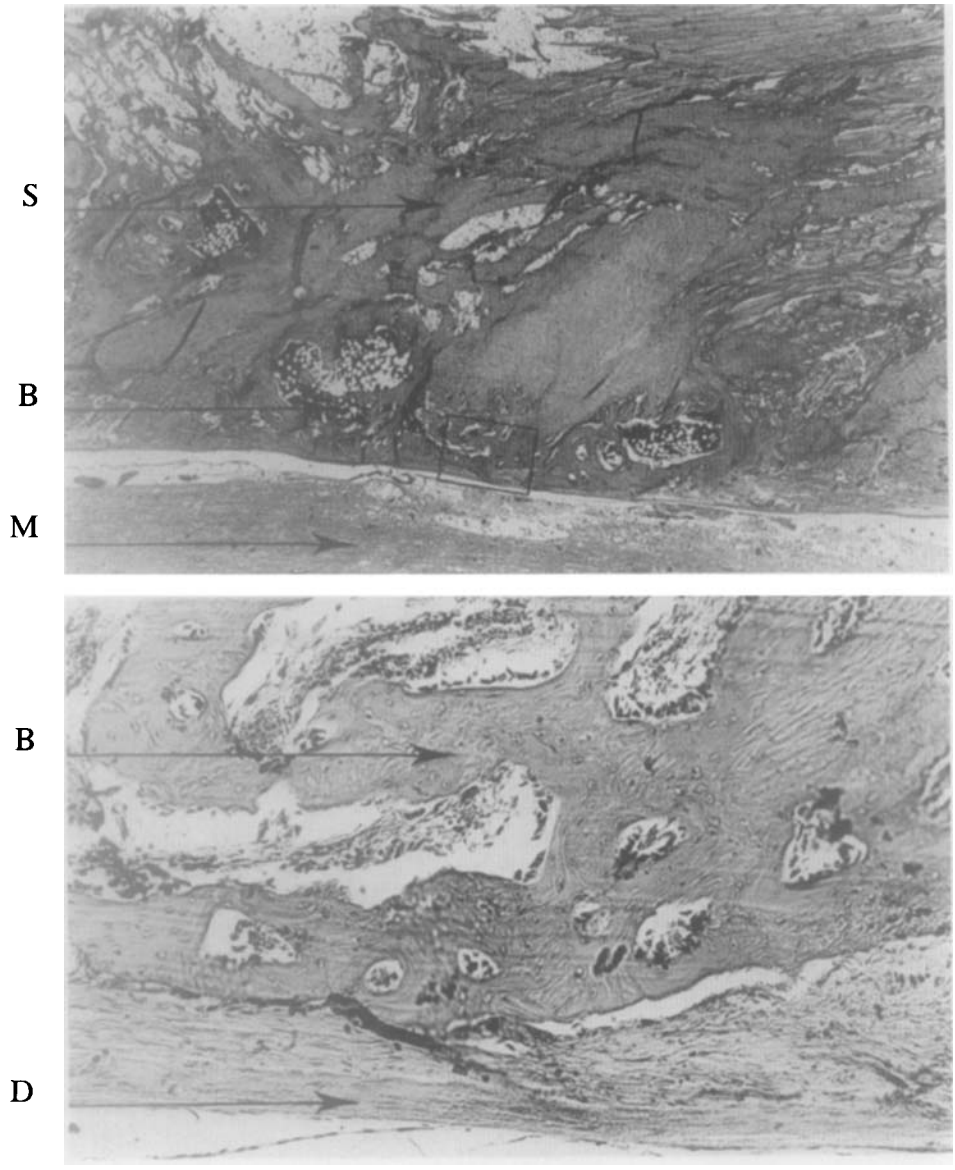

Fig. 7. Two photographs of a rabbit in the first series (without microscope and x 40). In the laminectomy site which was left to fill with blood and serum, scar (S) and bone (B) formation are seen. Bone and dura (D) are in close contact. M = medulla.

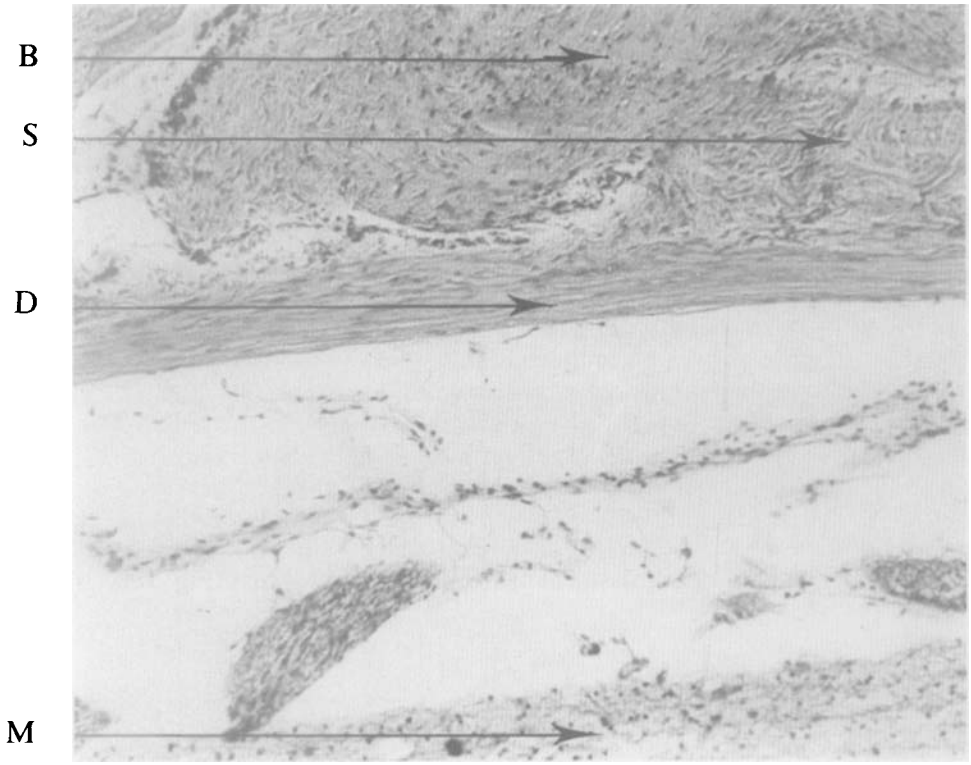

Fig. 8. A micrograph (x 100) of a rabbit in the first series (follow-up time 82 days). The laminectomy site left to fill with blood and serum illustrates the close contact of bone (B) and scar (S) to dura (D). M = medulla.

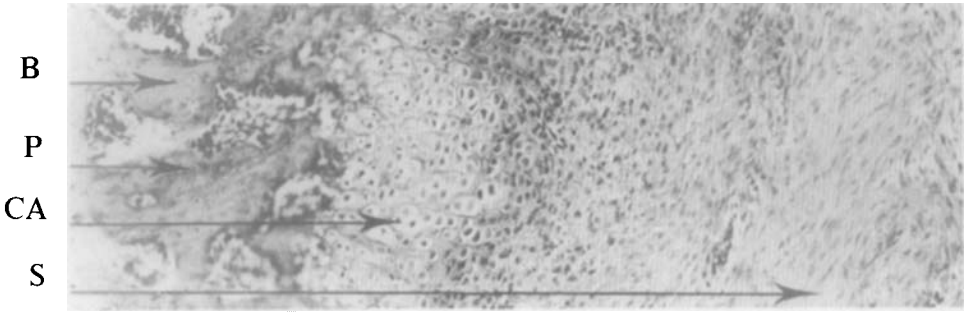

Fig. 9. A micrograph (x 100) of a marginal part of a laminectomy site near a spinous process (P) on the left. We can see bone (B), cartilage (CA), and scar (S). Observation time was 31 days (the first series). This laminectomy site was left to fill with blood and serum.

3.3.3. The second series (fat and fat + cortisone)

Sixteen rabbits belonged to this series. The histologic pattern of the operative areas to which fat had been transplanted was compared with the pattern which originated when cortisone installation was combined with the fat transplant. The preoperative weight of the rabbits was 2,110—2,650 g, mean 2,380 g. The lowest recorded weight at the time of sacrifice was 1,920, the highest 2,860 and the mean 2,420 g. The follow-up period in this group ranged from 31 to 52 days. The height and length of the fat in the sections was measured in the same way as before on page 26: height x length was 5 x 8 mm on average in cranial laminectomy site and 4 x 8 mm in caudal.

In histologic analysis the fat grafts were seen on the dura (Fig. 10—11). They showed clearly the close contact between them and the dura. The fat grafts consisted usually of almost nothing else but typical fat cells (Fig. 12—13) especially in the central parts of the grafts. However, cell infiltrations of leucocytes and macrophages, giant cells and fat cysts were often seen (Fig. 14), particularly in the marginal parts of the grafts. A connective tissue capsule encircled the grafts (Fig. 13).

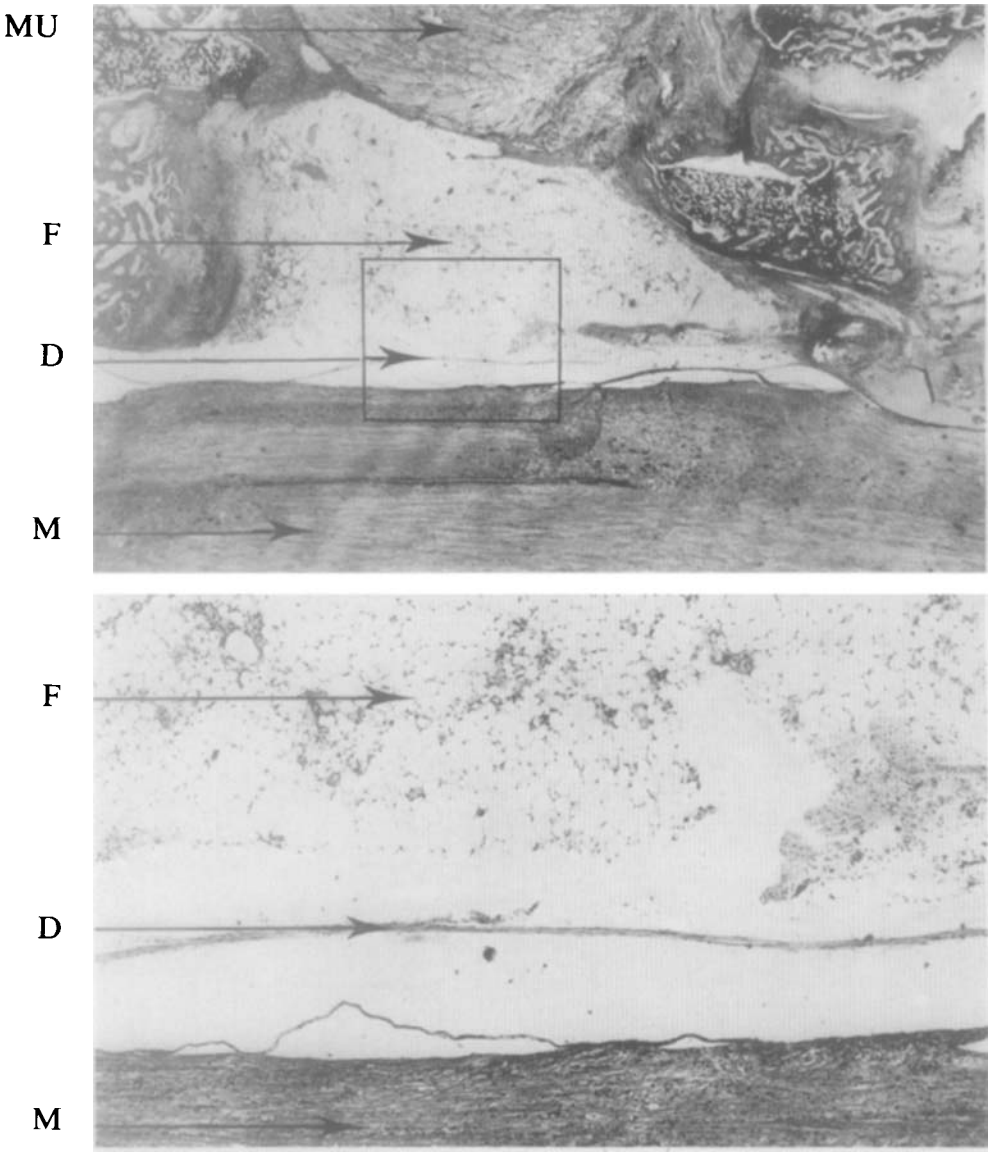

Fig. 10. Two micrographs of a section from a rabbit in the second series. Follow-up time was 51 days from the laminectomy in which fat tissue was transplanted onto the dura (magnification x 4 and 40). Fat tissue (F) is observed on the dura (D), which is better seen in the lower picture. MU=muscle, M=medulla.

