

The lateral wall of the pterygomandibular space is that portion of the medial surface of the ramus bounded inferiorly by the dissected insertion of the medial pterygoid muscle and superiorly by the lower border of the lateral pterygoid muscle. The medial fibres of the latter muscle can be noted passing posteriorly from their origin on the lateral surface of the lateral pterygoid plate to be inserted into the front of the neck of the mandible and the capsule of the temporo-mandibular joint.

The mandibular nerve enters the infratemporal fossa via the foramen ovale and immediately gives off the small nervus spinosus, a long branch passing to the medial aspect of the medial pterygoid muscle and branches to the tensor tympani and tensor palati muscles, before dividing into anterior and posterior parts. The posterior trunk gives off, by two roots, the auriculo-temporal nerve and ends by dividing into the inferior alveolar and lingual nerves.

When viewed in coronal section, both of the latter branches follow a flat S-shaped course as they run firstly over the medial surface of the lateral pterygoid muscle and then curve around its inferior border to approximate the bony contours of the ascending ramus on either side of the lingula (Fig. 5).

In this way the inferior alveolar nerve enters the mandibular sulcus and gives off the mylo-hyoid nerve before

Figure 5.



Fig. 5 - Photograph of the region illustrated in fig. 4.

entering the mandibular foramen. In its region of closest proximity to bone, the inferior alveolar nerve is shielded by the prominence of the lingula from possible trauma during intra-oral block injection.

The lingual nerve, medial to the lateral pterygoid muscle, is joined by the chorda tympani branch of the facial nerve and passes anteriorly to the lingula. It is in close proximity to the ridge of bone known as the temporal crest (Sicher 1965). A small vein accompanies the lingual nerve on its lateral aspect.

Because of the contour of the medial surface of the ascending ramus, the inferior alveolar nerve is situated more laterally than the lingual nerve and for this reason, both nerves can be anaesthetised along the one, obliquely directed, needle pathway. This pathway approximately corresponds to an imaginary line drawn parallel to the lower border of the body of the mandible at a level slightly above the mandibular foramen and extending from the posterior boundary of the mandibular sulcus to the premolar region of the opposite side. This is emphasized, because it is the route by which the inferior alveolar and lingual nerves are anaesthetised using the direct intra-oral approach.

This investigation is primarily concerned with the relation of this needle pathway to blood vessels of

sufficient calibre to permit partial or complete entry of the bevelled point of the twenty-five gauge needle commonly used for inferior alveolar nerve block injection.

The veins of the pterygomandibular space.

The two large maxillary veins, which drain the pterygoid venous plexus surrounding the maxillary artery and lateral pterygoid muscle, cross the neck of the mandible and join the posterior facial vein. This large vessel has already been noted within the parotid gland, forming the postero-medial limit of the pterygomandibular space. Another smaller vein, possibly associated with that portion of the pterygoid plexus on the lateral surface of the medial pterygoid muscle was noted passing directly backwards in contact with bone at the level of the mandibular foramen to join the posterior facial vein also. The inferior alveolar veins drain into these tributaries of the posterior facial vein, all of which are in close relation to both bone and to the needle pathway mentioned.

Arteries of the pterygomandibular space and infra-temporal fossa.

The external carotid artery is situated medially to the posterior facial vein in the retromandibular fossa and is not closely related to the pterygomandibular space. However, it turns sharply laterally behind the mandibular

neck and ends by dividing into the superficial temporal and maxillary arteries. The first part of the maxillary artery therefore, lies medially to the neck of the mandible with the maxillary veins and spheno-mandibular ligament on its medial aspect.

In this dissection, the inferior alveolar artery arose as a direct branch of the external carotid artery just before its terminal division. Whether the inferior alveolar artery arises in this unusual way or in the normal manner, as a branch of the first part of the maxillary artery, it is situated close to bone at its origin and during its course through the mandibular sulcus to the mandibular foramen. Here it gives off (a) the mylo-hyoid artery which passes downwards with the mylo-hyoid nerve in the groove of the same name and (b) a small lingual twig which accompanies the lingual nerve (Cunningham 1953).

Of the remaining branches of the first part of the maxillary artery, viz, the deep auricular, anterior tympanic, accessory meningeal and middle meningeal arteries, only the latter was traced in its upwards course between the two roots of the auriculo-temporal nerve to the foramen spinosum.

The second part of the maxillary artery usually runs upwards and forwards either superficial to the lateral pterygoid or between that muscle's deep surface and the

branches of the mandibular nerve (Cunningham 1953).

Sicher (1965) describes the artery as occasionally passing medially to the branches of the mandibular nerve as was the case in this dissection.

The following branches of the second part of the maxillary artery were noted. (a) The posterior deep temporal and masseteric arteries arising by a common trunk which passed around the inferior border of the lateral pterygoid muscle, (b) the anterior deep temporal artery, (c) small pterygoid branches.

The important structures within the pterygomandibular space are then, the inferior alveolar nerve, artery and veins, the lingual nerve and the spheno-mandibular ligament; the interstices being filled with loose connective tissue containing some fat. This type of areolar tissue would not be expected to require a large blood supply and histological examination of the prepared sections of the pterygomandibular space (Figs. 7-14), revealed no extensive capillary network such as was seen in the palatal specimens examined (Fig. 6).

With the exception of the spheno-mandibular ligament, all the important structures within the pterygomandibular space are either passing through to their sites of distribution (nerves and arteries) or returning from their source (veins), there being only a relatively small circulatory bed

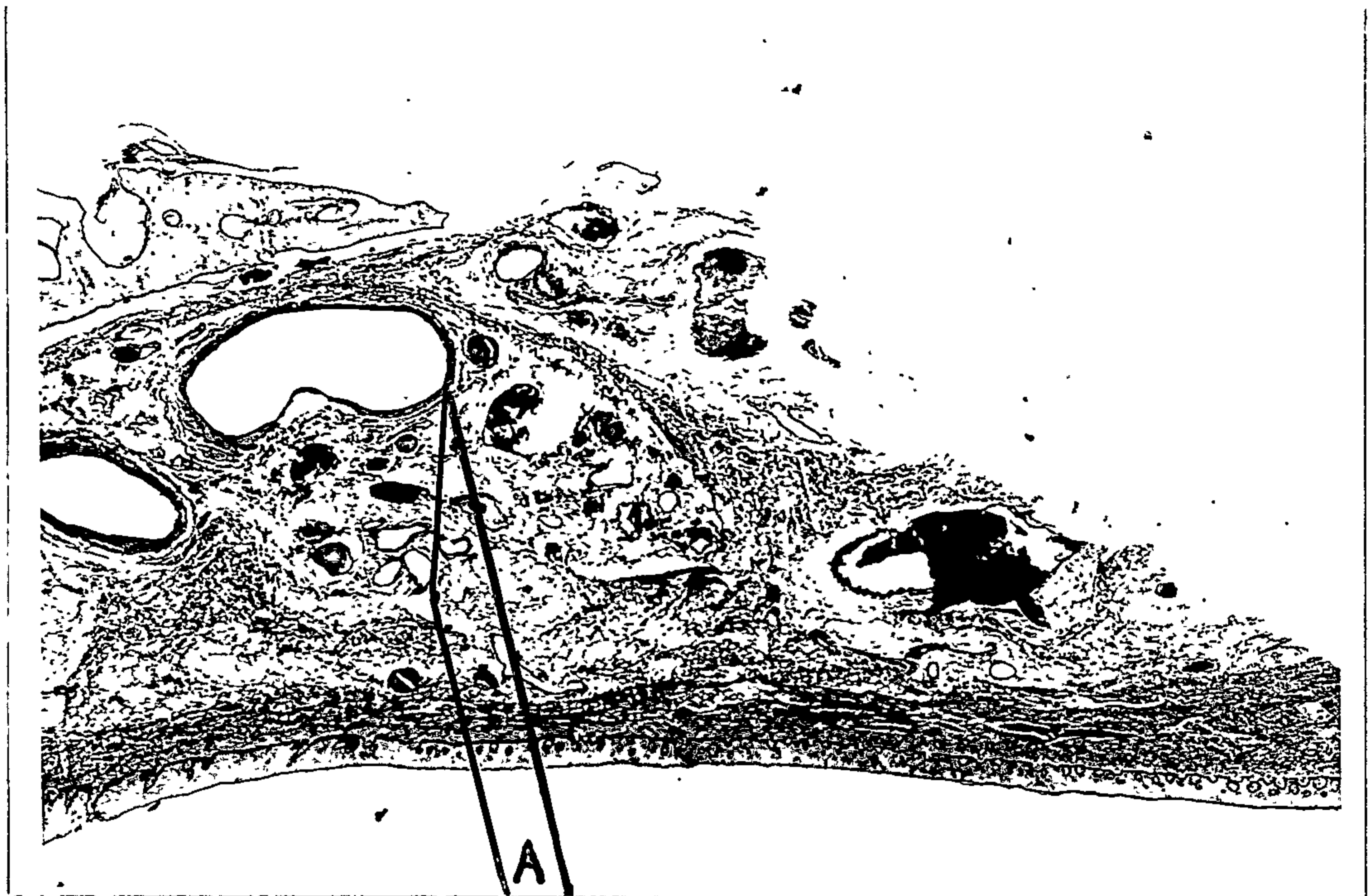


Fig. 6 - Coronal section 2-3 mm anterior to the greater palatine foramen showing the junction of the palatine and alveolar processes of the maxilla together with the overlying mucoperiosteum. Haematoxylin and eosin. 14 magnifications. "A" represents the comparative size of a 26 gauge needle.

Figures 7 - 14.

Serial horizontal sections of the pterygomandibular space from the level of the maxillary artery to the mandibular foramen. Haematoxylin and eosin. 8 magnifications.

- (A) inferior alveolar nerve
- (B) lingual nerve
- (C) maxillary artery
- (D) inferior alveolar artery
- (E) inferior alveolar veins
- (F) spheno-mandibular ligament
- (G) represents the position and comparative size of a 25 gauge mandibular block needle (Fig. 12).

