THE VEINS OF THE VERTEBRAL COLUMN AND THEIR ROLE IN THE SPREAD OF CANCER

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by

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Introduction

MALIGNANT DISEASE CONFRONTS us with two fundamental problems. On the one hand there is the enigma of the primary tumour itself and on the other that of its dissemination to distant sites in the body. Much effort is to-day devoted to studying the chemistry of the cell and the biochemical and genetic factors affecting its normal development and reproduction. Rather less attention is given to the manner in which tumour cells are transported about the body and to the varying circumstances that determine their destination; this is a matter of obvious significance, for the successful growth of tumour cells at a site distant from their point of origin spells defeat for curative surgery.

The work of Engell (1955), Cole *et al.* (1957), Moore *et al.* (1956), has shown that without question tumour cells can be identified in the blood stream of cancer patients and at all stages of their disease. These cells are particularly abundant in the venous blood draining from the tumour itself and there now seems little doubt that manipulation of the tumour leads to immediate increase in their number.

In the light of these new facts a clear knowledge of the venous pathways by which malignant cells can be disseminated and of the factors influencing the pattern of blood flow in the venous system becomes of considerable importance.

It is a tribute to the genius of John Hunter that his methods and principles, which transformed surgery from a primitive craft to a science, are to-day as valid as when first conceived. That surgery to be scientific must be based upon a sound knowledge of anatomy and physiology is among the most fundamental of Hunter's precepts. He was well aware that to obtain a clear concept of the nature of disease it is first necessary to understand normal structure and function.

It is, therefore, with a proper sense of debt to the great legacy provided by John Hunter that endeavour will be made to follow his precepts in presenting the findings of this investigation into the vertebral venous system. First to be considered will be the results of the anatomical studies in man and in animals; secondly, the factors influencing blood flow in the vertebral veins will be enumerated and, finally, these findings will be applied to the problem of the spread of cancer.

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Anatomy of the vertebral veins in man

The metastasis of a tumour directly from primary to secondary sites by venous pathways, without its cells first passing through the pulmonary circulation, is a familiar occurrence in the portal system. Batson (1940) was the first to suggest that just as a carcinoma of the gut may metastasize to the liver through the portal system, so a carcinoma of the prostate or breast might spread to the vertebral column and other bones of the axial skeleton by direct venous channels. This view was based upon injections made into the mammary and pelvic veins in the cadaver using radio-opaque media. He showed that the medium outlined a mass of vessels directly related to the vertebral column, which he termed the vertebral veins, and often now referred to as Batson's plexus; as more of the medium was injected it was seen to flow freely in these vertebral veins throughout the length of the spine and finally to reach the intracranial venous sinuses. In so doing a valveless venous pathway was revealed which by-passed the great systemic veins and the pulmonary circulation, having regular segmental connections with the rest of the venous system; directly linking such sites as the breast and prostate to the spine, and passing in the axis of the body between the pelvis and the cranium. Batson suggested that the distribution of these vessels could explain the frequency of metastasis to the vertebral column from primary tumours of the breast and prostate.

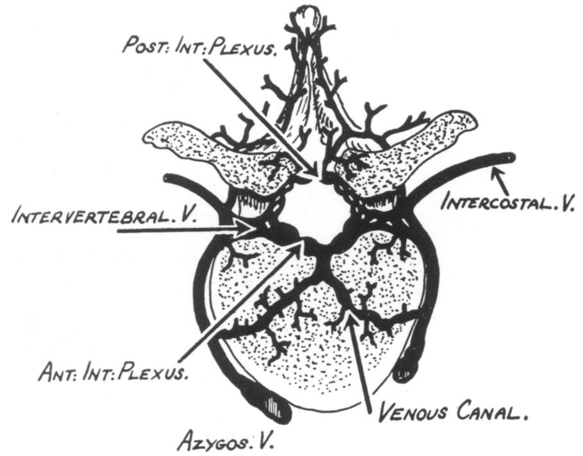
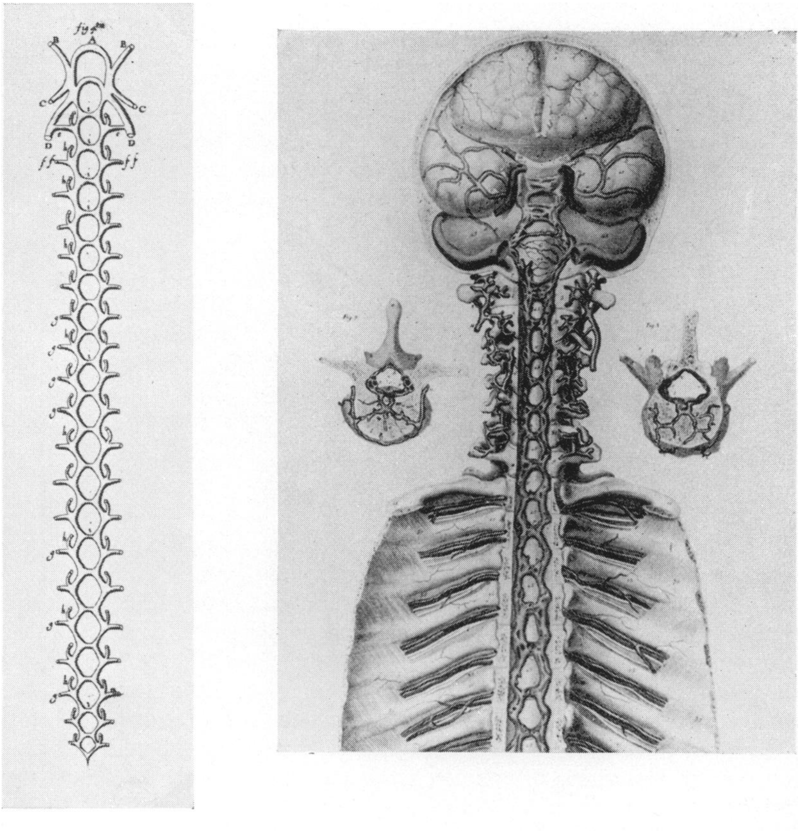


Fig. 1. Cross-section of a thoracic vertebra to show the disposition of the veins about the vertebral column and their main connections.