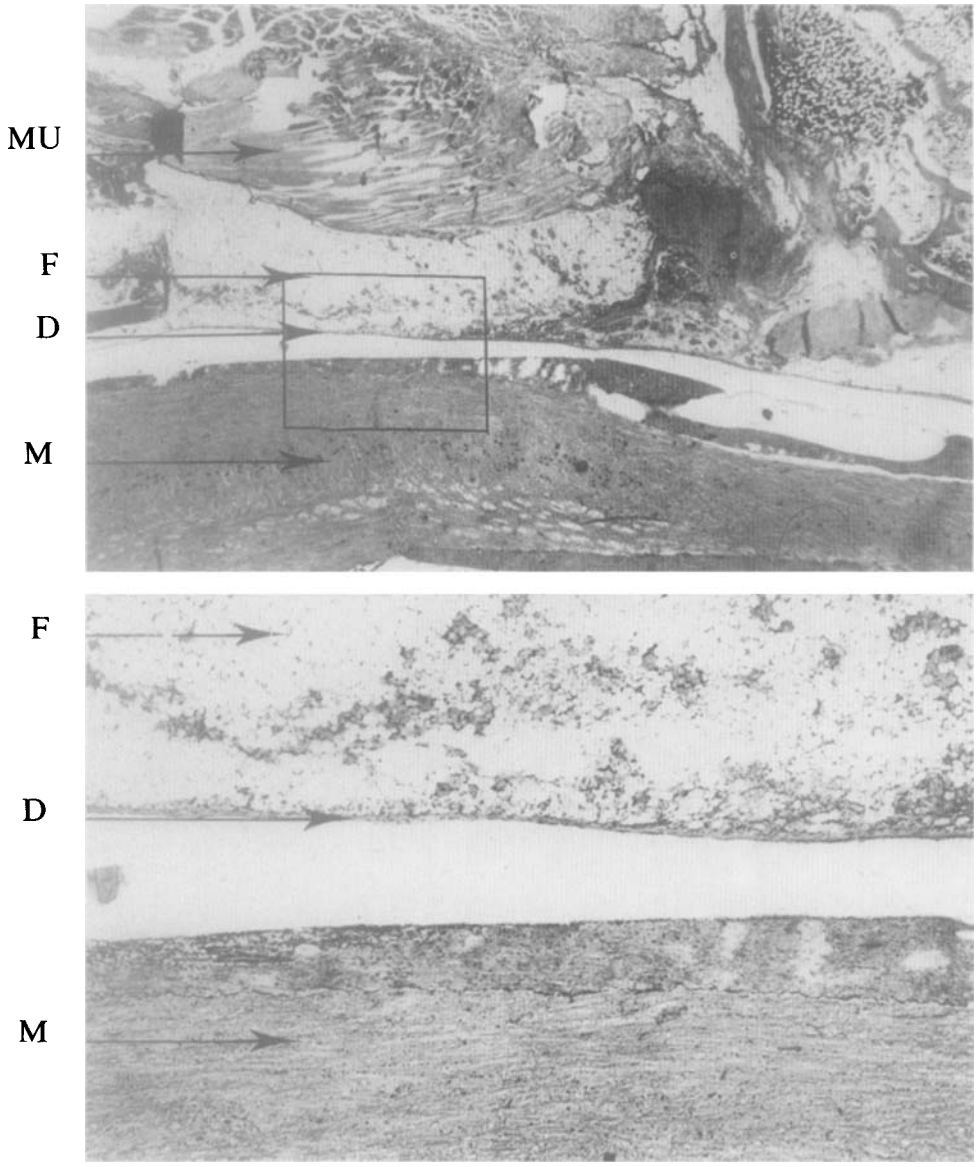

Fig. 11. Two micrographs of a section from a rabbit in the second series. Follow-up time was 51 days. Fat tissue and cortisone were put into the laminectomy site (x 4 and 40). Fat tissue (F) is observed, and the graft is lying on the dura (D). No significant difference is found between this graft with cortisone compared with the graft without cortisone in Fig. 10. MU = muscle, M = medulla.

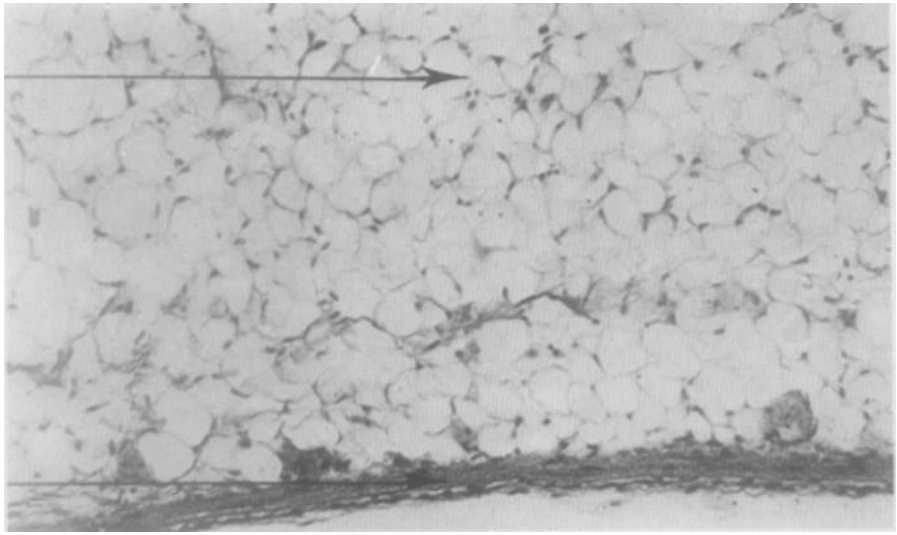

Fig. 12. A micrograph of a rabbit in the second series (magnification x 100). The observation time was 36 days. The picture presents the area on which fat tissue (F) and cortisone were placed. D=dura.

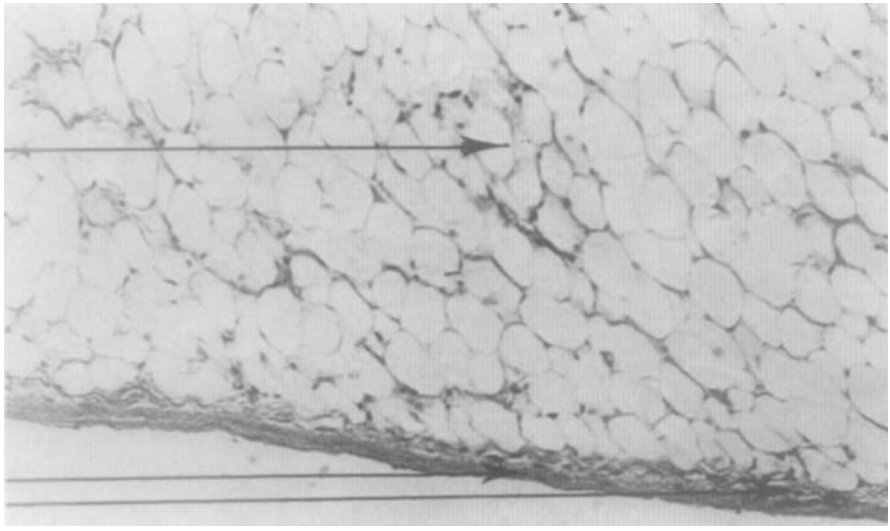

Fig. 13. A micrograph of a rabbit in the second series (magnification x 100). The observation was 36 days. A fat graft (F) without cortisone was transplanted on the dura (D). A part of the graft is seen and it looks similar to the graft with cortisone in Fig. 12. C = connective tissue capsule.

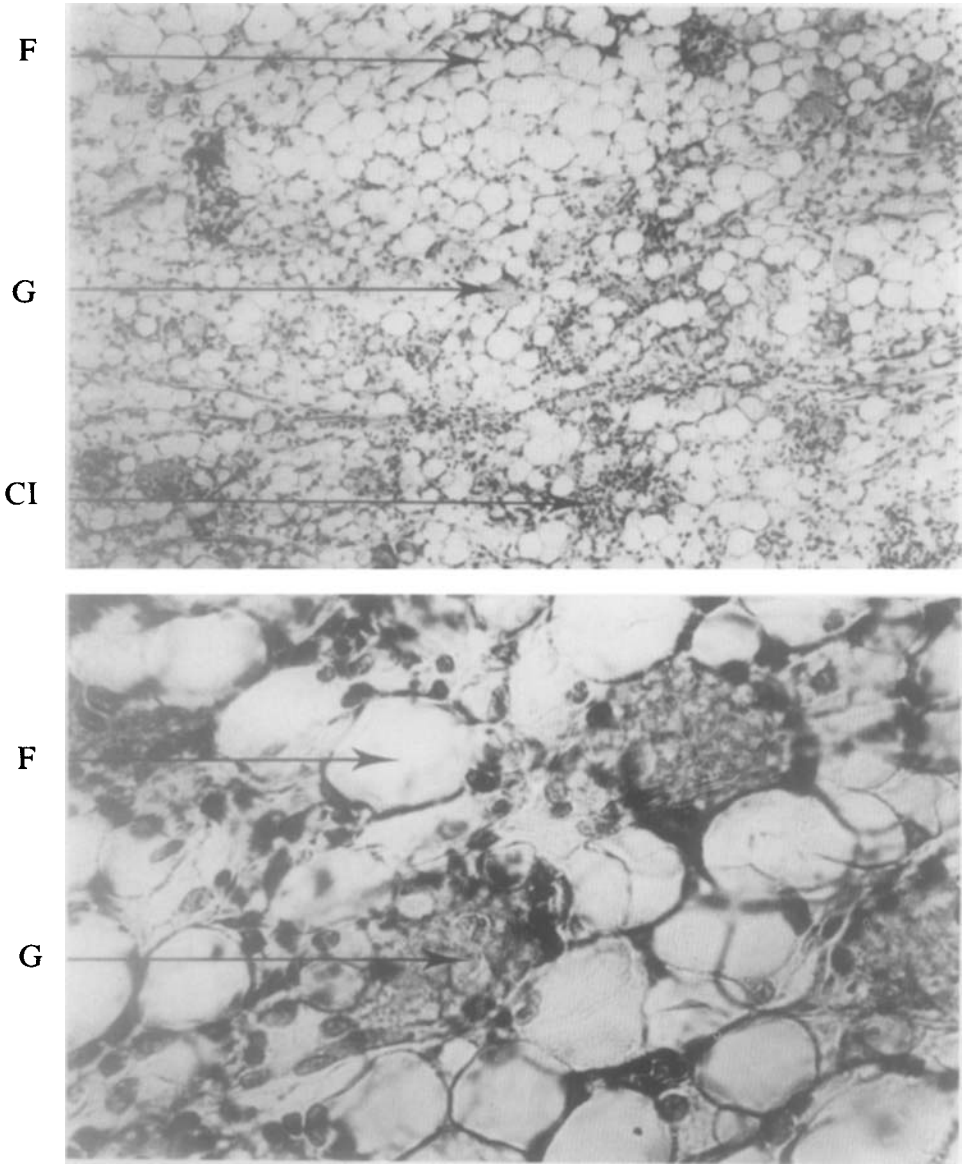

Fig. 14. Two micrographs of a section from a rabbit in the second series (magnification x 100 and 400). Fat tissue and cortisone were transplanted on the dura. The follow-up time was 34 days. A fat graft (F) in which giant cells (G) and cellular infiltration (CI) are seen in addition to fat cells.

In Table 8 the results of the second series are summarized. Fat tissue was preserved in every laminectomy site and there seemed to be no definite and regularly appearing histologic difference between the usual fat graft and the graft with cortisone.

Table 8. *Results of the second series (fat application and fat + cortisone).*

On each rabbit partial laminectomy was carried out on two vertebrae. In one of the laminectomy sites a piece of fat tissue was placed on the dura, in the other fat tissue + cortisone was placed on the dura.

Observation time (days)	Histologic findings at laminectomy site		No of rabbit
	fat	fat + cortisone	
31	fat + reaction	fat + reaction	37
33	fat + reaction	fat + reaction	39
33	fat + reaction	fat + reaction	41
34	fat + reaction	fat	34
34	fat + reaction	fat + reaction	35
34	fat + reaction	fat + reaction	38
36	fat	fat	106
41	fat + reaction	fat + reaction	48
46	fat + reaction	fat + reaction	52
46	fat + reaction	fat + reaction	53
46	fat + reaction	fat + reaction	54
48	fat + reaction	fat + reaction	51
49	fat + reaction	fat + reaction	45
51	fat	fat	46
52	fat + reaction	fat + reaction	43
52	fat + reaction	fat + reaction	44

3.3.4. The third series (cortisone and control)

This group comprised 16 rabbits. The comparison in this series was between two laminectony defects in one of which cortisone (Depo-Medrol 0,1 ml) was instilled onto the dura and the other site was left to fill with blood or serum. The preoperative weight of the animal was 1,940—2,690 g, mean 2,310 g. The weight at the time of sacrifice varied from 1,850 to 2,730 g, mean 2,360 g. The follow-up time was from 49 to 61 days.