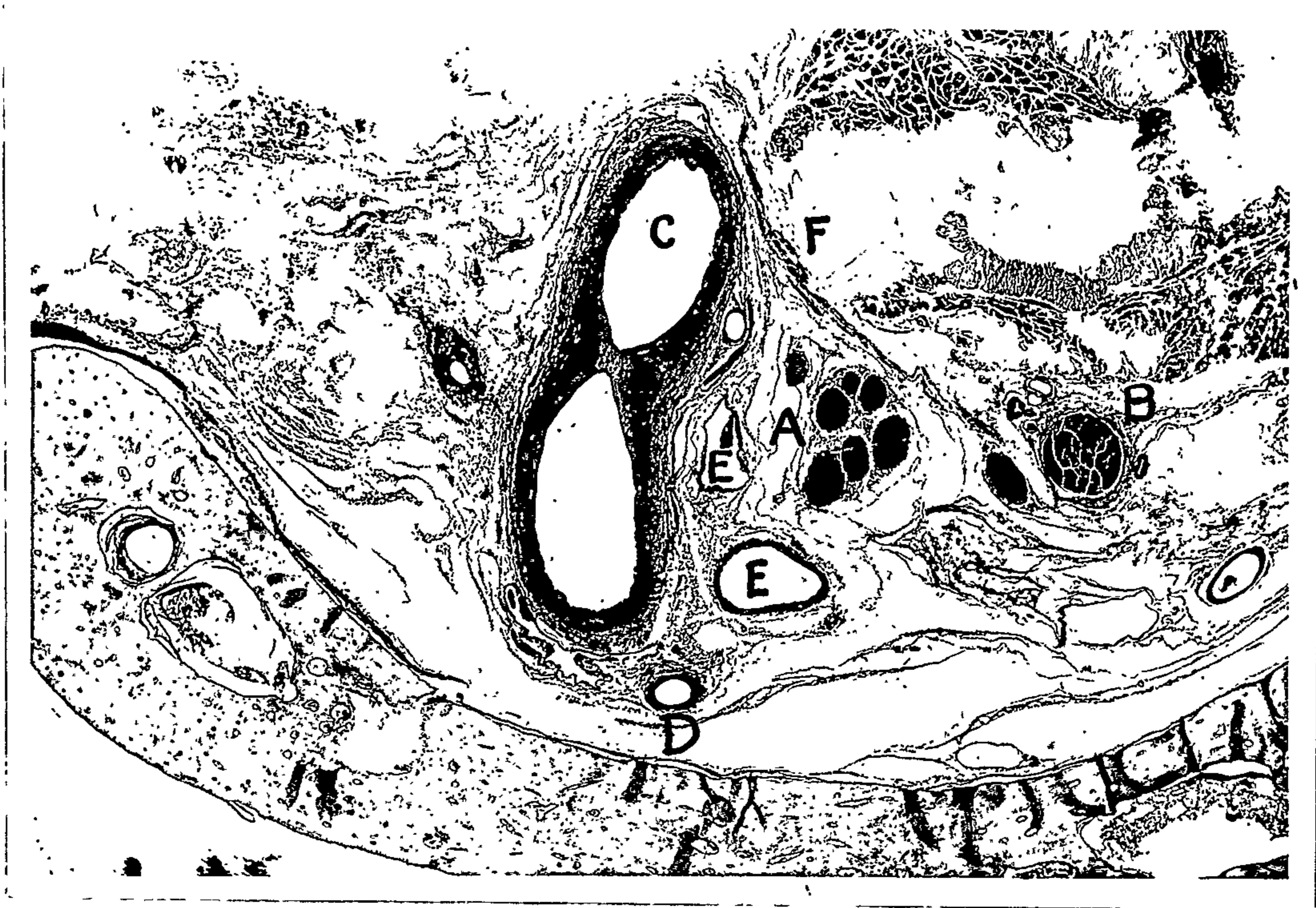


Figure 7.

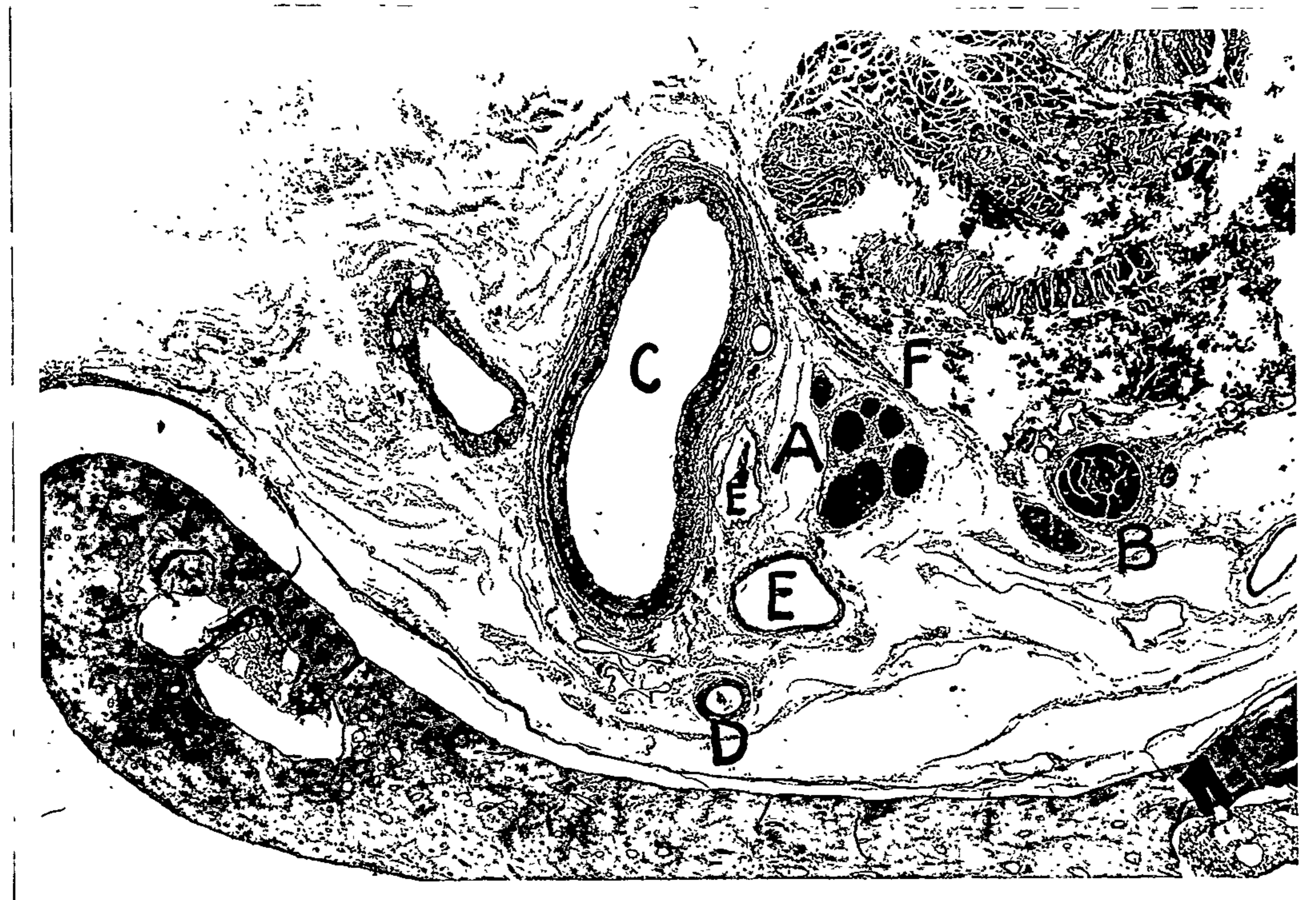


Figure 8.



Figure 9.



Figure 10.

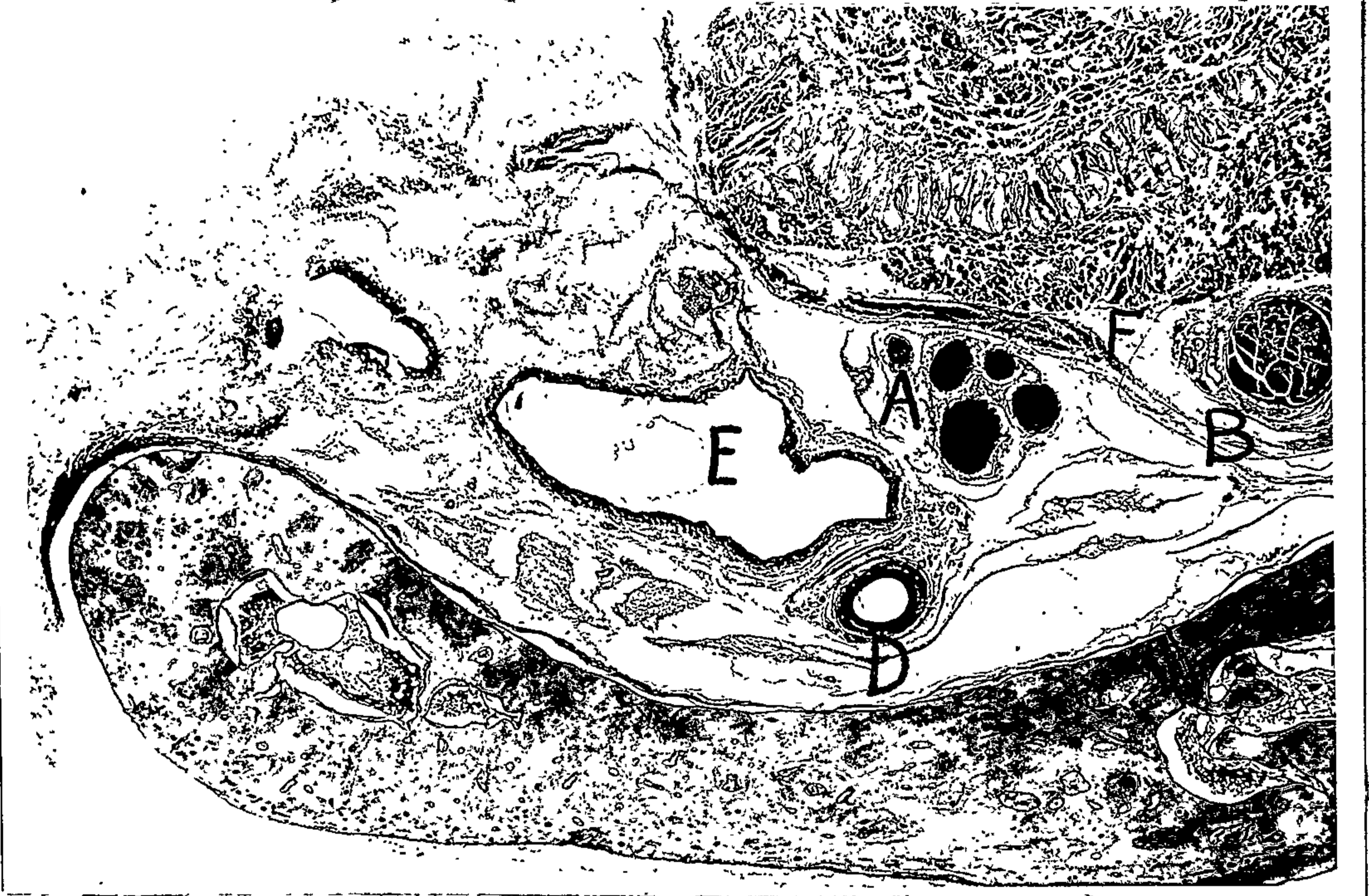


Figure 11.



Figure 12.



Figure 13.