The veins are disposed about the vertebral column in three concentric zones (Fig. 1). The central zone consists of vessels lying within the vertebral canal in the extradural fat. An anterior and a posterior internal venous plexus can be defined, of which the anterior is the larger and forms the main component of the vertebral venous system; these vessels are in fact the true vertebral veins. At the centre of each vertebral body the two halves of the anterior plexus are joined through a large cross-anastomosis, which in turn receives one or more emissary veins from the vertebral body. These regular cross-anastomoses (which are seen also in the posterior internal plexus) give the longitudinal arrangement of these vessels the appearance of a ladder, the gaps between the " rungs " occurring at the level of the intervertebral discs.



(a) (b)

Fig. 2. (*a*) Illustration from Thomas Willis's *Cerebri Anatome* (1664) showing the longitudinal arrangement of the vertebral veins within the vertebral canal (the anterior internal plexus); the ladder-like pattern, the segmental connections and the links with the intracranial venous sinuses are depicted; drawn by Christopher Wren. (*b*) An illustration of the vertebral veins from Gilbert Breschet's anatomical treatise (1828). The venous canals within the bone are seen in the two vertebral cross-sections.

At each vertebral segment the internal plexus is connected with the systemic veins of the corresponding body segment through the intervertebral veins. These latter vessels really consist of a venous plexus surrounding the segmental nerve as it passes through the intervertebral foramen.

Surrounding the central zone there is an intermediate zone of vessels within the bone substance; these vessels traverse the vertebral bodies to join the outer zone of veins on the bone surface.

The so-called external venous plexus consists, posteriorly, of veins draining the back musculature, and anteriorly of the named segmental veins such as the posterior intercostals or the lumbar veins.

The intermediate zone is thus seen to be the connecting link between the true vertebral veins on the one hand and the systemic veins on the other. The vessels forming this link either join the segmental veins, such as the posterior intercostals, or may enter the inferior vena cava and azygos veins directly. The only valves regularly to be found within the whole complex of vessels are situated at or near the junction of the posterior intercostal veins with the azygos and hemi-azygos vessels, such valves being absent from the lumbar veins.

Historical descriptions

Descriptions of the vertebral veins have appeared in anatomical works since the 17th century. An illustration from Thomas Willis's *Cerebri Anatome*, published in 1664 (Fig. 2*a*), shows clearly the ladder-like longitudinal arrangement of the vessels, their segmental connections and links with the intracranial sinuses, though being the handiwork of Christopher Wren it must be conceded that some anatomical accuracy has been sacrificed to the architect's love of symmetry. Our knowledge of the anatomy of the vertebral veins, and indeed of much of the venous system, comes from the work of the French anatomist Gilbert Breschet, who, working at the Faculty of Medicine in Paris, in 1828 published the first of his celebrated volumes on the venous system. The work is illustrated by life-size lithographs coloured by hand and drawn from specimens injected with a mixture of isinglass and Prussian blue (Fig. 2*b*). The typical pattern of the vertebral veins is again shown, though now with great attention to anatomical detail. He also depicts the vessels within the substance of the bone in which he was greatly interested and which are often given his name though his own title for them of " the Venous Canals of Bone " is the more descriptive. These canals are, as he pointed out, most numerous in the larger vertebrae.

As the cranium is approached the veins of the internal vertebral plexus increase in size and complexity and finally pass through the foramen magnum and condylar canals to join the intracranial sinuses. There is, indeed, a close similarity in structure between the intracranial sinuses and the vertebral veins; the latter with their sinus-like expansions possess no muscle in their walls, are devoid of valves and may reasonably be regarded as the continuation of the intracranial venous sinuses around the spinal cord.