In histologic examinations scar and bone could usually be found in the laminectomy sites (Fig. 15—16). There was often more scar than bone formation when cortisone was added compared with the laminectomy site left empty. Another example of that finding is presented in Figs 17 and 18. The scar or bone tissue was usually contiguous to the dura (Fig. 15—20). The bone formation was sometimes very abundant so that it was much thicker than the usual lamina (Fig. 16).

The results of this series are summarized in Table 9. S c a r a n d / o r b o n e w a s f o u n d i n e v e r y l a m i n e c t o m y s i t e.

3.3.5. The fourth series (fat + cortisone and control)

This group consisted of 15 rabbits. They were used to compare the histologic patterns at two laminectomy sites, one given fat + cortisone and the other nothing. The preoperative weight of the rabbits ranged from 1,900 to 2,420 g, mean 2,160 g. At the time of sacrifice the weight range was 1,810—2,550 g, mean 2,210 g. The follow-up period lasted from 31 to 59 days. The fat measured 6 x 9 mm on average in the longitudinal cross section of the preparation.

When the sections were studied in the microscope a piece of fat could usually be seen on the dura (Fig. 21). In control sections the laminectomy site was occupied by bone and scar (Fig. 22). In larger magnifications typical fat cells and bone structure could be identified (Fig. 23—24).

The results are summarized in Table 10, where it can be seen that i n e v e r y f a t t r a n s p l a n t w i t h c o r t i s o n e, f a t t i s s u e w a s p r e s e r v e d and the control laminectomy site was filled with scar and/or bone.

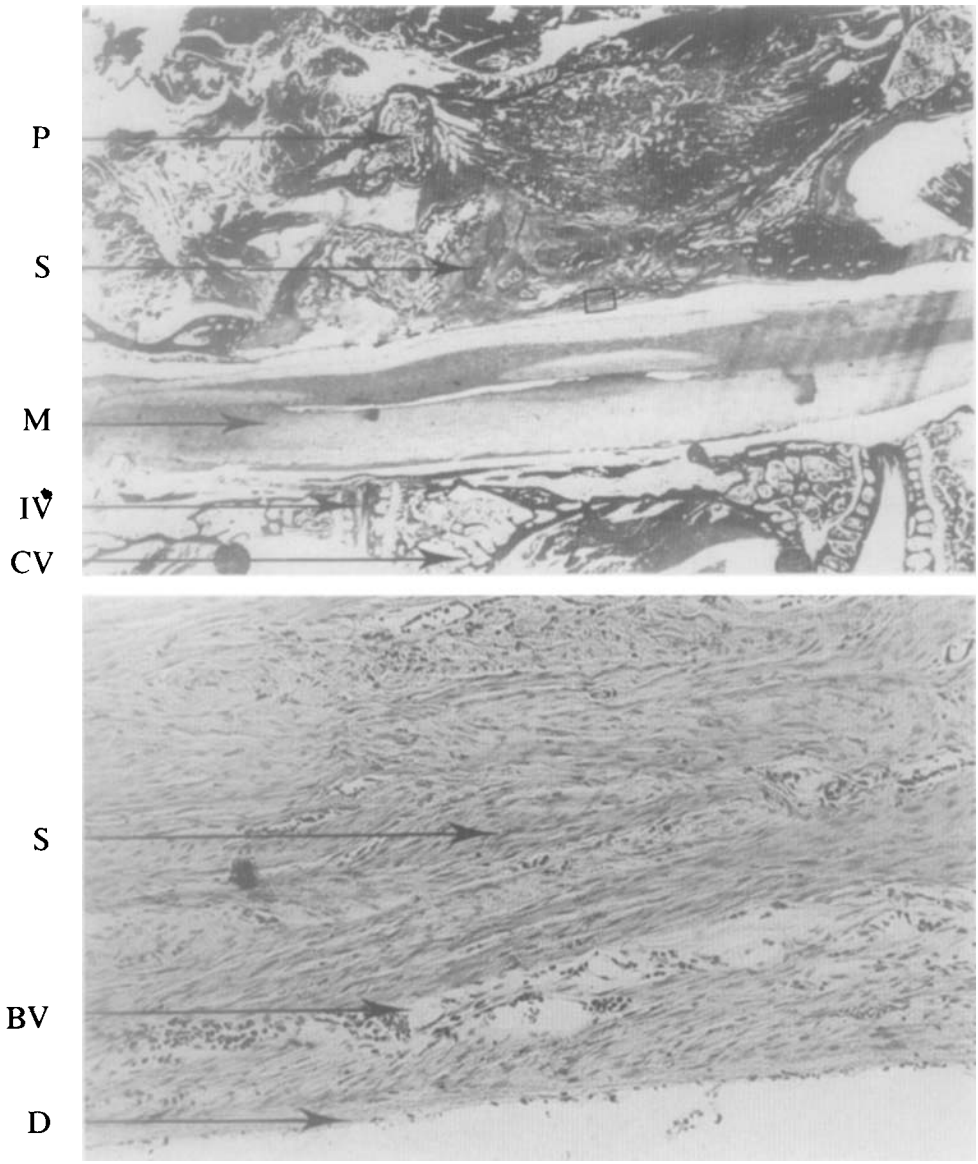

Fig. 15. Two photographs of a section from a rabbit in the third series. In this case cortisone was instilled onto the dura, the observation time being 52 days (x 4 and 100). Scar tissue (S) is seen in the laminectomy site contiguous to the dura (D). P = spinous process, M = medulla, IV = intervertebral disc. CV = vertebral body. BV = blood vessel.

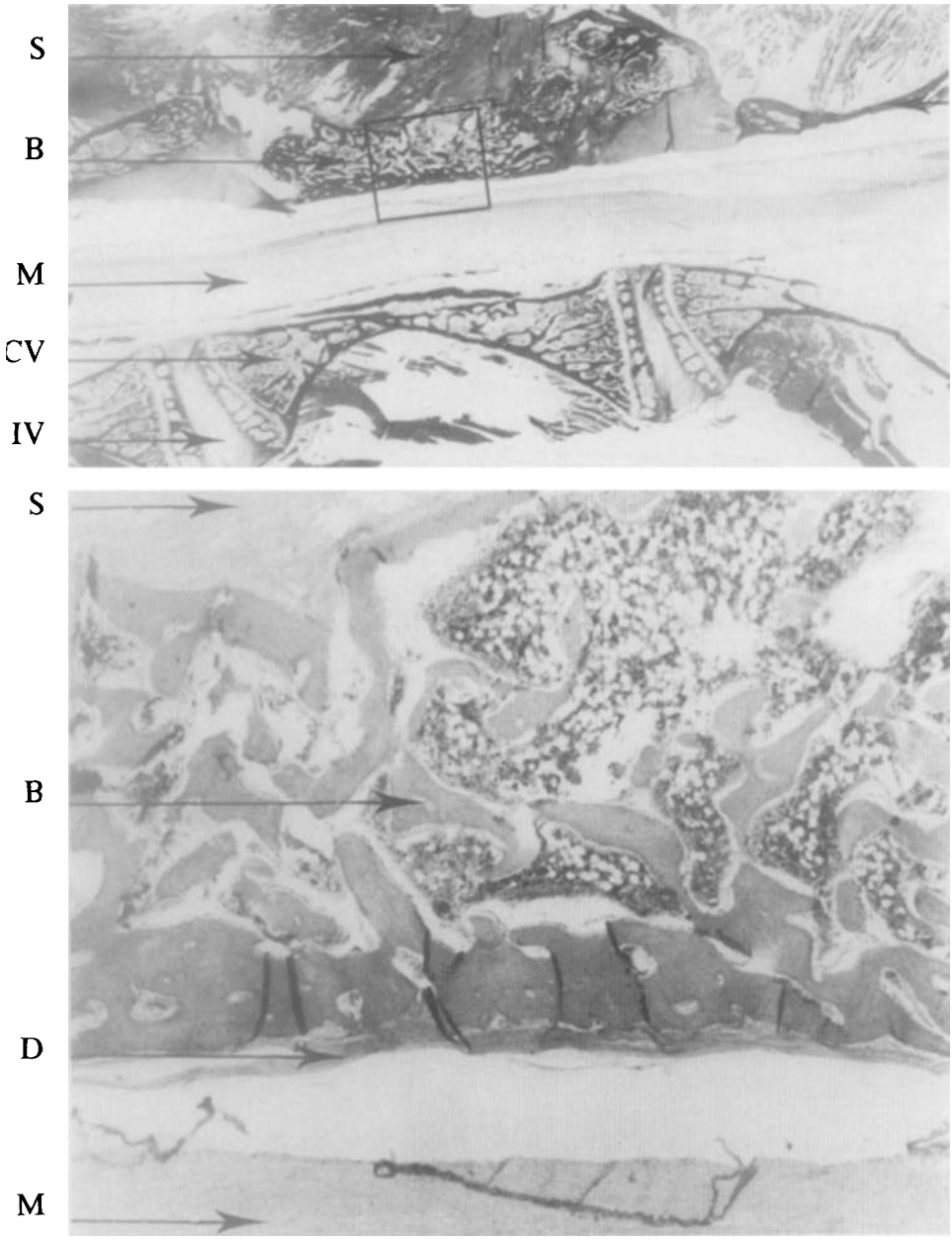

Fig. 16. Two photographs (x 4 and 40) of a section from a rabbit in the third series. The laminectomy site was left untreated and is now (52 days afterwards) filled with bone (B), which lies on the dura (D). S scar. M = medulla, CV = vertebral body, IV = intervertebral disc, L = lamina.

Fig. 17. A micrograph of a rabbit from the third series (magnification x 40). Cortisone was instilled onto the dura, the observation time being 58 days. Plenty of scar tissue (S) is seen in close contact to the dura (D). M =medulla.

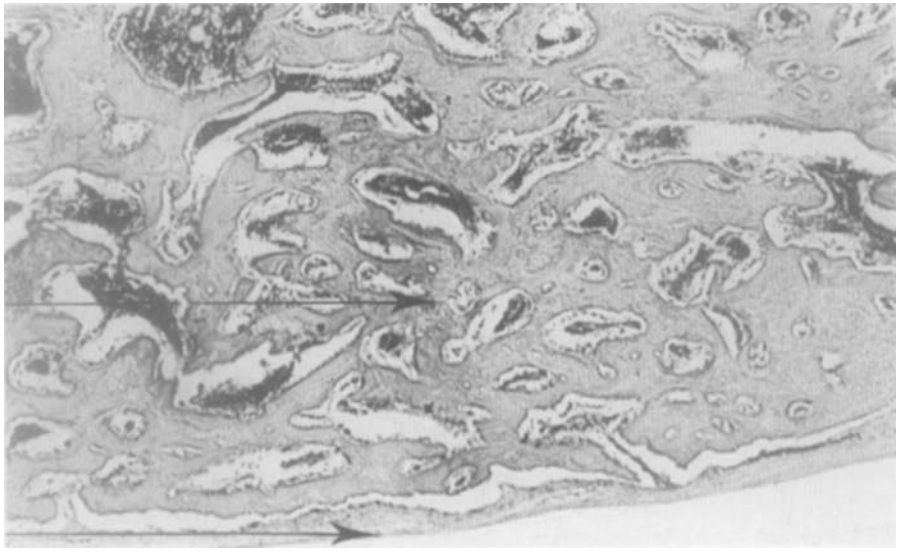

Fig. 18. A micrograph of a rabbit from the third series (magnification x 40). The laminectomy site was left untreated and the follow-up was 58 days. Bone (B) is seen on the dura (D), while there was scar instead of bone in Fig. 17 where cortisone was used.