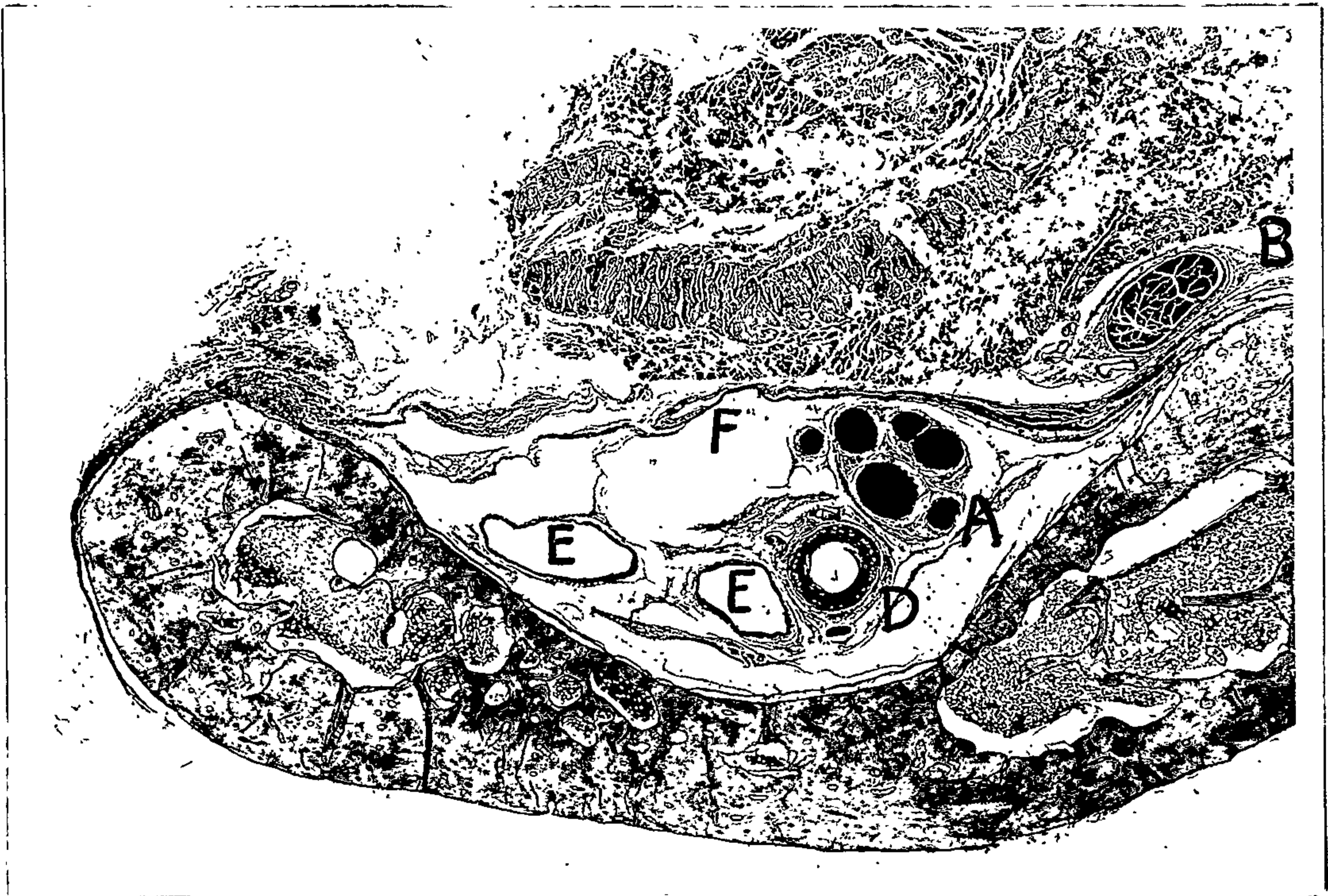


Figure 14.

to supply the loose connective tissue of the space itself. Posteriorly, the posterior facial vein and its tributaries, the maxillary veins, skirt the pterygomandibular space.

3B. DISCUSSION OF ANATOMICAL AND HISTOLOGICAL OBSERVATIONS.

The following extract from the report of an investigation of the effect of site of injection on the subsequent plasma level of local analgesic drugs (Scott 1964), may also apply to the pterygomandibular space.

"The results obtained in this study show that much higher plasma levels follow intercostal block, compared with epidural block. This would indicate that the epidural space is relatively avascular. The amount of blood flow through capillaries, is of course, the most important factor in absorption of deposited drug and though the epidural space contains an extensive network of veins, much of the blood in these veins is diverted from outside the space and is not, therefore, able to absorb local anaesthetics."

Harris (1957) in a survey of the results of aspiration before injection of dental local anaesthetics, writes, "where there is living tissue, there is vascularity and the smaller branches are abundantly and randomly distributed."

His observation seems less applicable to the loose connective and fatty tissue of the pterygomandibular space than to other parts of the oral environment. As previously

mentioned, histological examination reveals relatively few small branches, whereas the course of the large vessels is influenced by bony landmarks such as the mandibular neck and foramen and is, therefore, fairly predictable.

Sicher (1965) mentions, "it is surprising, in mandibular anaesthesia, how often the needle is found to have entered a vein. The reason for the high percentage of venous injuries seems to be the course of the inferior dental artery and veins. This course does not depend on the position of the maxillary artery and veins in the region of the mandibular neck. The lower alveolar vessels are in all individuals much closer to the inner surface of the ramus than to the lower alveolar nerve. The inferior alveolar artery and veins therefore are always closely related to bone and thus one of the veins is frequently punctured."

In blocking the inferior alveolar nerve contact should be made with the bony landmark provided by the posterior boundary of the mandibular sulcus (Nevin and Puterbaugh 1938, Sicher 1965), Figure 12 demonstrates the angle at which the mandibular block needle approaches the inferior alveolar vessels and the adjacent bone of the mandibular sulcus, to which they are closely related. It seems reasonable to suppose that, when vascular injury does occur, the inferior alveolar vessels have been caught

between the needle point and bone, and punctured. Although this type of accident would occur more easily to the flabby thin-walled veins, the artery, despite its thick elastic walls and tough slippery surface, is also vulnerable.

Using the accepted direct intra-oral technique of inferior alveolar nerve block, occasional injury to the vessels within the pterygomandibular space, and more particularly, within the mandibular sulcus, is unavoidable. The incidence of vascular injury associated with this injection has been the subject of a number of independent investigations.

Figures indicating the incidence of vascular injury with the mandibular block injection, vary from as low as 3.6 percent (Harris 1957), and 4.1 percent (Forrest 1959), to 11 percent (Schiano and Strambi 1964) and 12 percent (Frye 1963 and Shira 1962).

Individual differences in technique probably account for the differences in the results of the aspiration surveys cited. If the results of an aspiration survey are to have practical application, details of the way in which the survey is performed should be known. Therefore some of the variables which may influence the results of these surveys should first be considered. Then a technique of investigation can be devised which will indicate not only the incidence of vascular injury associated with mandibular

block injection, but also the location of such injury and the manner in which it occurs.

Clinical observation suggests that vascular injury in itself is not a serious complication of the mandibular block injection. If however, as a result of such injury the needle point occupies the lumen of a blood vessel while local anaesthetic solution is deposited, intravascular injection occurs. Therefore, it is of more practical importance to know the frequency with which vascular injury occurs at the inferior alveolar and lingual nerve injection sites as well as at any other sites within the pterygo-mandibular space where local anaesthetic is deposited. The value of applying the aspiration test prior to injection, as a means of limiting local anaesthetic systemic toxicity and reducing anaesthetic failures, can be assessed from such information.

4A. DISSECTION OF THE HARD PALATE.

An incision was made along the crest of the edentulous alveolar ridge and the epithelial layer separated from the underlying lamina propria of the mucosa.

Over the anterior region of the hard palate and along the palatine raphe and crest of the ridge, the mucoperiosteum is thin and closely applied to bone. In the molar region, the space between the lamina propria of the

mucosa and the periosteum covering the palatal and alveolar processes of the maxilla widens, to assume a roughly triangular shape when viewed in coronal section. The angle between these two bony surfaces becomes progressively less obtuse further posteriorly so that the triangular submucosal space is of maximum depth just anterior to the greater palatine foramen. The submucous layer contains the blood vessels and nerves which supply the palate enclosed in loose connective tissue which is therefore most voluminous around and immediately in front of the greater palatine foramen (Sicher 1965).

The submucosal layer in the molar-premolar region is traversed by fibrous bands which join the lamina propria to the periosteum thereby subdividing the intervening space into compartments. According to the content of these compartments, the palate is further subdivided into an anterolateral fatty zone and a posterolateral glandular zone (Orban 1966). It is necessary to sever these dense fibrous attachments to remove the lamina propria.

The spatial relationship of the vasculature in the posterior part of the hard palate is that the venous network is superficial to the arterial trunks (Maher and Swindle 1962). Here the submucosal network of fine veins was dissected from the surrounding glandular and loose

Figure 15.



Fig. 15. - (A) Greater palatine artery.
(B) Greater palatine nerve.
(C) Small veins.

connective tissue in an attempt to isolate the main collecting vessel which provided the venous drainage of that half of the hard palate.

The greater palatine foramen may be located 3-4 mm in front of the posterior border of the hard palate or in line with the distal half of the third molar when the latter is present. As the foramen was approached, the greater palatine artery was noted emerging and coursing forward in the groove in the bone between the palatal and alveolar processes of the maxilla. The greater palatine nerve followed a similar though slightly more superficial course. No venous counterpart of the greater palatine artery was found in the region surrounding and immediately anterior to the foramen.

Maher and Swindle (1962) state that "the venous drainage of the palate is to two main collecting veins that lead to a coarse venous network in the soft palate. This network is located quite posterior to the level of the entrance of the greater palatine arteries." The severed ends of several small veins can be noted behind the greater palatine foramen superficial to the artery and nerve (Fig. 15). Microscopic examination of prepared cross-sections of the other half of the hard palate immediately in front of the greater palatine foramen, showed the main trunk of the greater palatine artery and

several of its branches in close proximity to bone with the nerve at a slightly more superficial level. No main collecting vein was apparent and the largest of the veins present were of similar cross-sectional area to the arterial branches mentioned.

The main blood supply of the hard palate is derived from the greater palatine artery. Larger branches pass medially and smaller branches laterally from the main arterial trunk to form an arcade system of arterial anastomoses (Maher and Swindle 1962), so that the entire submucosal layer contains an extensive capillary network. Lateral branching progressively reduces the size of the main trunk as it courses forward. In the anterolateral region of the palate the spatial relationship of the blood vessels is reversed with arterial trunks superficial to many venous anastomoses (Maher and Swindle 1962). Further anteriorly the submucous layer can no longer be distinguished from the lamina propria or periosteum and here the small terminal portion of the greater palatine artery anastomoses with minute terminal branches of the sphenopalatine artery which has entered the oral cavity via the lateral incisive foramen.