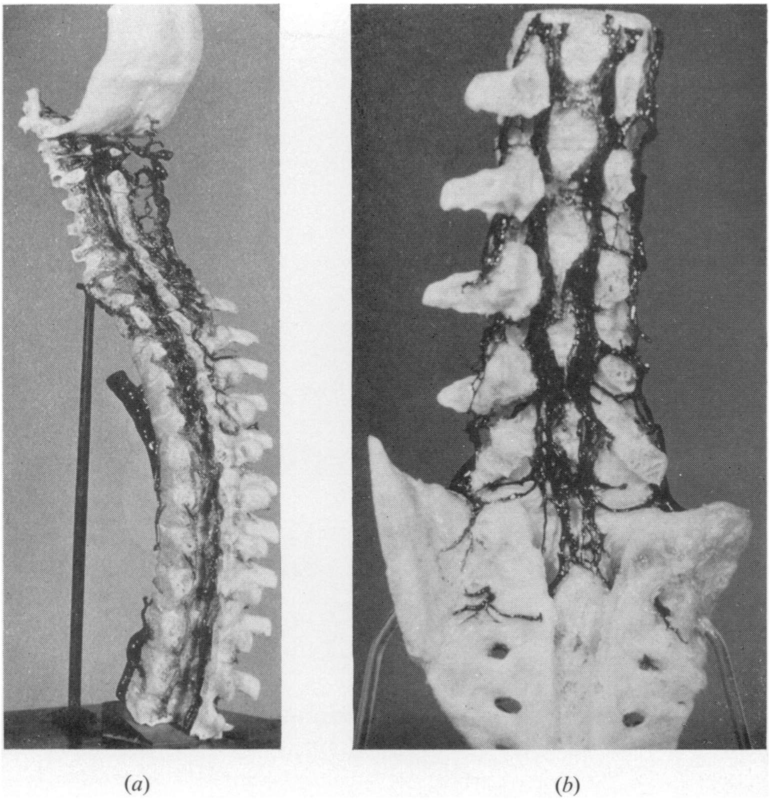
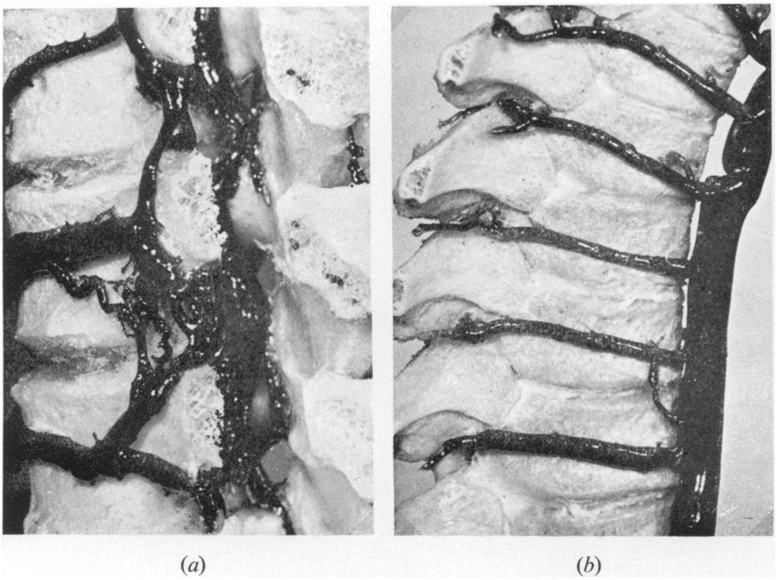


Fig. 3. (*a*) Resin cast of the vertebral veins prepared by retrograde injection of the azygos vein. The laminae have been removed to show the venous plexus within the vertebral canal and its segmental connections. The deep cervical vein, an integral part of the external vertebral venous plexus, is seen on the right-hand side of the specimen; it receives many emissary veins from the skull, one of which is depicted. (*b*) Resin cast of the vertebral veins in the lumbar and sacral region. The ladder-like arrangement of the vessels and their segmental links with the systemic veins are clearly evident.

Resin casts

The introduction of cold-setting polyester resins as an injection medium in anatomical studies (Tompsett, 1956), has made it possible to obtain more detailed and permanent casts of the vascular system than was ever previously the case; they are vastly superior to any drawings, diagrams or

X-rays upon which we have hitherto had to rely. A number of casts of the vertebral veins have been made in the Department of Surgery at King's College Hospital (Figs. 3 and 4); they were prepared by retrograde injection of the azygos vein, the soft tissues being subsequently removed, partly by dissection and partly by corrosion in four times normal sodium hydroxide at 80° C. It will be seen that from this one injection point a complex mass of vessels within the vertebral canal is filled and its multiplicity of connections with other vessels in the body is revealed. The vertebral veins, which in the cervical region reach considerable size, pass through the foramen magnum where they join the basilar and occipital sinuses and the anterior and posterior condylar veins. They are further linked to the intracranial venous sinuses through their regular segmental connections to the deep cervical veins since these vessels have as their tributaries many emissary veins in the occipital region of the skull (Fig. 3*a*). The typical pattern of the vertebral veins is well shown in the lumbar region (Fig. 3*b*). The vessels are seen to meet at the centre of each vertebral body where they receive emissary veins from the vertebra and then once more to part company as the intervertebral disc is approached.



(*a*) (*b*)

Fig. 4. (*a*) Resin cast of the vertebral veins in the lumbar region illustrating the complexity of the connections between them and the systemic veins. The laminae have been removed on one side showing the vertebral veins within the canal; a leash of vessels (the " intervertebral vein"), connects them with the lumbar veins at each vertebral segment. (*b*) Resin cast of the azygos and posterior intercostal veins. Emissary veins are seen at various points leaving the vertebral bodies to join the intercostal veins and in one instance to join the azygos vein directly.

The complex nature of the so-called intervertebral veins may be seen in a cast from the lumbar region (Fig. 4*a*); they seldom consist of a single vessel, most often being formed by a valveless plexus about the segmental nerve as it passes through the intervertebral foramen. Together with the venous canals of the bone they form the main segmental links between the vertebral and systemic veins.

The venous canals of Breschet are united to the systemic veins by means of emissary vessels, seen (Fig. 4*b*) emerging on the surface of the vertebral bodies to join the posterior intercostal veins and the azygos vein at various points. If these vessels are traced through the vertebral body (Fig. 5) it will be seen that, though tortuous, they pass directly through the bone substance without interruption to emerge through the nutrient foramen on the dorsum of the bone and there to join the internal vertebral plexus. This section also illustrates the considerable size of the vessels of the internal plexus when fully distended.