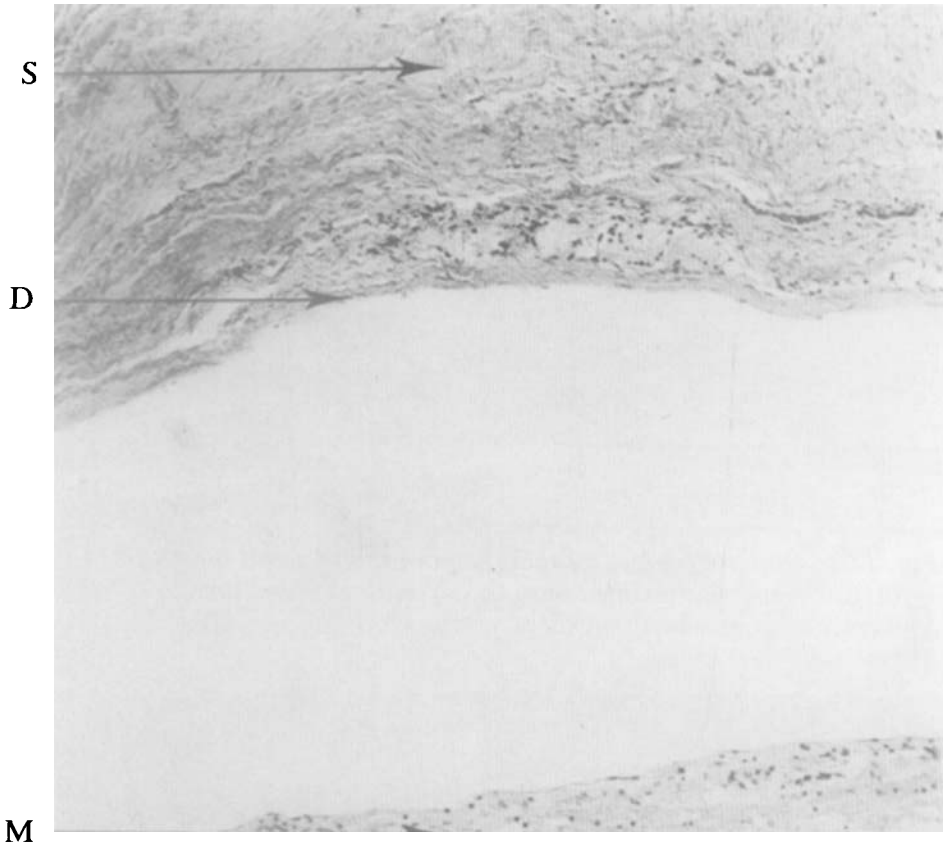

Fig. 19. A micrograph of a preparation from a rabbit in the third series (magnification x 100). The observation time was 52 days. The laminectomy site was left untreated. Abundant scar tissue (S) adjoining the dura (D) is seen. M = medulla.

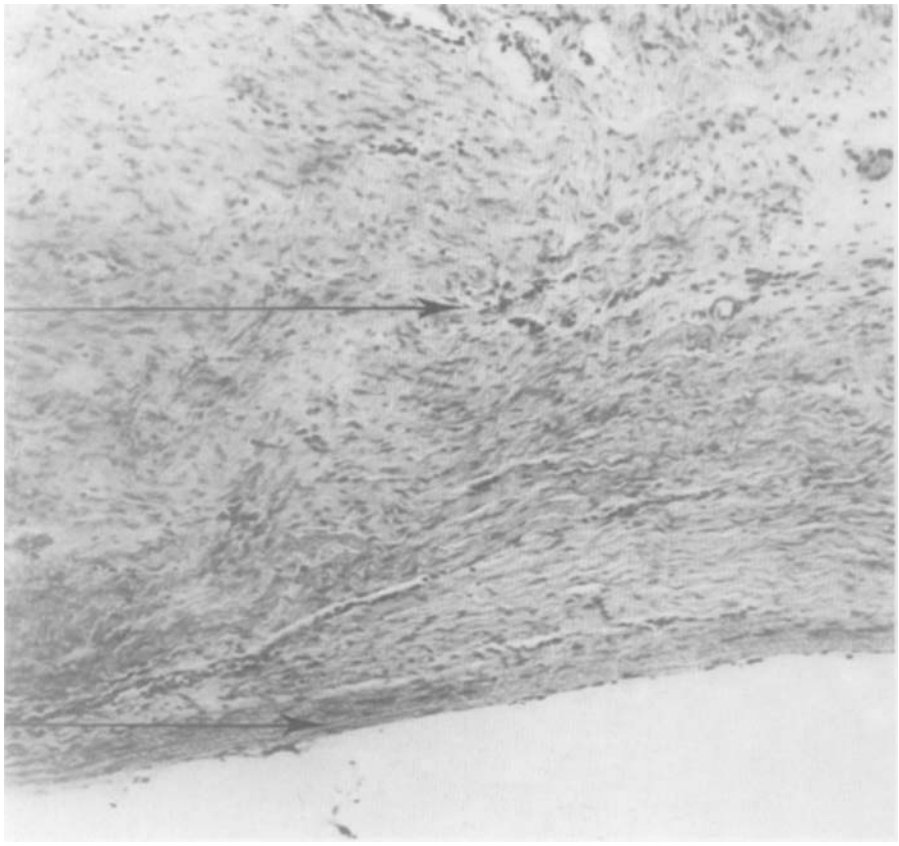

Fig. 20. A micrograph (x 100) of a rabbit from the third series. Cortisone was instilled into the laminectomy site and the follow-up was 58 days. Abundant scar tissue (S) is joining the dura (D).

Table 9. *Results of the third series (cortisone application and control). On each rabbit partial laminectomy was carried out on two vertebrae. In one of the laminectomy sites cortisone was placed on the dura, the other site was left to fill with blood or serum.*

Observation time (days)	Histologic findings at laminectomy site		No of rabbit
	cortisone	control	
49	scar	bone + scar	69
52	scar + bone	bone + scar	75
53	scar + bone	scar + bone	62
54	bone + scar	bone + scar	66
54	scar + bone	scar + bone	104
54	bone + scar	bone + scar	105
56	bone + scar	bone + scar	73
57	bone + little fat	bone + scar	59
57	bone + scar	bone + scar	60
57	scar	bone + scar	61
58	scar	bone + scar	63
59	scar	bone + scar	68
59	scar	scar	70
59	scar + bone	scar + bone	71
61	scar + bone	scar + bone	56
61	little fat + scar	bone	57

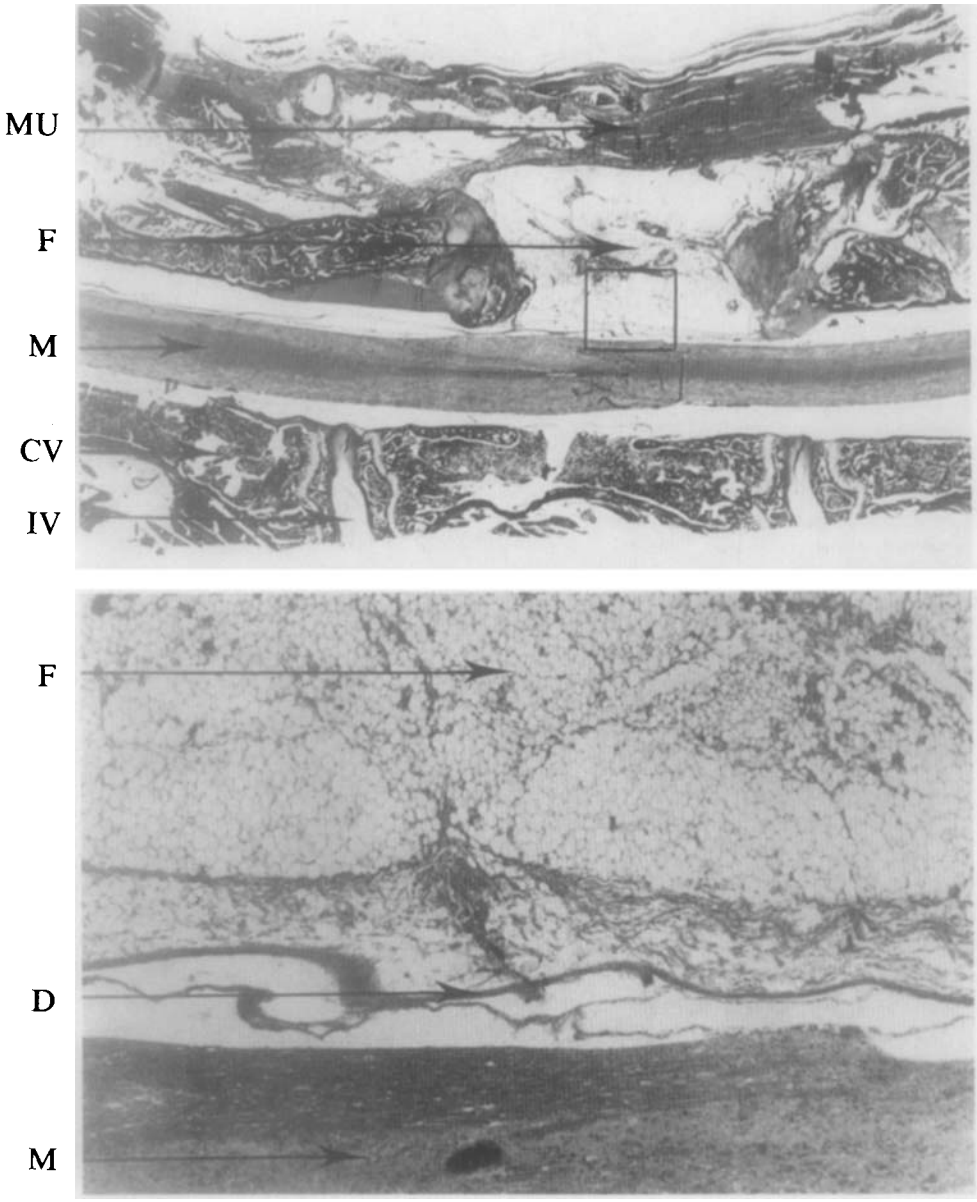

Fig. 21. Two photographs of a section from a rabbit in the 4th series (x 4 and 40). Fat tissue and cortisone were put onto the dura, and the observation time was 37 days. Fat tissue (F) is seen lying on the dura (D). MU = muscle, M = medulla, CV = vertebral body, IV = intervertebral disc.

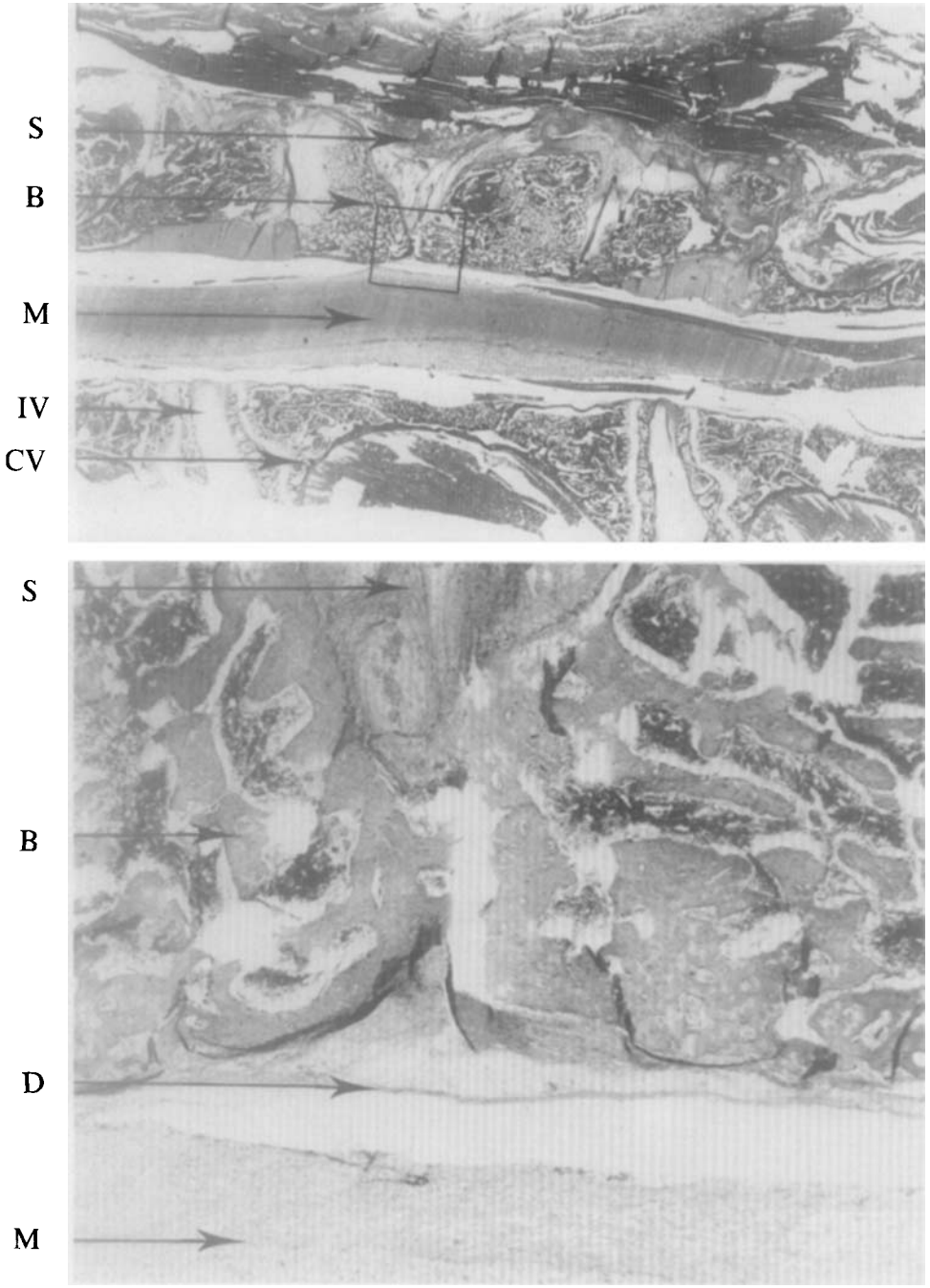

Fig. 22. Two photographs of a section from a rabbit in the 4th series (x 4 and 40). The laminectomy site was left to fill with blood and serum. Scar (S) and bone (B) are seen on the dura (D). The observation time was 37 days. M = medulla, IV = intervertebral disc, CV = vertebral body.