4B. DISCUSSION OF ANATOMICAL AND HISTOLOGICAL
OBSERVATIONS.

Local anaesthesia of the hard palate.

Complete unilateral anaesthesia of the hard and soft tissues of the palate and adjacent alveolar processes may be efficiently accomplished in two ways.

a) One injection blocking the maxillary nerve trunk and sphenopalatine ganglion in the pterygo-palatine fossa will desensitize one half of the palate since there is little nerve anastomosis with the opposite side (Corbett and Helmore 1948, Sicher 1965).

b) Two injections blocking the two nerves which supply the hard palate near their points of entry onto its oral surface will accomplish the same result. These injection sites are:-

(i) The greater palatine nerve is blocked at a point 2-3 mm anterior to the greater palatine foramen so as to avoid anaesthetising the lesser palatine nerves which supply the soft palate. The area anaesthetised by this injection includes the palatal tissues as far forward as the canine region.

(ii) The naso-palatine nerve (long sphenopalatine nerve) is blocked in the incisive fossa. This is the most suitable anterior injection site as the fossa provides a

limited region of loose connective tissue containing blood vessels of minimal size. The injection anaesthetizes the palatal tissues anterior to the canine region. The latter region is, therefore, the fringe area supplied by both the palatine and naso-palatine nerves, and requires either dual nerve block or local infiltration for desensitization (Ellis and McLarty 1963).

A notable feature of the greater palatine nerve injection site is that the region immediately beneath the lamina propria, while containing an extensive capillary network, is devoid of blood vessels of sufficient calibre to admit the twenty six gauge needle illustrated (Fig. 6). It is also significant that the larger vessels, which are those likely to admit the twenty six gauge needle, are situated deeper in the submucosal layer. Fig. (6), of course depicts only the post mortem appearance of the blood vessels in their collapsed state.

If the needle point is advanced to bone, one of these vessels may be caught between the two and punctured. For example, heavy contact with the bone of the groove enclosing the greater palatine artery is likely to injure this vessel.

It is suggested therefore, that in performing the greater palatine nerve injection the needle only be inserted to a position immediately beneath the lamina propria of the

mucosa, 2-3 mm anterior to the greater palatine foramen. A few drops of local anaesthetic solution deposited slowly in this position will anaesthetize the greater palatine nerve trunk with minimal risk of vascular injury.

CHAPTER III

AN INVESTIGATION OF SOME ASPECTS OF VASCULAR INJURY ASSOCIATED WITH THE MORE FREQUENTLY USED DENTAL LOCAL ANAESTHETIC PROCEDURES

I. AN INVESTIGATION OF THE INCIDENCE, LOCATION, AND CAUSE OF VASCULAR INJURIES ASSOCIATED WITH THE MANDIBULAR BLOCK INJECTION.

A. PURPOSE OF THE INVESTIGATION.

B. MATERIALS AND METHODS.

(a) Variable factors associated with the mandibular block injection which may influence the results of aspiration surveys.

(b) Description of the injection technique used.

C. SURVEY OF THE INCIDENCE AND LOCATION OF VASCULAR INJURY ASSOCIATED WITH THE MANDIBULAR BLOCK INJECTION.

(a) Explanation of the way in which the aspiration survey was carried out.

(b) Some pertinent aspects of the aspiration survey.

D. RESULTS.

E. DISCUSSION OF RESULTS AND RECOMMENDATIONS.

2. A SURVEY OF THE INCIDENCE OF VASCULAR INJURY ASSOCIATED WITH FREQUENTLY USED LOCAL ANAESTHETIC INFILTRATION PROCEDURES IN THE MAXILLA AND MANDIBLE, WITH PARTICULAR REFERENCE TO PALATAL TECHNIQUES.

A. THE PURPOSE OF THE INVESTIGATION.

B. MATERIALS AND METHODS.

C. RESULTS.

D. DISCUSSION OF RESULTS AND RECOMMENDATIONS.

AN INVESTIGATION OF SOME ASPECTS OF VASCULAR INJURY
ASSOCIATED WITH THE MORE FREQUENTLY USED DENTAL LOCAL
ANAESTHETIC PROCEDURES.

1. AN INVESTIGATION OF THE INCIDENCE, LOCATION, AND
CAUSE OF VASCULAR INJURIES ASSOCIATED WITH THE
MANDIBULAR BLOCK INJECTION.

A. PURPOSE OF THE INVESTIGATION.

The anatomy of the pterygomandibular space supports the hypothesis suggested by clinical experience, that the most frequent sites of vascular injury in mandibular block injection are the inferior alveolar vessels and that such injury is caused by these vessels being caught between the needle point and the bone of the mandibular sulcus. Therefore, it was decided to carry out a detailed aspiration survey in conjunction with mandibular block injection, the object being to provide additional information on this controversial aspect of local anaesthesia.

The aims of the investigation were

- a) To test the abovementioned theory.
- b) To determine other sites of vascular injury within the pterygomandibular space.
- c) To apply this information, if possible, to the avoidance of intravascular injection.

B. MATERIALS AND METHODS.

So as to eliminate the probable cause of the widely varying results recorded in previous mandibular aspiration surveys, factors influencing these surveys were examined so that a standardised technique of investigation could be established.

(a) Variable factors associated with the mandibular block injection which may influence the results of aspiration surveys.

(i) In mandibular block injection there are two neural target areas adjacent to the lingual and inferior alveolar nerves respectively. Therefore aspiration must be attempted in, at least, these two positions for each mandibular block injection.

(ii) Previous aspiration surveys do not indicate whether the test was performed with the needle point in contact with the bone of the mandibular sulcus; the inferior alveolar target area described by Nevin and Puterbaugh (1938); or just short of the periosteum, which is the correct injection site (Kemp 1965).

As mentioned previously, Sicher (1965) considers vascular injury to be a frequent complication of mandibular anaesthesia and adds that, because the inferior alveolar artery and accompanying veins are closely related to bone, one of the veins is frequently punctured. It has been

suggested in the previous chapter that a probable cause of such vascular injury is that the blood vessel is pinned between the needle point and the bone of the mandibular sulcus and punctured. If this were so, 2-3 mm withdrawal from contact with bone, which is the correct target area, should also disengage the punctured vessel and thus influence the result of aspiration.

(iii) In addition, Nevin (1952) couples the posterior facial vein with the inferior alveolar vessels as common sites of vascular injury during mandibular injection. Due to slight differences in regional anatomy or incorrect local anaesthetic technique, the needle may be advanced medially to the posterior boundary of the mandibular sulcus and enter the retromandibular space, particularly if penetration is too deep (Blaxter 1967, Anwandter 1944). Here the parotid gland is entered and the enclosed posterior facial vein frequently injured because of its size and prominence (Nevin 1952, Nevin and Puterbaugh 1938). Furthermore, if the puncture point is too high, or the needle is directed superiorly, one of the maxillary veins may be entered. The influence of the bevelled point in deflecting needles finer than 25 gauge from their intended course may also contribute to this complication (Smith 1968 A). However, the incidence of injury to either the posterior facial or maxillary veins depends mainly on the ability of

the clinician to accurately assess the anatomy of the pterygomandibular space. This introduces another variable which affects the results of aspiration surveys.

In this type of accident to the blood vessels which border the pterygomandibular space, there is no risk of intravascular injection being made if bone has not been contacted, since contact with bone is mandatory in inferior alveolar nerve block technique. Therefore, if local anaesthetic is not deposited intravascularly as a result of such injuries they have no effect on local anaesthetic systemic toxicity and this distinction should be made in recording the results of aspiration surveys. Nevertheless, whenever it is possible that the retro-mandibular space has been entered, aspiration of blood should be attempted at that position to determine whether the posterior facial vein has been injured. This is important because, injury to the large posterior facial vein or one of its tributaries, and subsequent haemorrhage, seems to produce a "pooling" of blood within the mandibular sulcus which may result in a false positive response to aspiration at the inferior alveolar nerve injection site on repositioning the syringe (Forrest 1959).

An explanation of why posterior facial vein injury seems to be associated more frequently with this phenomenon than injury to the inferior alveolar vessels

may be that, whereas the posterior facial vein may be torn in advancing through and past it, if penetration is too deep, the inferior alveolar vessels, lying close to bone, are usually only punctured causing less extravasation of blood.

(iv) High aspirating pressures should be avoided to minimise the risk of collapsing a penetrated vessel, which would lead to a false negative result. Furthermore, if fine gauge needles (28 and 30 gauge) are used, it is advisable to maintain low aspirating pressure for several seconds before assessing the response (Smith 1968, B).

(v) To eliminate the contingency of a false negative response resulting from the wall of the punctured vessel being drawn across and occluding the needle lumen during aspiration, it has been suggested that the barrel of the syringe be revolved. Kemp (1953) and Epstein (1958) advocate that aspiration be performed in two planes at right angles to each other while Foldes and McNall (1962) recommend aspiration in all four planes.

This refinement of technique would appear to be of more practical significance when venepuncture occurs with the needle almost parallel to the long axis of the vessel. It has already been noted that the inferior alveolar block needle approaches the mandibular sulcus and closely related inferior alveolar vessels obtusely,

Furthermore, if a vessel was lightly caught between the needle point and bone, revolving the syringe could actually cause venepuncture.

(vi) The delicacy of touch with which the anaesthetist explores deep bony landmarks must also influence the number of vascular injuries recorded.

b) Description of the injection technique used.

The technique of mandibular block injection used in this survey was the direct intra-oral approach. The puncture point is identified so as to allow uninterrupted passage of the needle between the anterior border of the medial pterygoid muscle and the tendinous insertion of the temporalis muscle. As previously mentioned, the needle pathway approximately corresponds to an imaginary line drawn parallel to the lower border of the body of the mandible at a level slightly above the mandibular foramen and extending from the posterior boundary of the mandibular sulcus to the premolar region of the opposite side.

In blocking the inferior alveolar nerve, the deep tissues are explored with the needle point to identify the posterior boundary and floor of the mandibular sulcus at a level slightly above the mandibular foramen. It has been established that when the mouth is widely opened, the inferior alveolar nerve is closely related to a needle in this position (Sieher 1946).

The needle is then withdrawn 2 - 3 millimetres from bone and here the local anaesthetic solution, usually 1.5 ml., is deposited. The lingual nerve is blocked along the same needle pathway by depositing approximately .5 ml at a position 5 mm deep to the puncture point. Frequently it is possible to use less than 1.5 ml. for the inferior alveolar nerve block and if the target area has been correctly assessed, labial paraesthesia is almost instantaneous and nerve block rapidly ensues.