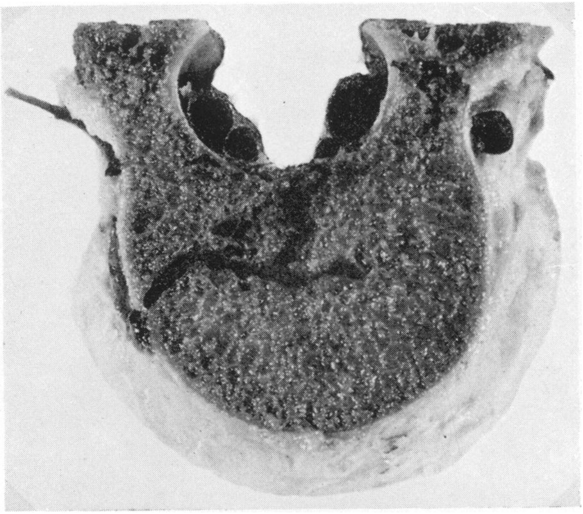


Fig. 5. Cross-section of the 12th thoracic vertebra showing the venous canals within the bone passing without interruption between the systemic veins on the bone surface and the vertebral veins within the vertebral canal. The size of the vertebral veins when fully distended is apparent. See also Figure 1.

The venous canals of the bone and the manner in which they link the central and the outer venous zones are best demonstrated by a corrosion cast in which all the tissues have been dissolved in concentrated hydrochloric acid to leave simply a cast of the vessels themselves.

It is fitting to observe at this point that the art of corrosion casting itself owes much to the work of William and John Hunter. One of their pupils, John Morgan, showed injected specimens of the blood vessels of the kidney at a meeting of the French Academy of Surgery in 1764. In his paper on " The Art of Making Anatomical Preparations by Corrosion ", published in 1786, he mentions that he gained the first rudiments of this art from the two Hunters and that the knowledge of it was at that time confined to Great Britain (Wakeley, 1955). There is thus the interesting possibility that the methods subsequently employed to such good effect by Breschet in Paris had their origins at the Hunters' school in Covent Garden. This country is still pre-eminent in the field of corrosion casting, thanks to the work of Dr. Tompsett in the Department of Anatomy in this College, and in collaboration with him a number of corrosion casts of the complete vascular system of the vertebral column have been prepared and may be seen in the Hunterian Museum.

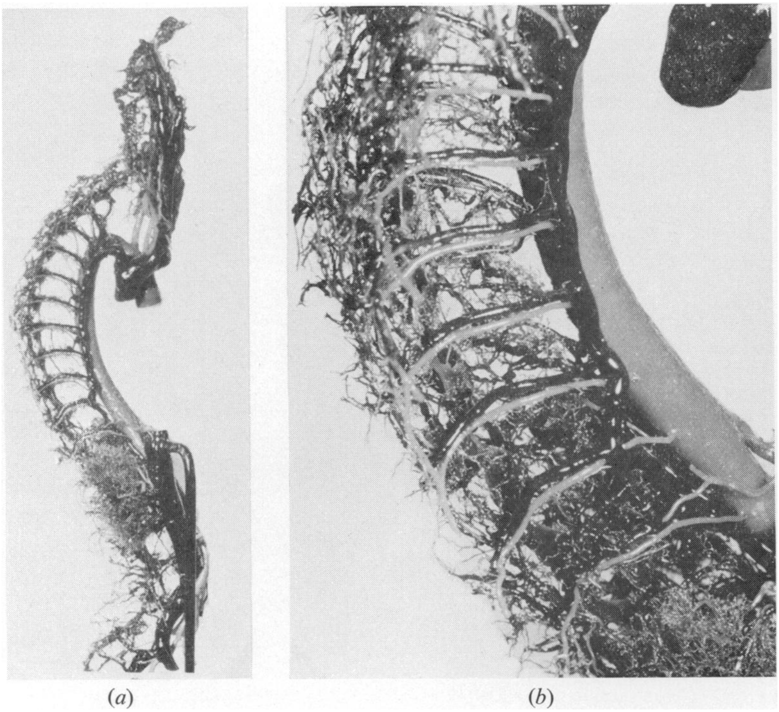

(*a*) (*b*)

Fig. 6. (*a*) Corrosion cast of the vascular system of the vertebral column from an adult female cadaver prepared by injection of the inferior vena cava and the aorta. The vertebral veins are seen to provide a collateral pathway to the caval and azygos system whilst segmentally linked to them. The cavernous sinuses are filled at the upper end of the specimen, which also includes casts of the thyroid and renal vessels. (*b*) Close view of the dorsal region to demonstrate the venous canals present within every vertebral body linking the vessels of the thoracic and abdominal cavities with the vertebral veins, which, being outside those cavities are not subject to the same pressure changes.

The cast illustrated (Fig. 6*a*) shows the relationship of the vertebral veins to the rest of the circulation and was prepared by injection of the inferior vena cava and the aorta in an adult female cadaver. The vertebral system is seen to provide a complex collateral pathway to the caval and azygos vessels, linked segmentally to them and extending throughout the axis of the body between the cavernous sinuses, seen at the upper end of the specimen, and the sacral veins at the lower end; the kidneys have also been included in the cast to show the venous links between them and the vertebral vessels. The venous canals within the vertebral bodies are seen throughout the vertebral column (Fig. 6*b*), increasing in size and complexity as the size of the vertebrae increases and reaching their zenith in the lumbar region.

As well as providing a collateral venous pathway it will also be clear that this extensive venous bed lies outside the body cavities, and is thus not subjected to the same pressure changes as the vessels within those cavities. Whilst this is a point of difference of the most fundamental importance it it does not justify the attempts that have been made by several authors to regard the vertebral veins as a separate venous system akin to the portal and pulmonary circulations. That this is a false concept has been emphasized by Harris (1941); he points out that a complex valveless venous network such as this, with an infinite number of links to the larger systemic veins, simply illustrates a persistence of the primitive venous plexus of the embryo and, far from implying any divorce from the rest of the venous system, emphasizes its close integration with it.