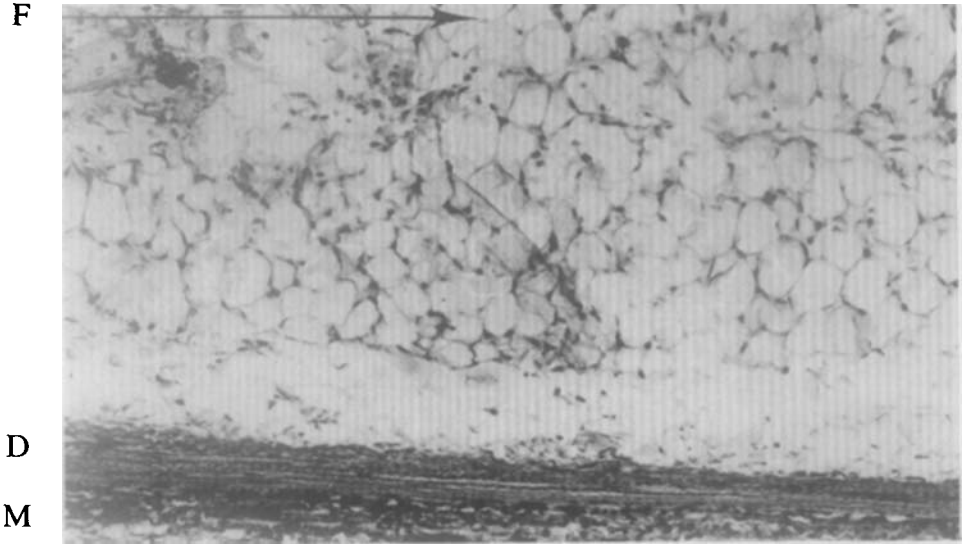

Fig. 23. A x 100 magnification of a rabbit in the 4th series. Fat tissue and cortisone was transplanted, and the follow-up period was 37 days. Fat tissue (F) is seen. D=dura, M=medulla.

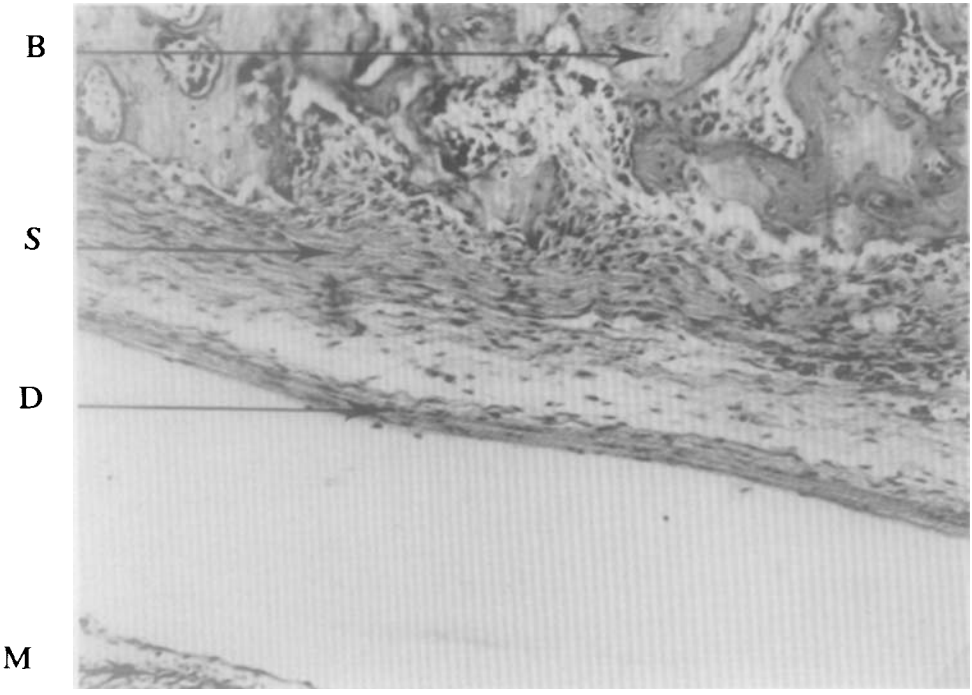

Fig. 24. A micrograph (x 100) of a rabbit in the 4th series. The laminectomy site was left untreated and the observation time was 37 days. Abundant bone (B) and scar (S) are seen on the dura (D) instead of fat tissue in Fig. 23.

Table 10. *Results of the fourth series (fat + cortisone application and control).*
On each rabbit partial laminectomy was carried out on two vertebrae. In one of the laminectomy sites a piece of fat tissue + cortisone was placed on the dura, the other site was left to fill with blood or serum.

Observation time (days)	Histologic findings at laminectomy site		No of rabbit
	fat + cortisone	control	
31	fat + reaction	scar	129
31	fat	bone + scar	130
31	fat + reaction	bone + scar	132
37	fat	bone + scar	142
37	fat + reaction	bone + scar	143
37	fat	bone + scar	144
41	fat + reaction	bone + scar	138
41	fat + reaction	scar	140
41	fat + reaction	bone + scar	141
42	fat + reaction	bone + scar	98
43	fat + reaction	bone + scar	133
43	fat + reaction	bone + scar	135
43	fat	bone + scar	136
43	fat + reaction	bone + scar	137
59	fat	bone + scar	102

3.3.6. The fifth series (fat + cortisone and control)

The fifth series comprised 12 rabbits. In this group, the histologic pattern at two laminectomy sites was compared. Fat and cortisone were introduced at one of them while the other was not treated. The animals' preoperative weight ranged from 1,700 to 3,000 g, mean 2,370 g. Their weight at the time of sacrifice was 2,500—3,475 g, mean 2,990 g. The follow-up period lasted from 122 to 142 days. The fat measured 5 x 10 mm on average in the longitudinal section of the preparation.

In the histological study the fat graft was seen well preserved (Fig. 25). There were less reactive changes in the marginal part of the graft than in other sections from all the other series, in which the observation time was shorter than in this series. In control sections plenty of bone was seen in the laminectomy sites (Fig. 26, 28). In this series, bone tissue was the dominant part in all controls, while in the rabbits with short observation scar tissue played a greater role. In the laminectomy left to fill with blood and serum, connective tissue was thus formed first and changed gradually to cartilage and then to bone. With greater magnification the connective tissue capsule was clearly seen surrounding the graft (Fig. 27, 29). In these sections, macrophages, leucocytes, giant cells or fat cysts were not seen. They were richly available in preparations with a shorter observation. It seemed as though a steady state between the graft and the host tissue had been reached, since the reactive changes had almost disappeared.

A summary of the results in this series is given in Table 11, where it can be seen that fat tissue was preserved in every case and often without reactive changes. The control laminectomy site was filled with bone.

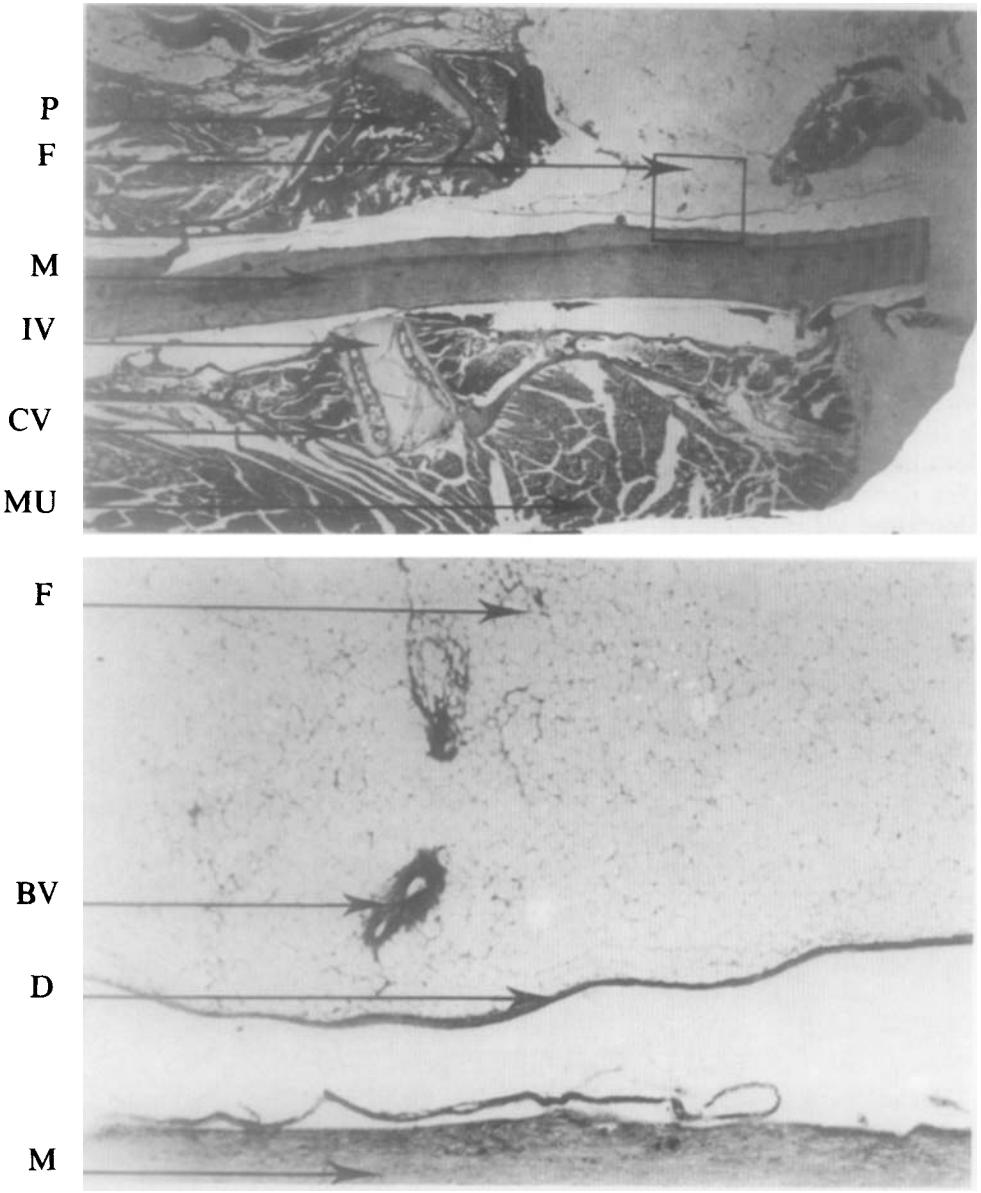

Fig. 25. ***Two photographs of a section from a rabbit in the 5th series*** *(x4 and 40). Fat tissue and cortisone were transplanted onto the dura, observation time being 138 days. The fat graft (F) is immediately contiguous to the dura (D). P = spinous process, M = medulla, IV= intervertebral disc, CV = vertebral body, MU =muscle, BV = blood vessel.*