The technique of depositing a "trail" of local anaesthetic from the mandibular sulcus to the puncture point (Locke 1962, Kobayashi 1968) is less efficient than the orthodox technique although, as will be demonstrated later, there is less likelihood of intravascular injection. However, an important principle of local anaesthesia is to use the minimum quantity of suitable concentration local anaesthetic solution consistent with the desired result (Harris 1960, Haywood 1962.). This purpose is best served by employing a precise technique based on established anatomical landmarks.

When inferior alveolar nerve block injection is given correctly, most of the local anaesthetic solution is deposited in two distinct positions. Intravascular injection in either of these positions will cause

- 1) increased systemic toxicity of the local anaesthetic solution (Shotwell 1948, Sadove 1952).

ii) anaesthetic failure (Forrest 1959). Harris (1957) found that the incidence of both these complications can be reduced by ensuring that injections are made extravascularly.

Therefore the incidence of vascular injury at the two injection sites for inferior alveolar and lingual nerve block is of particular significance.

Furthermore, as some clinicians prefer to deposit a little local anaesthetic in advance of the needle to minimise the pain of injection, the likelihood of intravenous injection at other points along the needle pathway should be considered also (Helmore 1963).

Finally, the possibility of puncture of the posterior facial vein with subsequent "pooling" of blood in the mandibular sulcus has been mentioned. As this may cause difficulty in subsequently interpreting the results of aspiration at the correct injection site, it also is worthy of investigation.

C. SURVEY OF THE INCIDENCE AND LOCATION OF VASCULAR INJURY ASSOCIATED WITH THE MANDIBULAR BLOCK INJECTION.

(a) Explanation of the way in which the aspiration survey was carried out.

The aspiration survey to be described was conducted on private patients receiving mandibular block injections for routine dental treatment. Mumford and Geddes (1959) consider that the extra manipulation associated with aspiration increases patient apprehension disproportionately to the small number of vascular injuries disclosed. In the survey described in this paper, aspiration was usually attempted four times during each mandibular block injection. While a high percentage of vascular injuries was apparent, abnormal apprehension was not. In fact, only the continued well-being of the patients made the survey practicable.

Mandibular block injections were performed on 1,000 occasions by the direct intra-oral route, employing solutions of 2 percent lignocaine with 1:50,000 sympathin and 2 percent lignocaine with 1:100,000 adrenaline. Aspirating cartridge syringes of 2.2 ml. capacity, fitted with 25 gauge x 1.5/8" needles of 18 degree bevel were used. The cartridges were of the highly efficient aspirating plunger type (Glover).

The oral mucosa was prepared and punctured, and the needle advanced about .5 cm into the pterygo-temporal space where an aspiration test was performed.

This position was designated "position 1". After depositing .5 ml. to anaesthetise the lingual nerve the syringe was inserted a variable distance gauged for each patient and usually varying between 1 and 1.5 cm. This position was designated "position 2" and was frequently found to be only 2 or 3 mm short of bone. Here again, aspiration of blood was attempted before advancing the needle to feel for the bony landmark provided by the mandibular sulcus. On contacting bone, designated "position 3", aspiration was again performed before withdrawing 2-3 mm, designated "position 4", where 1.5 ml. was deposited near the inferior alveolar nerve. The injection was made slowly after first aspirating to ensure that the local anaesthetic solution was not being administered intravascularly.

If the theory is correct that the main sites of vascular injury in the pterygomandibular space are the inferior alveolar vessels, and that injury follows their compression between the needle point and the bone of the mandibular sulcus, then this should be confirmed by the results of aspiration at position 3.

In actual fact, as was previously mentioned, a needle in position 2 was frequently found to be just short of bone and it was the next movement of 2-3 mm

to the mandibular sulcus (position 3) which resulted in puncture of a blood vessel and consequent positive response to aspiration. Withdrawal of the syringe 2-3 mm, with two exceptions, released the needle from the vessel resulting in negative aspiration. It was possible to confirm the relation of the injured vessel to bone by alternately advancing and withdrawing the needle while noting the results of aspiration in each position.

Furthermore, in advancing from position 2 to position 3, it was sometimes possible to feel the puncture of a blood vessel as it was caught between the needle point and bone. In such cases vascular injury could be confidently predicted and subsequently confirmed by aspiration. Whenever a clean puncture of a vessel in contact with the bone of the mandibular sulcus occurred, and it was possible to release and reenter the vessel, this was regarded as evidence supporting the proposed hypothesis of injury and the aspiration result was designated "classical".

(b) Several pertinent aspects of the aspiration survey should be mentioned.

(i) Where aspiration of blood has occurred, the needle lumen still retains a small amount of blood which should be allowed for in subsequent aspiration tests.

(ii) Although aspiration of blood into a cartridge does not affect the anaesthetic potency of the contained solution (Forrest 1959, Kennedy 1965), its discolouration does occasionally obscure the results of subsequent aspiration attempts and it is then advisable to reinject using a fresh cartridge.

(iii) On several occasions only a small quantity of blood could be aspirated and it was not possible to re-enter the vessel once released. Presumably a small blood vessel was involved which may have admitted only portion of the needle bevel.

(iv) On one occasion, with the needle point in light contact with bone, a negative aspiration was obtained. The syringe was revolved through ninety degrees and subsequent aspiration yielded a positive result. The possibility that a vessel was already lightly held between the needle point and bone when the initial aspiration was performed was considered. Rotation may then have produced the venepuncture evidenced by a positive response to the second aspiration.

(v) Four of the 58 positive aspirations recorded at position 3 followed an initial penetration which was too deep, bony contact having been missed. Aspiration

was not attempted at the incorrect position and on correctly repositioning the syringe, it was found difficult to obtain a negative aspiration response. It is possible that the posterior facial vein, or one of its tributaries had been punctured initially and that the resultant extravasation had produced a "pooling" of blood in the adjacent mandibular sulcus.

Therefore, these aspiration results were classified "doubtful", although they were obtained in the mandibular sulcus. Subsequently, as a result of these experiences, whenever it was judged that penetration was too deep, aspiration was performed at that position to ascertain the condition of the posterior facial vein before proceeding. This technique subsequently yielded one positive aspiration which probably resulted from injury to this vessel.

D. RESULTS.

The results of the aspiration survey for 1,000 mandibular block injections are recorded in Table II.

TABLE II

Posn.	No. of Aspirations	No. of Pos. Results	%age	Details of the Positive Responses
Posn. 1 .5 cm deep to puncture point	674	6	.89	One of the mandibular blocks yielded positive response at Posn. 3 as well as Posn. 1. Two of the positive responses occurred on opposite sides for the same patient.
Posn. 2 In mand. sulcus but not in contact with bone	1020	8	.78	The approx. distances of the sites of vascular injury from the floor of the mandibular sulcus varied between 10 mm and 2 mm. In the latter case the response to aspiration was slight possibly involving a small blood vessel which could not be re-entered once disengaged.
Posn. 3 In contact with bone of mand. sulcus	1097	58	5.2	53 of these responses conformed to the "classical" pattern described in the text, indicating a vessel punctured by compressing it against the bone of the mandibular sulcus. 4 responses were considered as possibly due to "pooling" of blood following puncture of the posterior facial vein and another was probably due to this cause. The 5 responses were classified "Doubtful".
Posn. 4 In mand. sulcus 2-3 mm from bone. The inf. alv. a. inj. site	1292	2	.15	In one response, a vessel punctured at Posn. 3 had not been disengaged at Posn. 4. In the other, the vessel was transfixed 2 mm from bone as it was possible to re-enter it by withdrawing a similar distance from bone. Three other slight responses to aspiration were disregarded as being due to pooling of blood from (a) puncture of an inferior alveolar vessel at Posn. 3. (1 case) (b) trauma associated with re-positioning the needle several times (2 cases).

Of 1000 mandibular block injections, 66 yielded a positive response to aspiration from vessels punctured within the pterygomandibular space. Three of these 66 injections yielded multiple responses to aspiration as follows:
 (a) at positions 1 & 2. (b) at positions 2 & 3.
 (c) at positions 3 & 4.

On five occasions, positive response to aspiration at position 3, followed possible injury to vessels lying outside the pterygomandibular space, viz the posterior facial veins.

The overall figure for vascular injury associated with 1000 mandibular block injections was found to be 7.1 percent. Contributing to this figure were the five "doubtful" cases where positive aspiration in the mandibular sulcus had followed too deep penetration with probable injury to the posterior facial vein and subsequent "pooling" of blood.

Where small doses of local anaesthetic are administered, as is the case with most dental procedures, manifestations of systemic toxicity usually follow venepuncture at an injection site with resultant intravascular injection (Moore 1955). In mandibular block injection the retromandibular space is not an injection site and therefore, injury to the posterior facial vein should not be regarded as a contributing factor in increasing local anaesthetic toxicity.

Consequently, an analysis of the figures for vascular injury actually occurring within the pterygomandibular space yields a figure of 6.6 percent.

One thousand and twenty aspiration attempts at position 2 (in the mandibular sulcus but not in contact with bone), yielded 8 positive results.

One of these was obtained 5 mm short of bone, it being possible to alternately leave and re-enter the vessel by advancing the needle to bone and then withdrawing it a similar distance. Presumably the vessel had been transfixed. Another occurred 2 mm from bone when it was suspected that only a small vessel was involved as

- (a) initially, little blood could be aspirated.
- (b) on advancing the needle to bone the vessel was released but could not be subsequently re-entered.

One thousand and seven aspiration attempts at position 3 (the bone of the mandibular sulcus) yielded 58 positive responses of which 53 conformed to the "classical" pattern indicative of a vessel caught between the needle point and bone before being punctured.

By this is meant that one or more of the following signs was associated with each so called "classical" venepuncture.

- (a) The vascular injury occurred in contact with bone, it having already been ascertained that no vessel had been encountered just short of bone (position 2).

- (b) in proceeding from position 2 to position 3, it was possible to feel the needle point puncture the vessel as it was held against bone.

- (c) the injured vessel could be disengaged by withdrawing the needle several millimetres from bone and

re-entered by re-inserting to bone.

The remaining five "doubtful" responses have previously been discussed.

It is worthy of mention that profuse response to aspiration was obtained in most of the cases observed, indicating that the needle lumen lay well within the lumen of the injured vessel.

One thousand two hundred and ninety two aspiration attempts at position 4, the neural target area for inferior alveolar block, yielded only 2 positive responses. In one instance the injured vessel had been penetrated at position 3 and subsequent withdrawal 2-3 mm from bone had failed to release the needle point from the vessel's lumen. In the other, the vessel was transfixed 2 mm from bone, it being possible to re-enter it by withdrawing a similar distance from bone.

Of the remaining 52 vascular injuries recorded at position 3, (in contact with bone), all yielded a negative response to aspiration at position 4, indicating that withdrawal of the needle point 2-3 mm from bone had disengaged the injured vessel.