As an example of this integration the vertebral veins can be shown to communicate with such vessels as the bronchial veins through the azygos system (Herlihy, 1947); with the renal veins, particularly on the left side (Anson *et al.*, 1948); and through a venous plexus on the front of the cervical vertebrae with venules on the back of the thyroid gland.

Comparative anatomy

Further evidence of the primitive origins of the vertebral venous system is afforded by the fact that throughout the mammal kingdom the pattern and arrangement of these vessels is constant to a remarkable degree. In certain species they have been developed to fulfil a special function.

Harrison and Tomlinson (1956) have shown how, in the dolphin, there are two longitudinal veins lying ventral to the spinal cord as in man. In the seal, however, these two vessels unite during development to form a single venous sinus of considerable size (Fig. 7); this communicates with the cranial venous sinuses and almost every part of the venous system. In the porpoise there is again a single large extradural vein and as these animals possess only a rudimentary jugular system it would appear that their intracranial venous drainage is almost entirely by their vertebral vessels.

Many authors suggest that these huge veins serve as a reservoir for the blood expelled from the animal's body cavities during diving. This provides some clue as to their function in man, for in those mammals possessing an enlarged vertebral system there exists an exceptional need to be able rapidly to redistribute venous blood and to accept sudden back-flow from other parts of the venous circulation.

HAEMODYNAMICS

Observations in man

Structure and function are closely related; what then do the anatomical facts that have been discussed mean in terms of function? The anatomy of the vertebral veins, as shown by the resin casts, indicates that a proportion of the venous blood from the cranium, neck and chest wall, and from organs such as the breast, thyroid, kidney and prostate, may well be carried by these vessels as a matter of routine. The human and comparative anatomy also provides evidence that the vertebral veins act as a collateral venous escape route for those occasions on which the vena caval return is impeded.

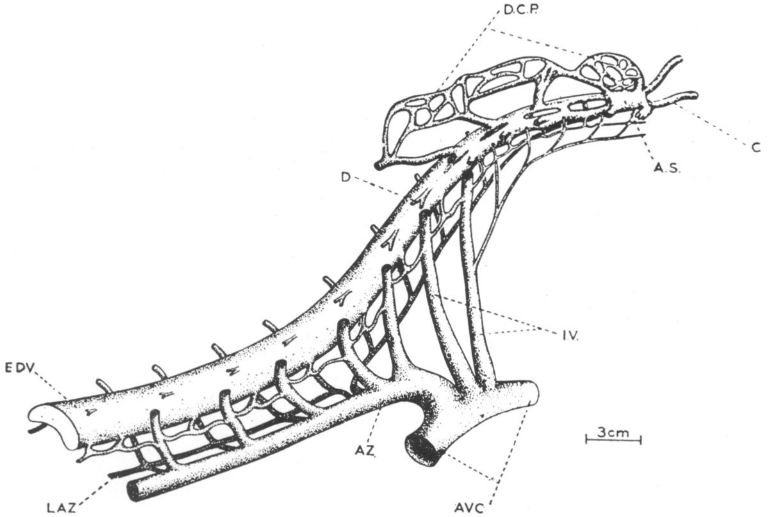


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Fig. 7. Diagram of the vertebral venous system in the seal (Harrison and Tomlinson, 1956). The two longitudinal veins unite during development to form one large venous sinus (E.D.V.) segmentally linked as in man to the azygos veins (Az) and intercostal veins (I.V.). C—communication to cranial sinuses; DCP—dorsal cervical plexus; AVC—anterior vena cava).

The physiological influences affecting venous return in this way are well known; John Hunter himself writes:

> " Breathing produces a stagnation of blood near the thorax for, during inspiration, the veins readily empty themselves but in expiration there is a degree of stagnation. Coughing, sneezing or straining in any way where the thoracic or abdominal muscles are concerned produces this effect." (*Works*, Vol. III, p. 228.)

Some indication of the degree to which venous return is influenced by the simple act of coughing is provided by the resulting pressure changes in the vena cava (Fig. 8*a*). These tracings were taken during cardiac catheterization, and it will be seen that with the tip of the catheter in the left axillary vein little pressure change is produced by coughing. As soon as the catheter passes beyond the protection of valves into the superior vena cava the pressure changes are dramatic. From a resting pressure between 0 mm./Hg. and 5 mm./Hg. peaks of up to 50 mm./Hg. are reached. Similar changes occur in the inferior vena cava (Fig. 8*b*) and here it will be noted that a series of lengthy expiratory efforts produces a more sustained pressure rise, in this instance the mean level being four times the resting pressure and lasting for six seconds. The actual pressure produced within the thorax by a cough has been estimated to reach on occasion 120 mm./Hg. (Hamilton *et al.*, 1944).