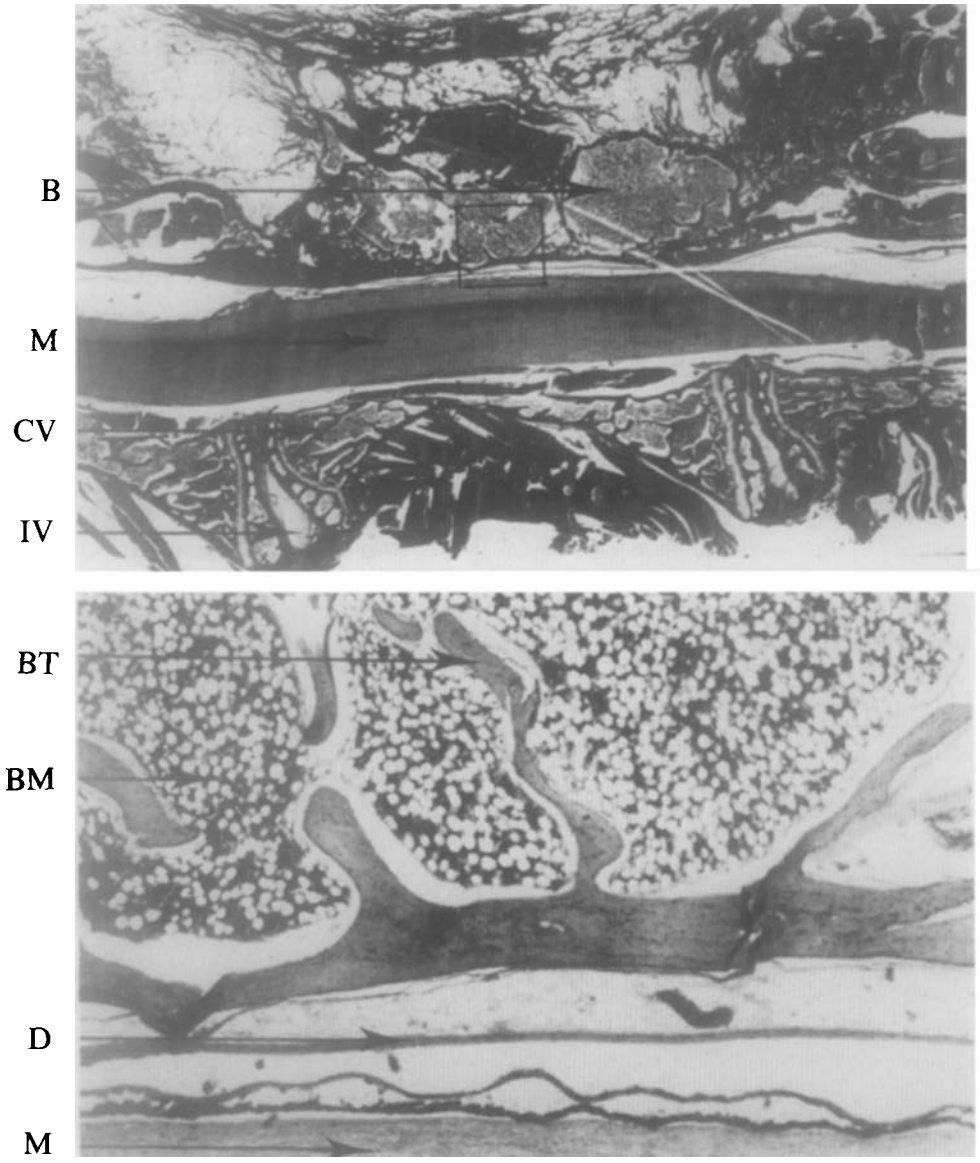

Fig. 26. Two photographs of the control sections from the same animal as in Fig. 25. Bone (B) is seen on the dura (D). M=medulla, CV = vertebral body, IV = intervertebral disc. BT = bone trabecle, BM=bone marrow.

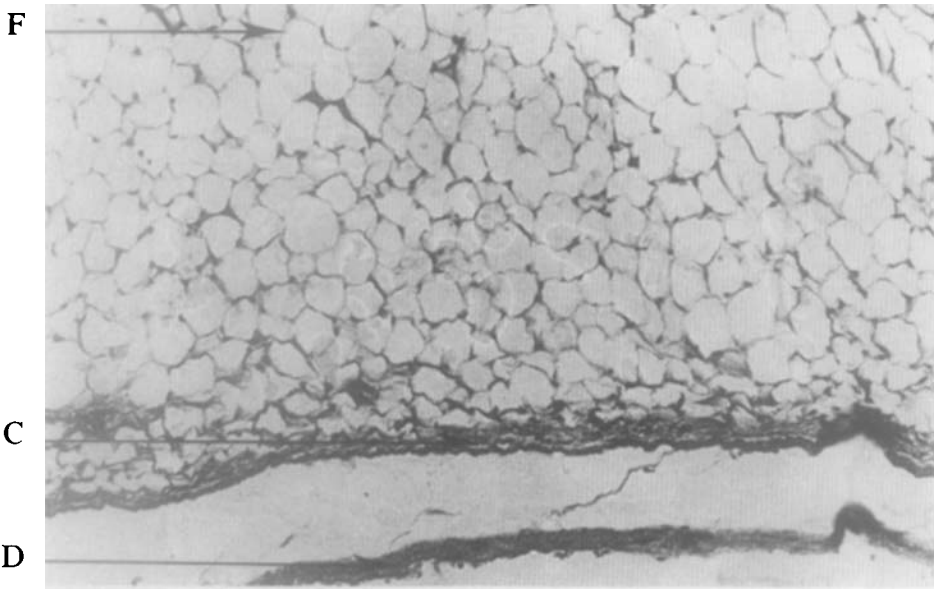

Fig. 27. A x 100 magnification of a preparation from a rabbit in the 5th series. Fat and cortisone were transplanted, the follow-up time being 122 days. Fat tissue (F) occupies most of the picture; it adjoins the connective tissue capsule (C) which has detached itself from the dura (D).

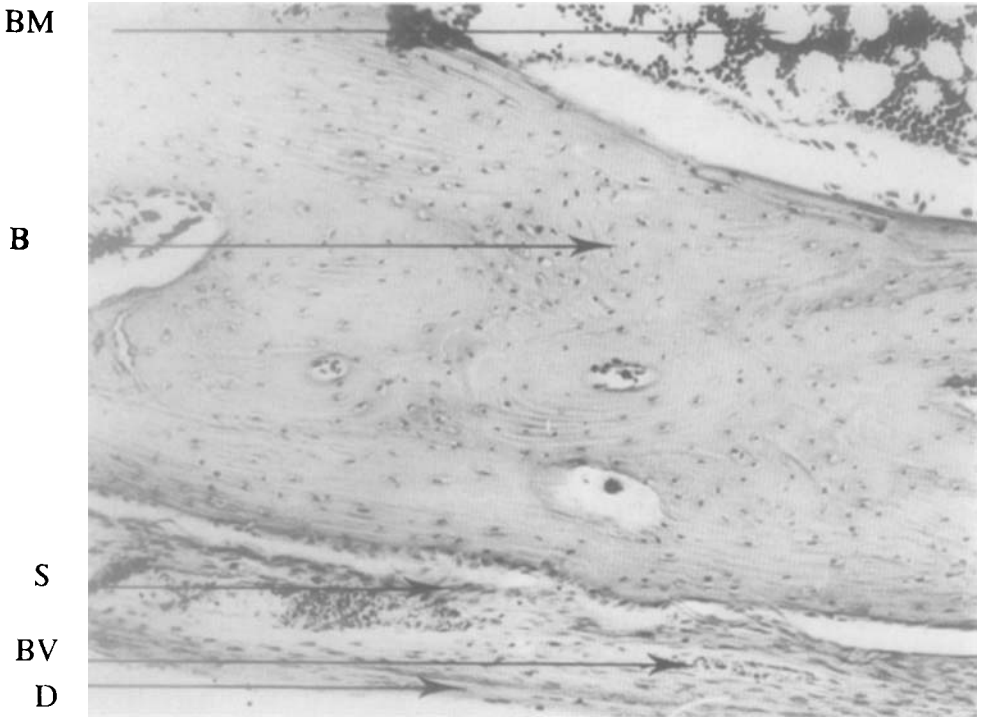

Fig. 28. A micrograph (x 100) of a rabbit from the 5th series. The laminectomy site was left untreated, the observation time being 122 days. Bony tissue (B) covers most of the area, with connective tissue (S)

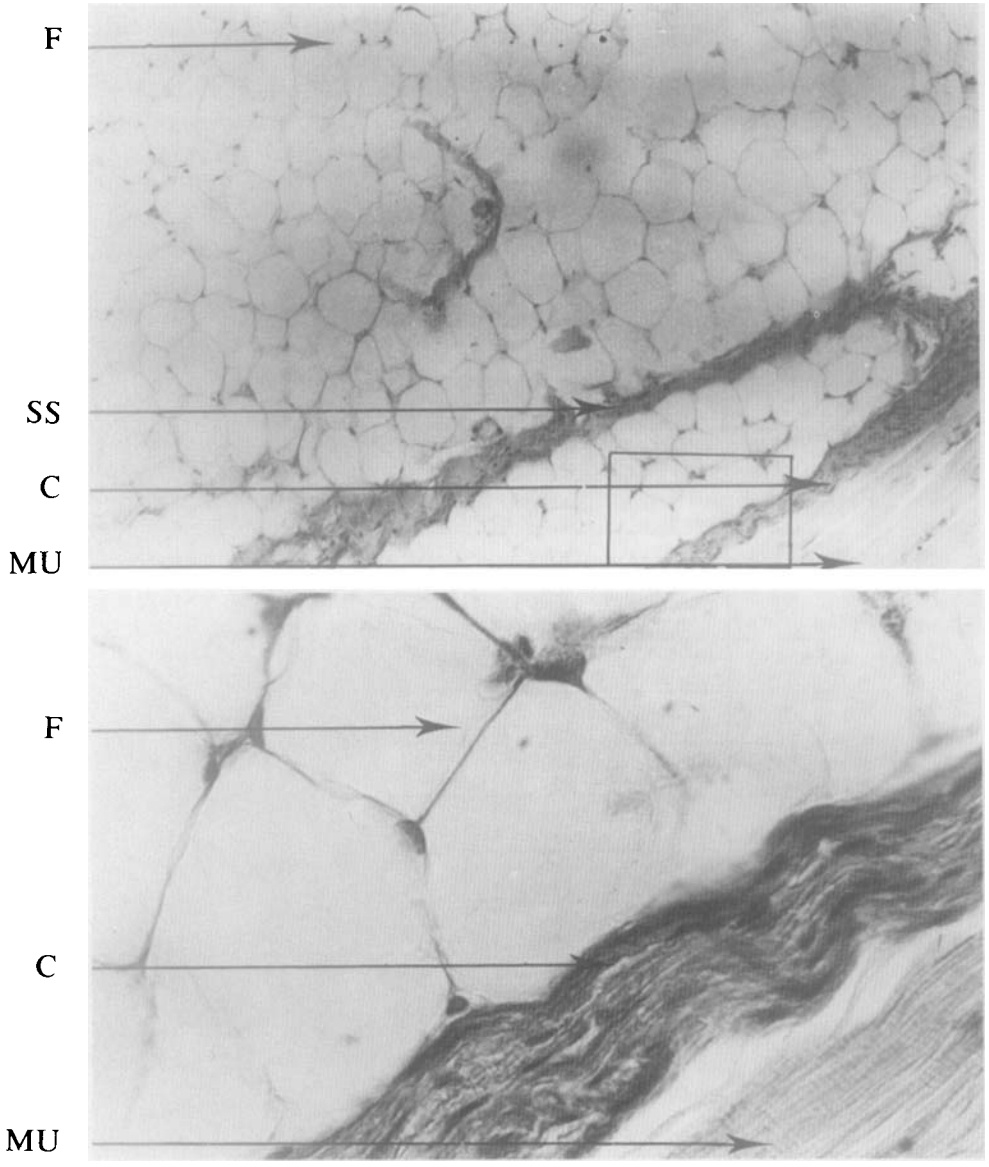

Fig. 29. Two magnifications (x 100 and x 400) of a preparation from a rabbit in the 5th series, showing the area to which fat tissue and cortisone were transplanted. The follow-up period was 122 days. The graft (F) adjoins the surrounding muscle tissue (MU). Fat cells are immediately contiguous to the connective tissue capsule (C) which, in turn, is in direct contact with the muscle. SS= connective tissue septum.

Table 11. *Results of the fifth series (fat + cortisone application and control).*
On each rabbit partial laminectomy was carried out on two vertebrae. In one of the laminectomy sites a piece of fat tissue + cortisone was placed on the dura, the other site was left to fill with blood or serum.

Observation time (days)	Histologic findings at laminectomy site		No of rabbit
	fat + cortisone	control	
122	fat	bone + scar	84
122	fat	bone + scar	85
122	fat	bone + scar	86
124	fat + reaction	bone + scar	94
124	fat + reaction	bone + scar	97
130	fat	bone + scar	78
132	fat + reaction	bone + scar	76
138	fat	bone + scar	89
138	fat	bone + scar	91
138	fat	bone + scar	92
142	fat	bone + scar	87
142	fat	bone	88

3.3.7. The sixth series (fat and gelatin)

The comparison in this series of 20 rabbits was between histologic sections obtained after transplanting fat at one laminectomy site and placing pieces of Spongostan in the other. The preoperative weight of the rabbits was 2,120—3,090 g, mean 2,570 g. The weight range at the time of sacrifice was 2,270—2,900 g, mean 2,590 g. The follow-up period was between 33 and 84 days. The fat measured 6 x 9 mm on average in the longitudinal section of the preparation.

In histological study the transplanted fat tissue was found on the dura, and it was sometimes divided in smaller parts by connective tissue septa as in this section (Fig. 30). The control site, in which gelatin was used, was replaced with scar and bone (Fig. 31—32). They were contiguous to the dura (Fig. 34). In fat grafts cellular infiltrations (macrophages and leucocytes) could be seen (Fig. 33), and especially in the marginal parts of the grafts with giant cells and fat cysts.

The results are summarized in Table 12, where it can be seen that the fat tissue was preserved and gelatin was unable to prevent scar or bone formation.