E. DISCUSSION OF RESULTS AND RECOMMENDATIONS.

a) These clinical results confirm the hypothesis, advanced as a result of clinical and anatomical observations,

that the most frequent sites of vascular injury in mandibular block injection are the inferior alveolar vessels, and that such injury is caused by the vessel being caught between the needle point and the bone of the mandibular sulcus.

b) If the results of this survey are to be applied clinically it is first necessary to clearly establish what is the correct technique of intra-oral mandibular block by the direct route. In the correct technique, there are two distinct neural targets where the anaesthetic solution is deposited.

(i) adjacent to the lingual nerve approximately 5 mm deep to the puncture point.

(ii) adjacent to the inferior alveolar nerve 2-3 mm from the bone of the mandibular sulcus (Kemp 1965).

Variations on the standard technique are:

(iii) to inject for the inferior alveolar nerve with the needle in contact with the bone of the mandibular sulcus.

(iv) having reached the position described in (iii) to deposit a "trail" of local anaesthetic solution from there to the surface as the needle is withdrawn (Locke 1961).

(v) to deposit a little local anaesthetic solution

ahead of the needle as it is advanced into the tissues to minimise discomfort (Orinjer 1949).

It is proposed to consider each of these techniques in the light of the information gathered and to make recommendations accordingly.

The accepted technique of mandibular block.

If aspiration is not practiced, the risk of intravascular injection associated with this technique is .15 percent at the inferior alveolar nerve injection site, and .89 percent at the lingual nerve injection site. Both figures are extremely small.

However, as all the local anaesthetic is deposited at these two positions, aspiration before injection is essential to ensure that a concentrated "slug" of local anaesthetic solution is not released directly into the general circulation as a result of rapid injection (Paton 1960, Crawford 1966). Intravascular injection would cause marked increase in systemic toxicity of the local anaesthetic solution and absence of local anaesthetic effect.

Technique (iii). If the needle is in contact with the bone of the mandibular sulcus while the inferior alveolar nerve injection is made and if aspiration is not performed, the likelihood of intravascular injection is a much higher 5.2 percent. Therefore, it is recommended

that aspiration of blood be not attempted in this position, but that the needle always be withdrawn a distance of 2-3 mm from bone before the test is applied prior to injection.

There are three reasons why this is desirable.

(1) The sensitive blood vessels and periosteum are thereby avoided.

(2) Unlike the inferior alveolar vessels, the nerve does not lie in contact with the ramus except at the mandibular foramen where the lingula offers it protection from needle trauma (Sicher 1965). Accordingly, a position just short of bone should be closer to the inferior alveolar nerve.

(3) The contents of the cartridge will always be clear when the neural target area is reached since blood will not involuntarily enter the syringe should vascular injury occur in contact with bone (Kennedy 1965, Shotwell 1948, Harris, 1957).

Technique (iv). This technique has the inherent deficiency that it fails to use the available local anaesthetic solution to the best advantage. However, the risk of depositing more than a few minims of local anaesthetic intravascularly is small, as the needle point is continually moving and the position where venepuncture is most likely to occur is left at the start of the injection.

Goldman and Gray (1963) in a trial of a new local anaesthetic agent, stated that aspiration prior to injection influenced neither the grade of anaesthesia nor the incidence of side reactions. Kennedy (1965) rightly disputes this claim which is hard to justify when applied, for example, to the abovementioned accepted technique of mandibular block injection.

However, if the majority of the 67 dentists engaged in this survey favoured technique (iv) it is possible that satisfactory though somewhat less than ideal results could have been obtained with little risk of side reaction despite the lack of preventive measures. Goldman and Gray (1963) recognised the limitations of their method of investigation which suffered from lack of rigid control due to the large number of operators involved. A critical appraisal of every aspect of local anaesthetic investigations is necessary before ascribing undue significance to their results.

Every local anaesthetic injection should be approached as an exercise in anatomy and not merely as a stereotyped procedure. The advantages gained thereby, in terms of rapidity and depth of anaesthesia with freedom from local and systemic complications, are abundantly obvious.

Technique (v). It has been claimed (Helmore 1963) as a strong argument against the technique of injecting as the needle is advanced, that aspiration should be performed whenever the needle point is moved within the tissues.

The results of this investigation indicate that a degree of safety from intravascular injection exists so long as the needle point is not in contact with bone while the injection is being made. However, for absolute safety, aspiration should be attempted wherever anaesthetic is deposited as the needle is advanced or withdrawn.

One aspect of mandibular anaesthesia relating to systemic toxicity which merits further study is the rate of absorption of local anaesthetic solution from the pterygomandibular space and the influence on this of vasoconstrictor drugs (Dhuner et al 1965).

2. A SURVEY OF THE INCIDENCE OF VASCULAR INJURY ASSOCIATED WITH FREQUENTLY USED LOCAL ANAESTHETIC INFILTRATION PROCEDURES IN THE MAXILLA AND MANDIBLE, WITH PARTICULAR REFERENCE TO PALATAL TECHNIQUES.

A. THE PURPOSE OF THE INVESTIGATION.

The purpose of this investigation was to determine the incidence of vascular injury associated with those

local anaesthetic infiltration procedures, both maxillary and mandibular, which are most commonly used in general dental practice (Kutscher and Mercadante 1958). These are the labial, buccal, lingual and palatal infiltration injections and also the greater palatine and naso-palatine nerve injections. Although the last two mentioned could be classified as regional procedures, for convenience they were grouped together with the infiltration injections.

B. MATERIALS AND METHODS.

In conjunction with the routine treatment of dental patients in private practice, a record of the results of aspiration with the abovementioned local anaesthetic procedures was made.

For this purpose aspirating cartridge syringes of 2.2 ml capacity, fitted with 25 gauge x 1* needles were used. The cartridges were of the aspirating plunger type (Glover). The needle bevel was always faced towards bone and the aspiration test was applied at the injection site prior to deposition of the solution.

With maxillary, labial and buccal infiltration injections, the aim in each instance was to deposit the local anaesthetic over the apical region of the tooth to be anaesthetised. Although 54 infiltration injections

were given in the lower anterior region, most were for deciduous extraction and therefore not deposited deeply in the mental fossa, a site in which vascular injury has occasionally been observed. (Personal observation, Schiano and Strambi 1964, Forrest 1959).

The naso-palatine nerve was blocked in the incisive fossa and the lingual and long buccal submucosal injections were deposited superficially, adjacent to the appropriate tooth.

The greater palatine nerve injections were given just beneath the lamina propria of the mucosa as described previously so as to keep well away from bony contact. In infiltrating on the palatal aspect of the maxillary premolar and canine teeth, frequently it was not possible to avoid contacting bone as here the submucosal layer is often thin and the mucoperiosteum dense and rigid. Furthermore the blood vessels are firmly held between the periosteum and lamina propria and are consequently exposed to the likelihood of injury by the needle point.

C. RESULTS.

The results of the aspiration survey on infiltration injections are recorded in Table III.

TABLE III.

Inject- ion site	buccal	labial	lingual	greater palatine inj.	naso- palatine inj.	palatal aspect of canine- premolar region
No. of infiltr. inject. given	1224	349	38	171	15	75
No. of Pos. resp- onses to asp.	0	0	0	0	0	4

D. DISCUSSION OF RESULTS AND RECOMMENDATIONS.

(a) When using a 25 gauge needle, venepuncture is an infrequent complication of buccal, labial and lingual infiltration injections in the maxilla and mandible.

(b) Because of the distribution of blood vessels in the sub-mucosa adjacent to the greater palatine foramen, shallow injection here minimises the incidence of vascular injury. This has the dual advantage of reducing the likelihood of, not only intravascular injection with its undesirable sequelae, but also the embarrassing haemorrhage which follows the puncturing of a large palatal vessel.

Sicher (1965) in dealing with the greater palatine nerve injection, states "it is the lack of resistance during this injection which is a sign that the needle has been

introduced at the right place". However, complete lack of resistance is strongly suggestive of intravascular injection, and this sign requires careful interpretation whether the aspiration test has preceded injection or not.

The palatal injection sites also provide signs which are useful aids in avoiding intravascular injection. With intravenous injection, the vasoconstrictor component of local anaesthetics produces only a transient blanching at the injection site due to the solution being rapidly dispersed into the general circulation. Intra-arterial injection, on the other hand, causes immediate widespread vasoconstriction of the arterial branches distal to the trunk involved. Therefore, the puncture point should be in view throughout the infiltration procedure. Slow injection then allows time for appropriate preventive measures, should these signs of intravascular injection be observed.

(c) The palatal tissues adjacent to the canine and premolar teeth present a poor site for injection. In this region, there is often little depth of investing soft tissue into which an injection can be made without causing pressure and pain, and possibly injury to the palatal vasculature lying therein. Therefore, if possible this region should be avoided as an injection site.

The greater palatine nerve injection blocks afferent impulses arising from the tissues on the palatal aspects of the molar and premolar teeth. Infiltration of local anaesthetic palatally to the premolars is neither necessary nor advisable, since it is both more painful and productive of more vascular injuries than the greater palatine nerve injection. It should be stressed however, that the latter injection be given as recommended, immediately beneath the lamina propria to minimise the risk of vascular injury, and 2-3 mm in front of the greater palatine foramen to avoid anaesthesia of the regions innervated by the lesser palatine nerves.

When palatal anaesthesia for the canine tooth only is required, shallow local infiltration is indicated. However, when other anterior teeth are also involved for which a naso-palatine nerve injection has already been given, the greater palatine nerve injection should be considered as an alternative to local infiltration for establishing palatal anaesthesia of the canine region.

The removal of sound deciduous maxillary canine teeth for orthodontic reasons often produces little trauma to the palatal gingiva. Palatal anaesthesia in these cases can be accomplished by topical application rather than local infiltration, which in this region, produces considerable discomfort to the patient and some risk of vascular injury.

Where excessive pressure is used to deposit local anaesthetic in the dense palatal tissues of the canine-premolar region, the rubber plunger of non-aspirating type cartridges is frequently distorted. When pressure on the plunger is released, its elasticity creates suction within the cartridge which is often sufficient to aspirate blood from a punctured vessel (Cowan 1959). Although the combination of high injection pressure and venepuncture seems contradictory, the two situations may coexist presumably where the long bevel of the needle only partially enters the lumen of a small blood vessel.

This phenomenon has been observed personally, both in teaching clinics and in private practice, though never with a glass syringe, and may explain the reports of spontaneous aspiration of blood reported in the literature (Shotwell 1948, Goldman and Gray 1963).

(d) The surprisingly low incidence of vascular injury associated with the greater palatine canal approach to the pterygo-palatine fossa (Corbett and Helmore 1948, Personal observation), may be explained by the absence of greater palatine veins from the canal. The findings of this dissection support the observation of Maher and Swindle (1962) that the main venous drainage of the hard palate is via collecting vessels to a coarse network in the soft palate.

(e) The small calibre of the terminal blood vessels occupying the incisive fossa reduces the likelihood of vascular injury associated with the naso-palatine injection.