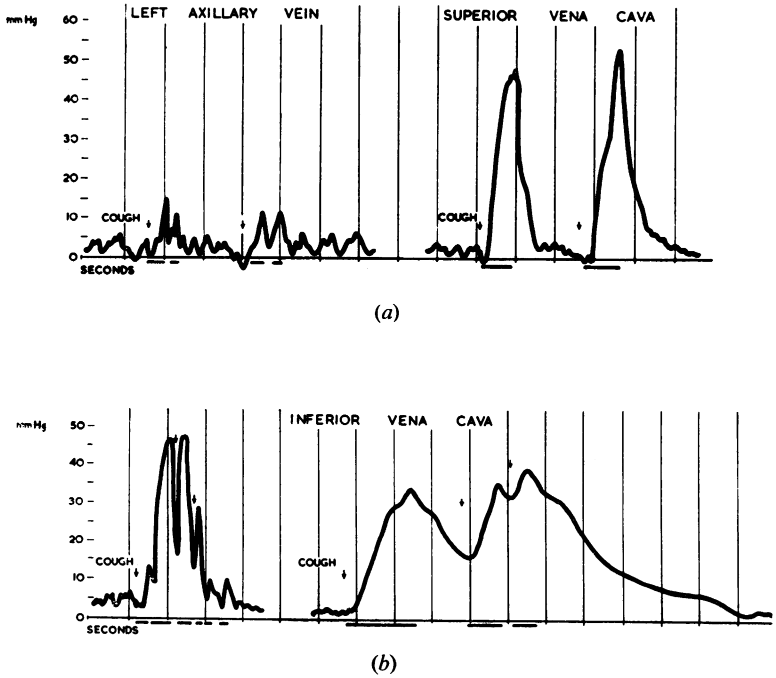

Fig. 8. Tracing taken during cardiac catheterization to show the effect of coughing on the pressure within the venae cavae. (*a*) With the catheter in the left axillary vein pressure change is minimal. Once the superior vena cava is entered the pressure rises from 5 mm./Hg. to 50 mm./Hg. when the subject coughs. (*b*) Similar effect is seen with the catheter in the inferior vena cava. More lengthy expiratory efforts (right-hand tracing) produce a four-fold pressure increase in the inferior vena cava lasting some six seconds.

It has been shown by Sharpey-Schafer (1953) that in extreme cases prolonged bouts of coughing, producing rises of intrathoracic pressure between 150 mm./Hg. and 300 mm./Hg., may so interfere with the venous return as to lead to a fall in cardiac output and consequent loss of consciousness. On the other hand Werkö (1947) and Hubay *et al.* (1954) have shown that quite small sustained increases in intrathoracic pressure, of as little as 100 mm. H_2O, will lead to a reduction in superior vena caval blood flow by as much as 30 per cent. within a few seconds.

It must be stressed that all these changes are within the physiological range, and under these circumstances blood must normally be accommodated in vessels outside the zone of pressure change in much the same way as it is in the seal and the porpoise during diving.

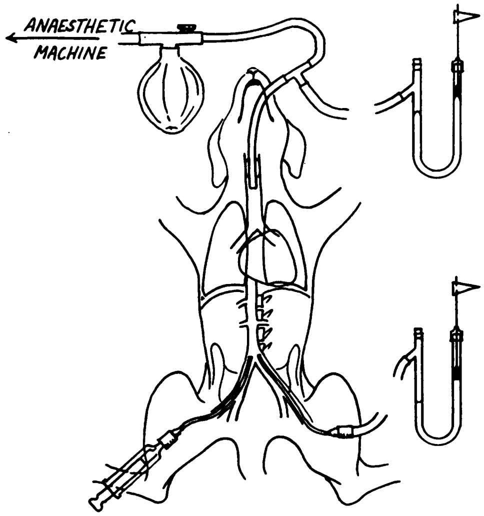

Fig. 9. Diagram to show the experimental layout used in the dog to investigate the effect of different intrapulmonary pressures on the pressure in the inferior vena cava. For details see text.

The obvious importance of changes in intrapulmonary pressure in the production of this collateral venous flow in the vertebral system led to its further study in a series of experiments using the dog and the calf, both of which animals possess a vertebral venous system closely resembling that in man (Worthman, 1956; Crock, 1960). This work was undertaken at the Buckston Browne Research Farm in collaboration with R. G. Smith, F.R.C.S., the Laming Evans Senior Research Fellow in Orthopaedic Surgery.

The animals were anaesthetized and fixed in the supine position. An endotracheal tube was passed and its cuff was inflated; the tube was then connected to a standard Boyle's anaesthetic machine, the pressure within the circuit being recorded by a mercury manometer (Fig. 9). Heparin was given to reduce the risk of clotting; a polythene catheter was introduced into the inferior vena cava through the left femoral vein and connected to a water manometer to record the vena caval pressure. Tracings from both manometers were recorded on a standard kymograph. A second polythene catheter introduced through the right femoral vein enabled venograms to be taken at various stages of the experiment. The intrapulmonary pressure was varied either by compression of the anaesthetic bag or by alteration of the valve opening and the rate of flow of the gases.

It will be seen from an example of the tracings obtained from these experiments (Fig. 10) that if the animal simply breathes against a gas flow of 8 litres/minute with the valve open, although the rise in intrapulmonary pressure is minimal (Fig. 10*a*); there is, however, an immediate increase in the vena caval pressure, from a resting level of 30 mm. H_2O to 80 mm. H_2O (Fig 10*a*). If the anaesthetic bag is now compressed at regular intervals in much the same way as during assisted respiration at operation, so as to produce peaks of 10 mm./Hg. intrathoracic pressure (Fig. 10*b*), the vena caval pressure mounts by a further 20 mm. H_2O. A sustained intrapulmonary pressure of 10 mm./Hg. causes the pressure in the vena cava to rise to a maximum level of about 110 mm. H_2O (Fig. 10*c*). It will be seen that at these pressures, which may be regarded as within a physiological range, spontaneous respiration still occurs and each breath by the animal produces a small pressure peak in the tracing from the vena cava.