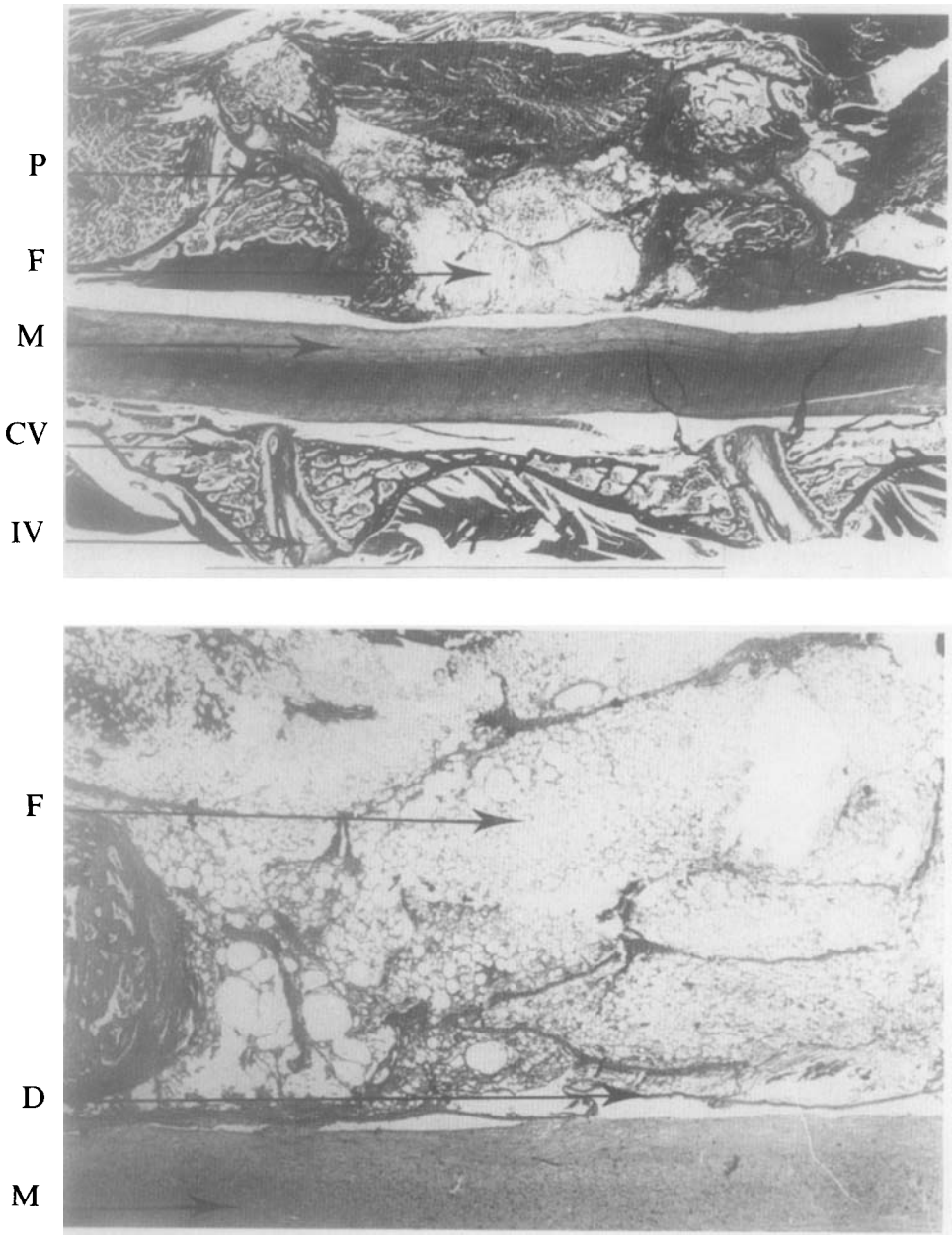

Fig. 30. Two photographs of a section from a rabbit in the 6th series (x 4 and 25). A fat graft was transplanted on the dura, observation time being 39 days. The fat graft (F) is seen lying on the dura (D). P = spinous process, M = medulla, CV = vertebral body, IV = intervertebral disc.

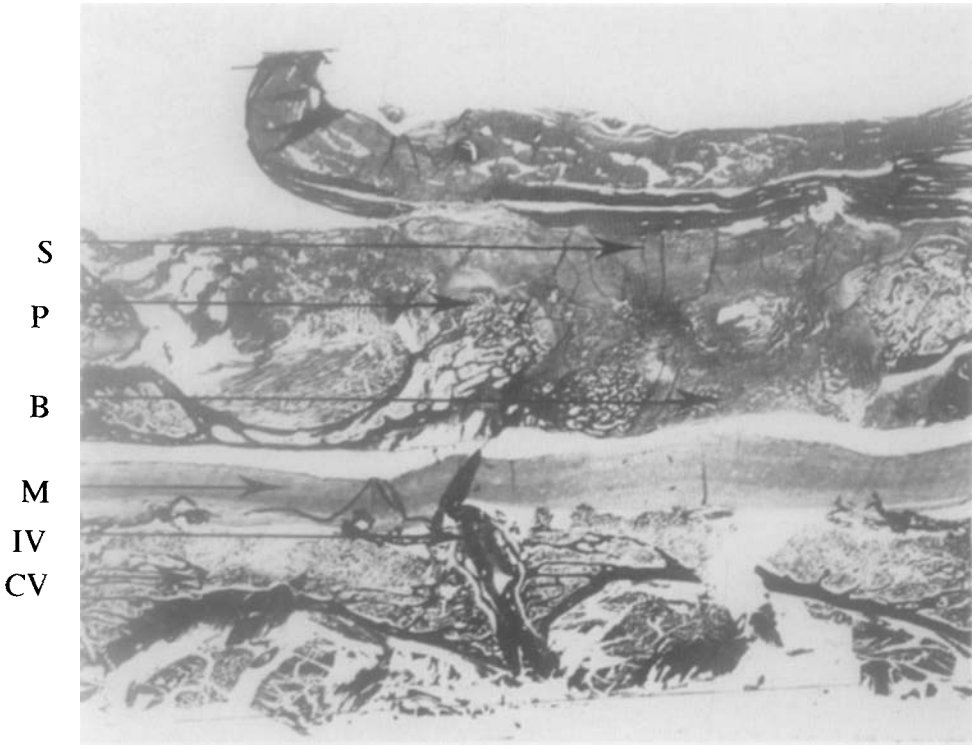

Fig. 31. A photograph (x 4) of a section from a rabbit in the 6th series serving as a control to the corresponging picture in Fig. 30. Spongostan was set on the dura. We can see scar tissue (S) and bone (B), which are contiguous to the dura (D) . P = spinous process, M = medulla, IV = intervertebral disc, CV = vertebral body.

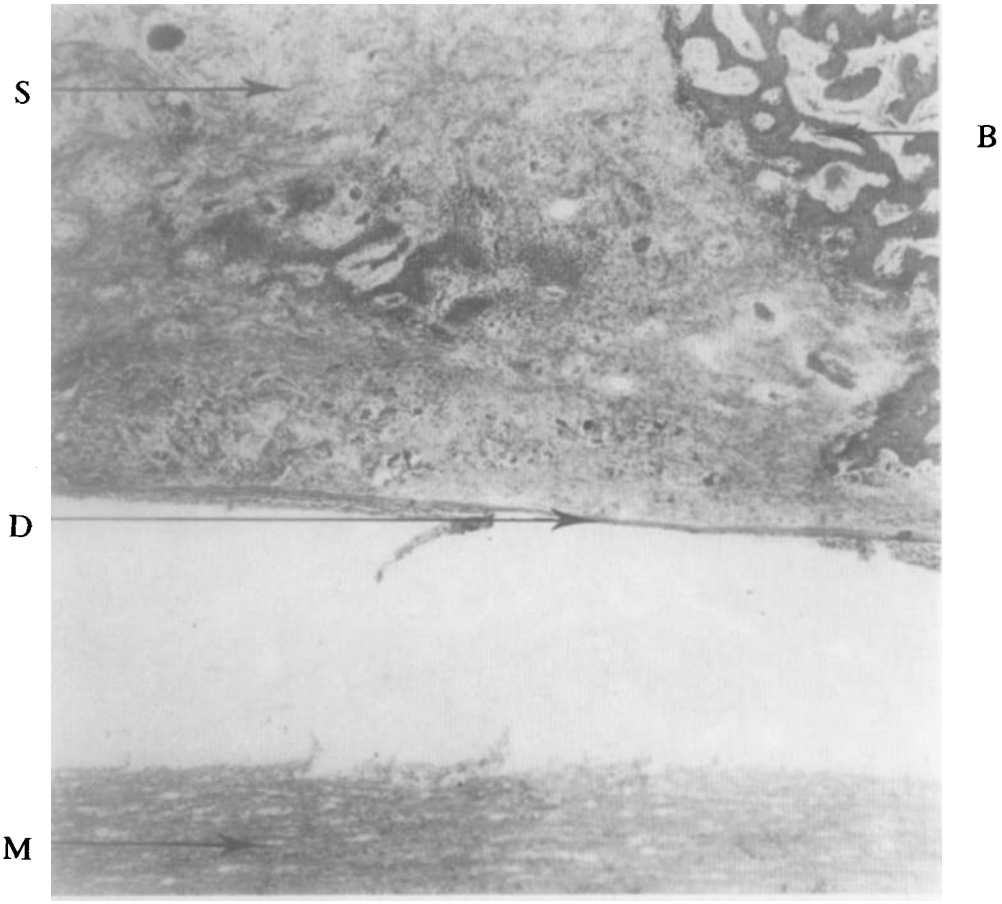

Fig. 32. A micrograph (x 40) of a laminectomy site in the 6th series. Spongostan was put on the dura, the follow-up being 39 days. Scar (S) and bone (B) are joining the dura (D). M=medulla.

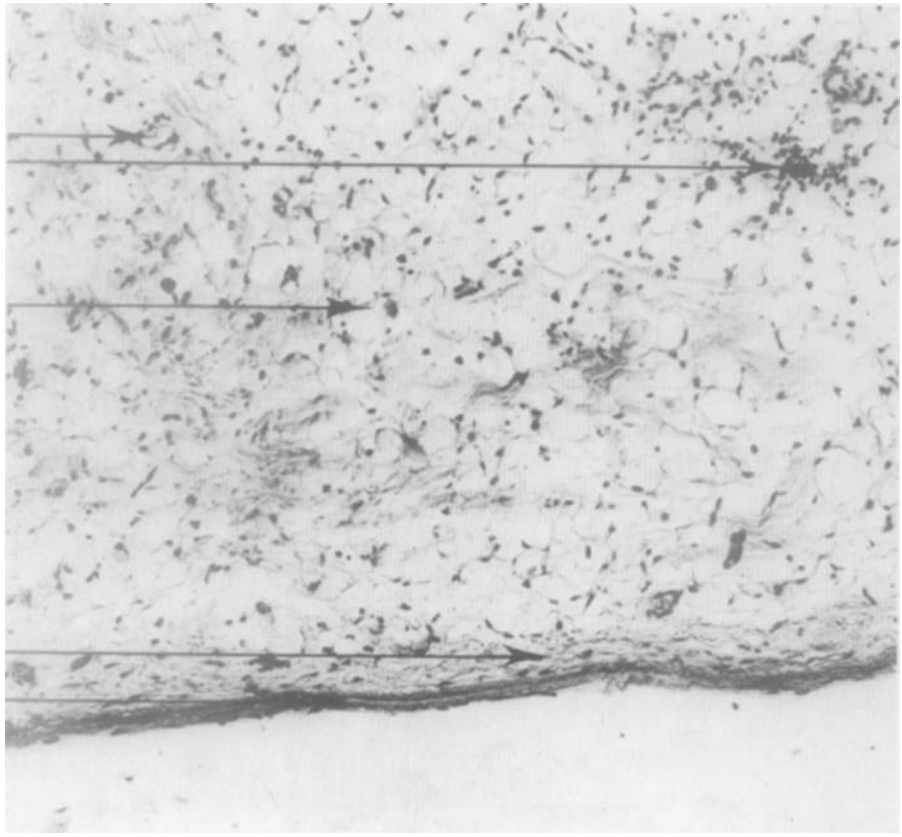

Fig. 33. A x 100 magnification of a preparation from a rabbit in the 6th series. The area to which fat tissue was transplanted is seen. The follow-up period was 46 days. Fat tissue (F) predominates and is contiguous to the thin connective tissue capsule (C), which adjoins the dura (D). Some cellular infiltration (CI) is seen in the right upper corner. BV = blood vessel.