(f) As 26 gauge needles were preferred to the larger 25 gauge recommended for satisfactory aspiration studies (Foldes and McNall 1962), this test was discontinued for infiltration injections on completion of the short survey reported in Table III. Recent investigations indicate however that aspiration can be successfully accomplished with finer than 25 gauge needles (Wittrock and Fisher 1968, Smith 1968 B). Since completion of the survey, a large number of greater palatine injections have been given as recommended, just beneath the lamina propria of the mucosa, 2-3mm in front of the greater palatine foramen. The incidence of successful anaesthesia has not been adversely affected by this technique and the complication of blood flowing from the puncture point has been entirely eliminated. Furthermore, it is considered that all the injections were deposited extravascularly. This claim is based on

- (i) the appearance of the injection site during infiltration of a local anaesthetic solution containing 1:100,000 adrenaline.
- (ii) the incidence of satisfactory anaesthesia despite the small amounts of solution used.

CHAPTER IV.

VASOCONSTRICTORS.

1. INTRODUCTION
2. LOCAL EFFECTS OF VASOCONSTRICTORS.
 - A. Sympathetic vasomotor control.
 - B. The absorptive capillary bed.
3. SYSTEMIC EFFECTS OF VASOCONSTRICTORS.
 - A. Cardiovascular effects.
 - B. Central nervous system effects.

VASOCONSTRICTORS.

1. INTRODUCTION.

The term "local anaesthesia" describes that state of localized insensibility to pain, without loss of consciousness, achieved by the application of drugs to sensory neurones in which they reversibly depress conduction of afferent impulses (Current Clinical Dental Terminology 1963, Wood-Smith and Stewart 1962). Therefore the object in local anaesthesia is to deposit and retain the anaesthetic solution within a small circumscribed area around the nerves to be anaesthetised. As all local anaesthetic agents, except the natural alkaloid cocaine, are vasodilators (Glover 1968, Braid and Scott 1966, Dhuner and Lewis 1966), they hasten their own absorption into the general circulation. Their vasodilatory effect is undesirable, not only because of the fleeting anaesthesia it produces when the anaesthetic is used alone, but also because rapid dissemination of the drug markedly increases its systemic toxicity. (Foldes 1966, Nevin 1952). Therefore a vasoconstrictor agent is usually included in local anaesthetic preparations to provide a "chemical tourniquet" effect which delays their absorption (Moore 1955).

Although added to delay absorption and thus reduce the toxicity of the potent local anaesthetic component, vasoconstrictor drugs themselves have a strong systemic toxic potential. However, the margin between their therapeutic and toxic dosages is wide and it is the incidence of side reactions which causes most concern. It is generally accepted that the vasoconstrictor reduces the toxicity of the total preparation in submucosal injection (Dobbs and Kader 1950). The deposition of local anaesthetic solution directly into the blood stream as a result of accidental venepuncture is, of course, contrary to the concept of local anaesthesia.

There are two aspects of vasoconstrictor action which influence the systemic toxicity of the local anaesthetic solutions in which they occur.

(a) The local effect of increasing smooth muscle tone in the walls of blood vessels, thereby producing vasoconstriction. This is the principal therapeutic action of dental vasoconstrictors.

(b) The systemic effect of vasoconstrictors, on entering the blood stream, which is an undesirable side effect of the dental use of these drugs.

In recent years the vasoconstrictor content in dental local anaesthetic preparations has been steadily

decreasing. This trend has been influenced by the introduction of the anilide local anaesthetic agents which exhibit high anaesthetic potency and penetrating ability and therefore require less vasoconstrictor to enhance their effect. Collectively they are less vasodilatory than their ester counterparts and are therefore more easily retained at the injection site (Dhuner and Lewis 1966). In addition, it has been recognised that there is an individual vasoconstrictor concentration suited, not only to each local anaesthetic agent but also to each procedure for which it is used (Harris 1961). For example, the duration of anaesthesia can be reduced by decreasing the vasoconstrictor content although, it should be realised that, in so doing, local anaesthetic toxicity is increased because of more rapid absorption.

An important influence on the trend towards decreasing vasoconstrictor concentration is the clinical impression that signs of systemic disturbance following the injection of local anaesthetic solutions, are frequently those for which adrenaline may be responsible. When signs of emotional alertness as evidenced by, fear, anxiety, restlessness and tremors are observed in a previously calm patient, the vasoconstrictor component is more likely to be the cause than the local anaesthetic

agent itself (Everett 1949, Moore 1955, Fisher 1965). Surveys involving ester local anaesthetic agents (Kutscher and Mercadante 1958, Costich 1956), revealed an increase in reactions under local anaesthesia with increase in vasoconstrictor concentration. However, although certain local anaesthetics derived from para-amino benzoic acid potentiate the action of adrenaline, this effect has not been observed with the amides (Wiedling 1954).

Adrenaline is regarded as the prototype vasoconstrictor drug (Goodman and Gilman 1966) and, for the purposes of this paper, unless specifically stated otherwise, the two terms "adrenaline" and "vasoconstrictor" have been regarded as synonymous. Of the several sympathomimetic agents available for use as dental vasoconstrictors e.g. cobefrin, neosynephrine, noradrenaline and adrenaline, there is a direct relation between therapeutic efficiency and systemic toxicity (Dille 1963, Glover 1954). Therefore, although adrenaline is the most potent vasoconstrictor agent (Holroyd et al 1960), it has also the greatest systemic effect (Dobbs and Kader 1950). Because of this, it is not only possible but often desirable to reduce its concentration to the minimum level which satisfies the requirements of the contemplated procedure.

Associated with the reduction of vasoconstrictor content of dental local anaesthetic solutions, is the

need for particular attention to two aspects of their administration. (a) rate of injection. (b) extravascular injection.

(a) Rate of Injection.

Although vasoconstrictor concentration has been progressively decreased over a period of some years, the local anaesthetic component has shown a trend towards greater systemic potency.

(i) because of the intrinsic potency of the newer agents themselves, particularly the anilide drugs.

(ii) because of the higher concentrations in which they are sometimes used.

The result is a local anaesthetic preparation which is potentially more toxic, and therefore it is necessary to observe a slower rate of deposition, so that the vasoconstrictor can exert its maximum therapeutic effect of localizing the solution to the injection site. Rapid injection increases the spread of the solution, allowing greater dilution by tissue fluid, and thus reducing the local efficiency of both the anaesthetic and vasoconstrictor components. As a result of the larger absorptive area and the reduced vasoconstriction, the drugs are rapidly absorbed into the bloodstream.

Slowing the rate of entry into the general circulation reduces the possibility of producing a toxic blood level of drug and allows larger amounts of local anaesthetic agent to be used with safety. In addition metabolism of small amounts of some readily hydrolyzable local anaesthetic agents, e.g. meprylcaine (Glover 1965, Foldes 1966), and a small proportion of the vasoconstrictor content, commences in the tissues, further minimising their systemic effects (Crout 1968, Foldes 1966). A rate of injection of 1 ml each 30 seconds is generally regarded as satisfactory for dental procedures (Glover 1968).

(b) Extravascular injection.

Although a more intense systemic response may be obtained from local anaesthetic preparations containing adrenaline; that is, the patient may feel more nervous or apprehensive than when the vasoconstrictor is omitted, the threat of serious consequences is much less when this agent is present (Dick 1953, Wallace et al 1956, Holroyd et al 1960). This opinion is based mainly on

(i) the vasoconstrictor's ability to delay absorption of the more toxic local anaesthetic component when deposited extravascularly.

(ii) Evidence indicating that the addition of adrenaline increased the lethal intravenous dose

of ester type local anaesthetics, in experimental animals, by 50 to 100 percent over that recorded for the plain local anaesthetic drug. Following intravenous injection, the vasoconstrictor's stimulatory effect on the cardiovascular system presumably maintained vital cerebral function while larger amounts of local anaesthetic drug were detoxified (Tainter and Thronson 1933, Tainter and Thronson and Moose 1938).

Subsequently, with the advent of the anilide local anaesthetic agents and their use in combination with lower concentrations of adrenaline, the incidence of cardiovascular side effects of a stimulatory nature due to the vasoconstrictor agent, has been reduced. One reason for the decreased cardiovascular response is that the local anaesthetic and vasoconstrictor agents are, to some extent, pharmacological antagonists in their direct toxic manifestations on the heart and blood vessels (Wiedling 1964, New York Heart Assoc. 1955). Presumably the addition of adrenaline to anilide local anaesthetic solutions is not as effective in stimulating the cardiovascular system and reducing the intravenous toxicity of the overall preparation, as with ester drugs. Furthermore, since the heart is the first organ reached by drugs deposited intravenously in dentistry, the characteristic depressant

effect of local anaesthetic agents on the cardiovascular system in general, and the myocardium in particular, should be avoided by injecting extra-vascularly. This is especially important when using concentrated solutions of plain local anaesthetic drug.

2. LOCAL EFFECT OF VASOCONSTRICTORS.

To understand how sympathomimetic agents limit toxicity by delaying the absorption of local anaesthetic drugs, it is necessary to examine some aspects of the anatomy and physiology of

(A) Sympathetic vasomotor control.

(B) The absorptive capillary bed.

A. Sympathetic vasomotor control.

Post ganglionic fibres of the sympathetic system accompany most blood vessels, with which they are associated in the form of a perivascular plexus; an arrangement which permits sympathetic control of vascular tone (Mason 1968, Cunningham 1953). Evidence of parasympathetic influence on the mandibular circulatory bed has been presented by Bishop and co-workers (1961), but it is generally agreed that vascular tone is regulated by a pressor amine liberated at the terminals of sympathetic nerves in response to sympathetic outflow. The peripheral transmitter

substance liberated at sympathetic nerve terminals is noradrenaline (Goodman and Gilman 1966), which acts as the chemical mediator between the neurone and the receptor site which, in this instance, is situated in the smooth muscle component of the vascular wall.

Receptor sites are hypothetical entities which conveniently explain some aspects of drug action (Paton 1960, Foster 1966). Furthermore, it is suggested that the excitatory postsynaptic potential is transmitted from receptor sites to further muscle fibres as a result of functional contact between them, and that not all smooth muscle fibres have receptor components capable of direct stimulation.

(a) The sympathetic neuro-effector junction (or synapse).

Perivascular sympathetic axons are extensions of nerve cells centrally located within sympathetic ganglia. The postganglionic axon terminates in an enlargement called the synaptic knob which is a structure designed to deliver quantities of the chemical transmitter substance noradrenaline, into the synaptic cleft which separates the synaptic knob from the receptor site in the smooth muscle component of the vascular wall (Eccles 1965, Katz 1961). Adrenaline is also liberated from sympathetic nerves in smaller quantities.