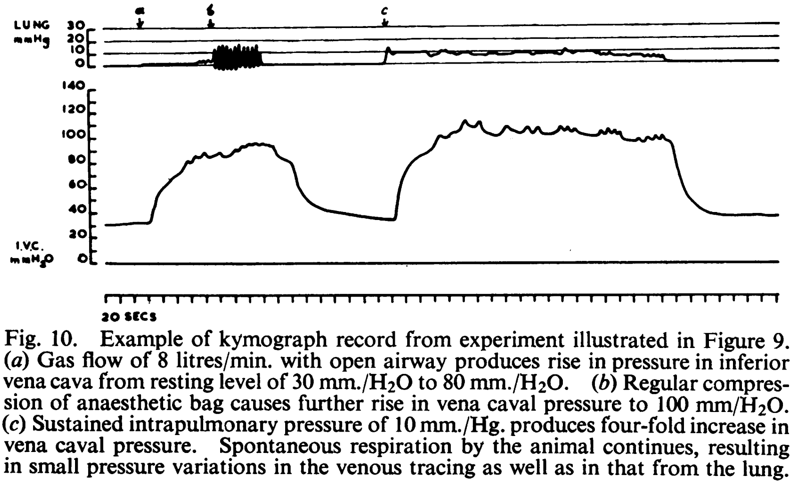

Fig. 10. Example of kymograph record from experiment illustrated in Figure 9. (*a*) Gas flow of 8 litres/min. with open airway produces rise in pressure in inferior vena cava from resting level of 30 mm./H_2O to 80 mm./H_2O. (*b*) Regular compression of anaesthetic bag causes further rise in vena caval pressure to 100 mm/H_2O. (*c*) Sustained intrapulmonary pressure of 10 mm./Hg. produces four-fold increase in vena caval pressure. Spontaneous respiration by the animal continues, resulting in small pressure variations in the venous tracing as well as in that from the lung.

Some idea of the changes in the pathways taken by the returning venous blood under these circumstances is obtained by venography. The normal flow pattern in the inferior vena cava in the dog is shown (Fig. 11*a*) following an injection of 20 c.c. of 60 per cent. hypaque; the renal veins discharging their blood into the vena cava produced two clear streams in the dye contained in that vessel. It will be noted that the vertebral veins are not demonstrated and there is nowhere any evidence of reflux. When the intrapulmonary pressure is raised to 20 mm./Hg. and the injection into the vena cava is repeated (Fig. 11*b*), the vertebral veins are to be seen clearly, discharging their collateral function whilst the flow in the vena cava is impeded at the level of the diaphragm. In addition reflux is seen to occur in many vessels, notably the hepatic, renal, lumbar and intercostal veins.

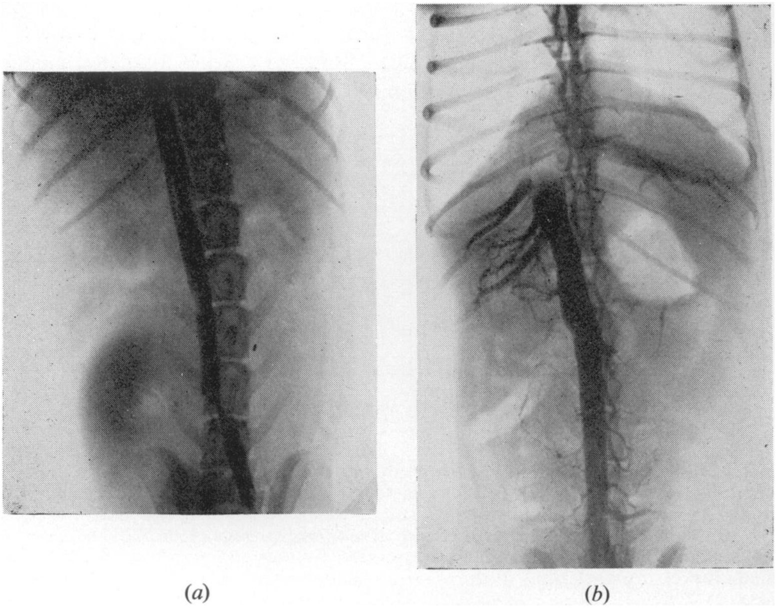
(*a*) (*b*)

Fig. 11. (*a*) Venogram to show the pattern of blood flow in the dog's vena cava under resting conditions. (*b*) When the intrapulmonary pressure is raised the blood flow in the inferior vena cava is impeded at the level of the diaphragm, and the vertebral veins take over as a collateral pathway; reflux is seen to occur in many intra-abdominal veins.

A similar effect can be demonstrated in the cervical region by injecting the dye into the superior vena cava whilst increasing the intrapulmonary pressure, and reflux again occurs into the vertebral veins of the cervical and dorsal spine.

Thus in the dog it can be shown that blood shunts under physiological pressures into the vertebral veins, which serve as a collateral path for venous blood when the vena caval return is impeded.

The next important point to be elucidated is whether, in the process of a similar shunting of blood in man, cancer emboli and cancer cells might be carried through the venous canals within the bone itself and thereby metastases in the vertebral column be facilitated. Are the venous canals in the bone in fact capable of acting as venous shunts, or do they simply serve the venous drainage of the bone itself? To investigate this problem a further series of animal experiments was undertaken in the dog and the calf (Fig. 12). The method of varying the intrapulmonary pressure was that previously employed. The animals were again heparinized and a polythene catheter was introduced into the vena cava. In order to trace the path taken by the venous blood, radioactive phosphorus (^{32}P) was employed in the form of orthophosphate in isotonic solution. As this substance emits beta particles only, with their short range of about 4 mm., the confusion from background radiation in the general circulation was minimal. A scintillation counter was placed over the animal's heart, and a Geiger probe counter 3 mm. in diameter was inserted by means of a trocar and cannula into the body of the second or third lumbar vertebra. The sensitive portion of the probe counter was positioned with the aid of X-rays so that it lay as nearly as possible in the centre of the vertebral body. A preliminary venogram, using the trocar to inject the dye, confirmed that there was free communication with the vertebral veins.