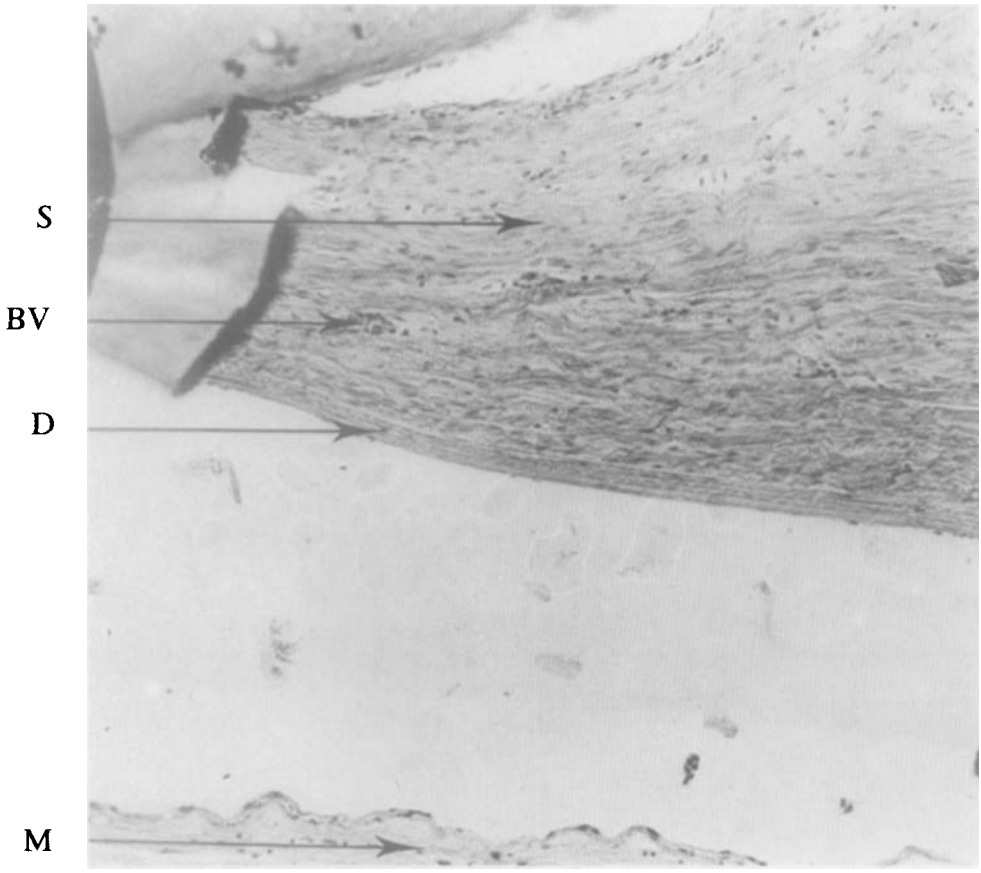

Fig. 34. A micrograph (x 100) of a rabbit from the 6th series. Spongostan was put on the dura, the follow-up being 39 days. Abundant scar tissue (S) is seen adjoining the dura (D). BV = blood vessel, M = medulla.

Table 12. *Results of the sixth series (fat application and gelatin). On each rabbit partial laminectomy was carried out on two vertebrae. In one of the laminectomy sites a piece of fat tissue was placed on the dura, in the other Spongostan was placed on the dura.*

Observation time (days)	Histologic findings at laminectomy site		No of rabbit
	fat	Spongostan	
33	fat + reaction	scar + bone	123
33	fat	bone + scar	124
33	fat + reaction	scar + bone	125
35	fat	scar	120
35	fat + reaction	scar	121
35	fat + reaction		122
39	fat	scar + bone	114
39	fat + reaction	bone + scar	115
39	fat + reaction	scar + bone	116
39	fat + reaction	scar	117
39	fat	scar + bone	118
39	fat	bone + scar	126
45	fat + reaction	scar + bone	110
45	fat + reaction	bone + scar	111
45	fat + reaction	bone + scar	112
45	fat + reaction	bone + scar	113
46	fat + reaction	bone + scar	107
46	fat	bone + scar	108
84	fat	bone + scar	127
84	fat + reaction	scar + bone	128

3.3.8. Summary of the results

The mean results for each series are summarised in Table 13. 145 rabbits were operated. From these 16 belonged to the pilot study, 37 were excluded because of complications (Table 5, p. 24 and the rest (92) were divided into six series. The transplanted fat tissue remained in situ above the dura and prevented a scar from forming in every case. When no fat was used, scar tissue and bone formed and usually adhered to the dura. Cortisone did not cause any clearly discernible changes in the fat transplant. Scar formation did not decrease when Spongostan was used. The reactive changes in the fat transplants were smaller when the observation period was longer. When cortisone was instilled onto the dura at one laminectomy site and the other site was left to fill with blood or serum there seemed to be less bone formation in the cortisone group than in the controls. The laminectomy site left to fill with blood and serum was first replaced by connective tissue, which was gradually changed to bone.

Table 13. *Summary of the results.*
Laminectomy sites were studied microscopically in 92 rabbits. On each, partial laminectomy was carried out on two vertebrae. Fat, fat + cortisone, or Spongostan was placed on the dura or the site was left empty to fill with blood or serum. Different comparisons were made in the six series.

Series No	1 (=fat and control)	2 (=fat and fat + cortisone)	3 (=cortisone and control)	4 (=fat + cortisone and control)	5 (=fat + cortisone and control)	6 (=fat and Spongostan)
Number of rabbits	13	16	16	15	12	20
Observation time (days)	31—84	31—52	49—61	31—59	122—142	33—84
Size of fat transplant measured on sections (mm)	6 x 9	5 x 8		5 x 10	6 x 9	6 x 9
Histologic findings	Fat was preserved, the other laminectomy site was filled with scar and/or bone (Fig. 2—9)	Fat was preserved in both sites, no difference found between the two laminectomies (Fig. 10—14)	Scar and/or bone in both laminectomies (Fig. 15—20)	Fat was preserved, the other site was filled with bone and/or scar. The fat transplant had less reactive changes in the fifth than in the fourth series (Fig. 21—29)		Fat was preserved, the other site was filled with scar and/or bone (Fig. 30—34)

4. DISCUSSION

4.1. Free fat transplants

A voluminous literature on free fat transplants has been published since the first half of the 19th century. The publications have generally reported the survival of the autogenous fat graft, but somewhat reduced in size (May 1941, Peer 1950 and Schörcher 1957).

In 1959 Peer presented a summary of the microscopical picture of the fat graft. He found profuse accumulation of leucocytes during the first four days after the transplantation. Four days after the operation there were numerous red and white cells in the vessels of the graft which migrated into the tissue. Circulation was established in this phase between the host and the transplant. Foreign body giant cells were also seen at this stage. On the fifth and sixth days fibroblast proliferation was observed. On the tenth day numerous large histiocytes with some disintegrated fat cells in their vicinity were visible. Some large blood vessels also began to function normally in this phase. Histiocytes were most profuse 60 days after the operation; they contained one or more fat droplets which gave them some resemblance to fat cells. Fat cysts of dirrering sizes were also seen up to two months. The cells participating in the reaction decreased in number during the third and seventh months and the graft began to take on a normal appearance. Some walled-off cystic spaces remained with normal fat cells around them. The thick connective tissue capsule around the transplant became thinner. From less than a year up to 13 years postoperatively the transplant resembled normal fat tissue encircled by a connective tissue layer reminiscent of the capsule of a lipoma.

4.2. Own studies and comparison with earlier investigations

A total number of 130 free fat transplantations were perfomed in 6 series. In 92 laminectomy sites which could be studied histologically fat was preserved and prevented scar from forming on the meningeal dura in all of them. In 38 animals the histology could not be studied because of premature death (22), inflammation (6) or paralysis (9). The microscopical follow-up period ranged from approx. one to four months.

Normal fat cells were seen almost all the time, as has been reported in earlier studies. The formation of fat cysts was clearly discernible and can be seen in the photographs presented in connection with the results. Giant cells were noticeably numerous in the preparations, whereas no great number of histiocytes was detectable. The connective tissue capsule was also visible. In addition, fibrosis which changed gradually into cartilage and then into bone was established at the junction of the graft and bone. Some degree of bone formation was thus demonstrable at the edges. The preservation of the autogenous fat transplant as normal fat tissue in this study is in agreement with the information gained from earlier investigations.

When the observation period was four months there were less reactive changes in the fat transplant than when the follow-up lasted only from one to two months. The same findings have also been made earlier concerning the role of time in fat transplants (Peer 1959).

Cortisone seemed to make no observable change in the fat transplant. In the third series the comparison was made between two laminectomy sites, in which cortisone was instilled onto the dura at one laminectomy site and the other site was left to fill with blood or serum. It seemed that there was less new bone forming in the cortisone group than in the control group. In the literature it is generally accepted that cortisone has an inhibiting influence in the repair of bones (Blunt et al., Sissons and Hadfield, Koskinen).

Spongostan seemed to achieve abundant bone and scar formation in this study. Gelatin acted as a space obliterator in the treatment of bone cavities in jaws. It was replaced by fibrous tissue, which incorporated into bone (Thoma and Sleeper).

The laminectomy site which acted as a control and was left to fill with blood or serum, was later filled with scar and/or bone. In the marginal parts of the laminectomy site it was often possible to find chondroblasts and chondrocytes. These findings are in agreement with the repair of bones described on page (Ham).

In the literature I have been unable to find any studies where the fat transplant has been placed on the spinal dura.

4.3. Intervertebral disc surgery

Prolapse of the disc is a common contition. Roentgenograms of persons aged over 50 always reveal degenerative changes, but they are also often encountered in younger people. Most cases are treated conservatibely, but many patients have to submit to surgery for removal of the prolapse. This does not always mean a permanent cure, and the complaint may recur and necessitate reoperation. Reoperation of this kind is not common. The reoperation rate was 24 per cent in a series of 140 patients reported by Aitken and Bradford in 1947. In the following year, Falconer and his co-workers presented a material of 100 patients, 14 of whom had to be reoperated. Waris's material of 347 patients (1948) had a reoperation rate of 2 per cent. Epstein and his co-workers reported in 1967 that a second operation was performed on 4 per cent of a series of 900 patients, and Mattmann's (1969) figures were 10 per cent and 3,000 patients, respectively.

Falconer described the technique employed in reoperations. When the ligamentum flavum or a part of the lamina had been removed the dead space filled with scar tissue which adhered firmly to its environment and could extend to the dural sleeves. The scar makes it difficult to operate. To obviate this problem, surgeons at the Orthopedic Hospital of the Invalid Foundation and the Department of Orthopaedics and Traumatology, Helsinki University Central Hospital, have since 1965 transplanted free fat onto the dura in operations for prolapsed disc (A. Langenskiöld, unpublished observations). The clinical experience at the reoperations has been good. It has been easy to move the fat transplant aside and gain access to the dura.

4.4. Conclusions

Free fat grafts placed on the dura of rabbit are preserved. They prevent scar formation on the dura when the fat is placed in a space which would have been filled by a haematoma. Cortisone in itself is incapable of preventing scar tissue from forming and seemed to provide no added benefit when used together with a fat graft. Spongostan (Ferrosan) cannot prevent the formation of scar or bone.

Free fat transplants may be useful in surgery for prolapsed disc.

5. SUMMARY

The purpose of this study was to investigate whether the use of a free fat transplant prevents scar formation on the dura that has been exposed by surgery. A procedure to prevent epidural scar formation could be expected to be beneficial in surgery for intervertebral disc prolapse. Reoperation has been complicated hitherto by the scar tissue that forms at the site of the first operation. Clinical observations of the benefit of free fat transplants placed on the dura have been made since 1965 (Langenskiöld and Kiviluoto).

A total of 145 operations were performed on rabbits each of which was submitted to two partial laminectomies on the lumbar spine. Care was taken not to damage the dura. A second incision was then made between the scapulae and subcutaneous fat tissue was taken for transplantation. It was taken in one piece for each laminectomy as far as possible. The fat tissue was placed on the dura with the graft extending beyond the edges of the bone. The other laminectomy site one arch away from the first served as a control. In 56 animals it was left to fill with blood or serum. The wound was closed with catgut and the skin with nonresorbing suture. The rabbits were killed 1—4 months postoperatively. The spinal column in the operative area was decalcified and cut in the middle so that the control was located in a separate piece.

Both pieces were sectioned so that the sample included the vertebral body, the medulla and the hemilaminectomy site.

The fat tissue was regularly found to have retained a practically normal appearance in all 92 laminectomy spaces into which fat was transplanted and which could be studied histologically. Giant cells, fibrosis, fat cysts and cellular infiltration were seen in the marginal parts of the graft. The transplants decreased in size. In the control laminectomy site spaces which were filled with blood or serum, scar tissue and bone formation were regularly established. The following comparisons were made in the other series: between fat and fat plus cortisone in the second series, between cortisone and control in the third, between fat plus cortisone and control in the fourth and fifth series, and between fat and gelatin in the sixth series. Cortisone did not appear to have any effect on the fat transplant but seemed to reduce new bone formation when used alone. The gelatin series displayed abundant scar and bone formation. The longest follow-up period was four months. The reactive changes had decreased by then compared with the situation at 1—2 months and the graft looked like normal fat tissue.

Free fat grafts placed on the dura in surgery for prolapsed disc may facilitate a possible reoperation for recurrence.

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