Sympathomimetic or adrenergic drugs used as vasoconstrictors in dentistry are so called because, by acting directly on the sympathetic receptor sites, they produce effects similar to those of stimulation of post-ganglionic sympathetic nerves. Other sympathomimetic drugs (e.g. ephedrine, amphetamine), produce their therapeutic effect by stimulating the release of endogenous noradrenaline from stores within the sympathetic axon (Trinker et al 1967, Ellis et al 1967). These stores of noradrenaline are located within the cytoplasm of the axon and in granular varicosities of the mitochondria which are more prevalent near the synaptic knob. Sympathetic stimulation causes the release of noradrenaline from either the cytoplasm reserves or storage granules into the cytoplasm and thence to the synaptic cleft and receptor site; a physiological process which is continually operating at sub-threshold levels to maintain normal vascular tone. Noradrenaline is metabolized in the cytoplasm of the nerve by the enzyme monoamine oxidase and if this process is inhibited, the axon reserve of noradrenaline is increased (Rond and Trinker 1966, Foster 1966).

Termination of sympathetic effect is not brought about by enzymatic destruction of noradrenaline at the synapse but by (i) re-absorption into the sympathetic axon where it is either metabolized by monoamine oxidase

or stored.

(ii) diffusion away from the site and metabolism mainly in the liver by the enzyme catechol-o-methyl transferase.

As previously mentioned, injected sympathomimetic drugs, such as adrenaline and noradrenaline, have their sites of action at the neuro-effector junction, and this action is terminated by the same processes as their endogenous counterparts (Greene 1968).

The effect of sympathomimetic drugs can be blocked by sympatholytic agents which have an affinity for, but produce no stimulus in, the sympathetic receptor site, e.g. dihydroergotamine and phentolamine (Ariens 1963, Goldberg 1964). Whereas certain sympathomimetic amines, e.g. amphetamine and ephedrine, rely on the release of stored noradrenaline to indirectly mediate their sympathomimetic effect, others impair the binding of noradrenaline within the axon (Rand and Trinker 1966, Trinker et al 1967, Ellis et al 1967).

Potentiation of the effect of some sympathomimetic agents may be caused by other drugs which prevent the re-uptake and binding of noradrenaline within the axon, which is the normal avenue for termination of sympathetic activity. Cocaine inhibits the uptake of noradrenaline

which results in the potentiation of adrenergic responses, including the unique vasoconstrictor characteristic of this drug (Greene 1968). Monoamine oxidase inhibitor drugs saturate tissue stores of adrenaline and noradrenaline in the brain and other organs by inhibiting deamination within the neurone cytoplasm. When tissue stores of noradrenaline are saturated, termination of the effect of either injected or released sympathomimetic drugs by uptake, is inhibited. Potentiation of their effect depends on this alone (Elis et al 1967).

Goldberg (1964), Elis et al (1967), and Trinker et al (1967), consider that MAOI drugs do not potentiate the effects of the catecholamines adrenaline and noradrenaline. How amino oxidase inhibitors bring out the pharmacological effects of circulating noradrenaline is not clearly understood (Robsen and Stacy 1962). However the patient under MAOI therapy is poorly prepared for the additional stress of dental procedures and the possible cardiovascular effects of injected adrenaline (Burch et al 1966).

B. The absorptive capillary bed.

Opinions differ on the calibre of blood vessels affected by vasoconstrictor action. Abrahamsen (1962) states that injected adrenaline will produce vaso-

constriction of all vessels in the region containing smooth muscle. Goodman and Gilman (1966) consider that, although capillaries have no muscular coat, they also may be affected, but Abrahamson (1962), and Fulton et al (1958), failed to substantiate this concept experimentally. The latter investigators obtained constriction of arterioles, precapillary sphincters and muscular venules in the buccal pouch of hamsters by the topical application of both adrenaline and noradrenaline, but neither amine produced any detectable change in the calibre of true capillaries.

In a similar experiment using a rubefacient (eugenol), the dilatory response was limited to the arterioles and muscular venules. The area of vessels involved was larger than the point of application indicating a conduction system with nerve-like properties. Possibly the non-myelinated perivascular plexus was responsible (Abrahamson 1962).

It is interesting to note that, although smooth muscle is absent from the walls of capillaries and small venules, vasoconstriction may be possible by changes in the lining endothelial cells which may vary in shape from flattened to columnar, thereby reducing the lumen size. Large bundles of filaments, which may be contractile, are found within the cytoplasm of these cells (Abrahamson 1962).

Increase in physiological tone of most blood vessels is effected by the action of noradrenaline liberated on stimulation of the perivascular sympathetic plexus. A similar response occurs in such vessels to analagous exogenous sympathomimetic amines, which also act through the adrenergic receptor site. In contrast, the posterior pituitary hormone, vasopressin, and its synthetic derivative felypressin, act directly on the contractile elements and are not impeded by adrenergic blocking agents such as phentolamine (Light 1965). Although capillaries may be contractile, they do not contain smooth muscle. Neither do small venules and it is doubtful if either is affected by sympathomimetic drugs or posterior pituitary derivatives.

Only blood reaching the capillary bed can serve in the process of exchange essential for cellular metabolism. The tissue cells are bathed by an intermediary tissue fluid which acts as an exchange medium, supplying nutrients and receiving the products of metabolic activity. The lymphatic system is also involved in this process. Like the blood vessels, the lymphatics are, for the most part, closed vessels and lymphatic capillaries have the same relation to tissue spaces as have blood capillaries. Lymphatics are absent from the central

nervous system and bone marrow. In voluntary muscle they are found only in the fascial planes and are generally not as prevalent as blood vessels. The larger lymphatics are contractile, reacting to both adrenaline and acetylcholine, and even smaller lymphatics show contractility in certain conditions (Abrahamson 1962).

The blood pressure necessary for adequate oxygenation of the tissues is responsible also for transudation of protein from the capillaries and this outflow is normally balanced by the resultant oncotic pressure in the tissue spaces. It is the function of the lymphatic system to maintain proper cellular environment by clearing the tissue spaces of substances which have leaked out and not been reabsorbed by the blood. For example, approximately 40 percent of circulatory protein escapes and has to be returned to the blood stream. A pressure gradient exists from the interstices to the lymphatic capillaries wherein tissue fluid becomes lymph. Since the lymphatic capillaries are freely permeable to macromolecules; escaped circulatory protein, metabolic byproducts, and foreign substances, including local anaesthetics are returned to the general circulation with minimal loss (Abrahamson 1962). Both lymphatic and blood capillaries are involved in this process of clearing the tissue spaces.

Blood vessels of all sizes from the aorta down to the smallest arterioles possess a muscular coat and are, therefore, susceptible to the action of vasoconstrictors. Bishop et al (1961), claimed that the addition of a vasoconstrictor to a local anaesthetic solution deposited in the pterygomandibular space, did not cause a decrease in blood flow through the inferior alveolar artery. Perhaps when applied locally at the concentration used in dental local anaesthetics, the vasoconstrictor does not affect blood vessels of a size comparable to the inferior alveolar artery.

However the vasoconstrictor is added to dental local anaesthetics to (i) localize the solution and (ii) delay its absorption. Both these processes involve the vasculature at capillary level and, since it is doubtful that capillaries are contractile, interest therefore centres on the vasoconstrictor's effect on the arterioles and precapillary sphincters. Vasoconstriction in the arterioles and precapillary sphincters reduces capillary blood flow thereby retarding the process of metabolic exchange necessary for absorption of local anaesthetic from the tissue spaces. In addition, lymphatic absorption is impeded by the reduced blood flow and resultant decrease in pressure gradient from the tissue spaces to the lymphatic capillaries. The possible pressor effect of vasoconstrictors

on the smaller lymphatics may also contribute (Abrahamson 1962).

3. SYSTEMIC EFFECTS OF VASOCONSTRICTORS.

Having considered the local action of vasoconstrictor drugs which, by regulating the rate of absorption, limits the systemic toxicity of local anaesthetic preparations, the systemic effects of these drugs on entering the blood stream should be discussed. The systemic effects produced by circulatory vasoconstrictor drugs are principally on the cardiovascular system and, to a minor degree, on the central nervous system.

With the small amounts used, signs of toxicity from dentally administered adrenaline are seldom observed unless influenced by rapid absorption into the blood stream. When deposited slowly extravascularly, the vasoconstrictor delays its own absorption, allowing some of the drug to be metabolised in the tissues at the injection site. The remainder is slowly absorbed and, although relatively stable in the blood stream, is taken up by other tissues, mainly the liver, in which it is rapidly metabolised. The greater part of a dose injected in man is excreted by the kidneys after inactivation by catechol-o-methyl transferase and, to a lesser extent, monoamine oxidase (Crout 1968, Green 1968, Foster 1966, Goodman and Gilman 1966, Trinker et al 1967).

Vasoconstrictors are as complex in their pharmacological actions as any drugs in use today (Monheim 1961); yet a great deal is known of the way in which they act. They are usually sympathomimetic drugs. That is to say they produce the same response as follows the stimulation of post ganglionic non-medullated fibres of the sympathetic nervous system. Of the sympathomimetic vasoconstrictor drugs suitable for use in combination with local anaesthetic agents, adrenaline and noradrenaline are most often used.

The autonomic nervous system is primarily concerned with the regulation of the body's internal environment and the maintenance of its stability. When confronted with stimuli such as fear, emotion, or pain, the sympathetic component responds by preparing the internal environment to meet the changed external circumstances (Livingston 1953). Adrenaline and noradrenaline are the physiological agents which mediate the effect of sympathetic outflow and are always present in variable amounts in the blood stream and at sympathetic neuro-effector junctions. In addition some sympathetic activity is mediated by acetylcholine (Foster 1966). Adrenaline, and to a lesser extent its adrenal precursor noradrenaline, are secreted directly into the circulation from the adrenal medulla (Goodman and Gilman 1966).

Noradrenaline derives mainly from the sympathetic nerve terminals of synapses in physiological amounts which, under normal conditions are sufficient to maintain vascular tone. Sympathetic stimulation causes the release of noradrenaline from the adrenergic axon in much larger amounts so that the threshold level necessary for vasoconstriction is attained.

The degree of stress associated with dental procedures can be gauged from the increase in plasma level of steroids which occurs in patients awaiting treatment (Shannon et al 1961). The response of the sympathetic nervous system to stimuli such as stress, fear, pain etc., is to prepare the body for activity. Reflex regulation of cardiovascular performance to increase cardiac output is the main autonomic effect by which this is accomplished.

Cardiac output

Three basic factors influence cardiac output.

- (a) cardiac function,
- (b) peripheral resistance,
- (c) degree of filling of the circulatory system.

(a) As a pump, the heart is directly responsible for cardiac output, but rarely works to the limit of its capacity, and does not actually regulate output except under abnormal conditions. Sympathetic stimulation and parasympathetic inhibition cause an increase in rate and force of contraction (of the heart) and thus pumping capacity is increased.