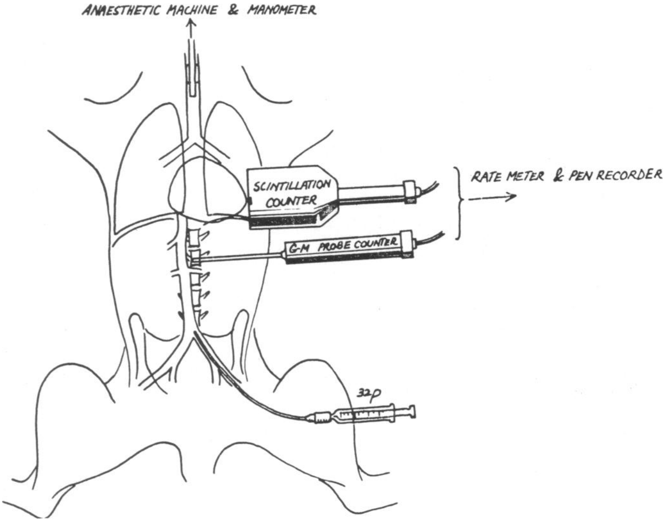

Fig. 12. Diagram of the experimental layout in the dog and the calf to investigate the possibility of venous reflux through the substance of the vertebral body during increase in intrapulmonary pressure. For details see text.

Both counters were connected through rate meters to simultaneous pen recorders. An injection of 250 microcuries of ^{32}P was then given through the vena caval catheter. Under control conditions its arrival in the heart was registered by the scintillation counter immediately and no change was recorded by the Geiger counter, apart from a slight rise in background activity. When, on the other hand, the intrapulmonary pressure is raised to a sustained level of 20 mm./Hg. at the moment of injection of the isotope there is a different sequence of events. In four of eight animals (three dogs and one calf) the arrival of the isotope was recorded in the vertebral body immediately prior to its arrival in the heart (Fig. 13). The possibility that the probe counter was responding to isotope temporarily arrested in the vena cava was excluded by placing a double dose (400 microcuries) on the front of the vertebral body without any detectable change in the Geiger counter record. The fact that not all the animal experiments gave this result is probably explained by the difficulty of placing the sensitive part of the probe counter in communication with one of the venous canals in the bone.

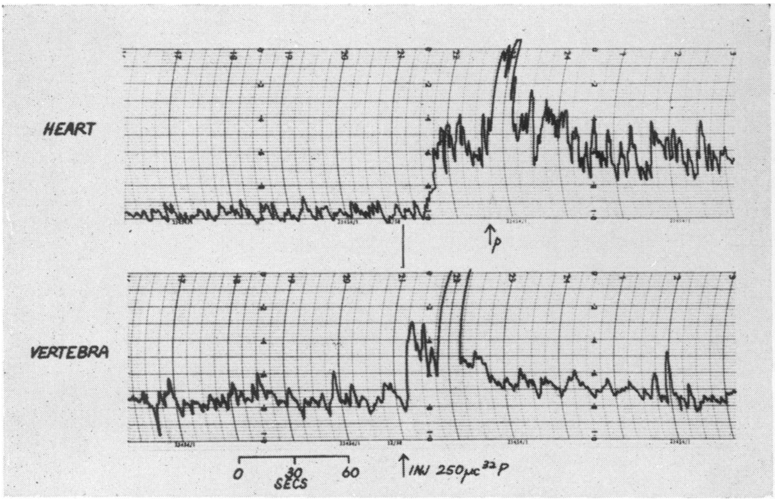

Fig. 13. Record obtained from the experiment illustrated in Figure 12. When the intrapulmonary pressure is raised an injection of radioactive phosphorus into the inferior vena cava arrives in the body of the second lumbar vertebra before reaching the heart. At the point P the pressure in the lung was released, resulting in an immediate increase in the radioactivity in the heart as the blood flow temporarily impeded in inferior vena cava returns to normal.

These findings strongly support the concept of venous reflux across the vertebral body. It should be remembered, however, that similar venous canals exist in many other bones, an obvious example being the skull. The vertebrae were chosen for these experiments because their venous canals are among the largest to be found in the skeleton. The venous canals can therefore be legitimately regarded as acting as shunts for the passage of blood from a zone of high pressure to one of low pressure during pressure changes within the body cavities.

CLINICAL STUDIES

Collateral vertebral venous flow in clinical conditions

The clinical evidence that collateral venous flow in the vertebral veins occurs regularly and in a variety of circumstances in man can only be briefly touched upon. The chief indication that the vertebral veins are acting in this capacity is provided by their becoming distended. Thus the outline of a myelogram alters with respiration as the dural sac is compressed at regular intervals by the increased volume of blood in the vertebral veins during each inspiratory phase (Reitan, 1941).

The violent pain experienced on coughing by a patient with a prolapsed intervertebral disc is probably produced by a sudden venous engorgement in the vertebral vessels and the intervertebral venous plexus surrounding the nerve root.

The manner in which venous congestion, and therefore bleeding, may be reduced at laminectomy by the avoidance of abdominal compression is well known (Pearce, 1957). Conversely the congestion produced in the vertebral and cranial veins by positive pressure respiration is recognized by anaesthetists and neurosurgeons alike.

Much radiological evidence is available to show how reflux occurs into the vertebral veins at all levels during such activities as coughing, straining or performing the Valsalva manoeuvre and Queckenstedt's test (Anderson, 1951; Abeshouse and Ruben, 1952; Taylor, 1960).

The comparative freedom from oedema of the head and neck following a bilateral block dissection shows that the vertebral veins are capable of taking on the duties of the jugular system, just as in the seal and porpoise, when necessary. Even ligation of the inferior vena cava itself is attended by less serious consequences than might be anticipated, due to the collateral venous pathway provided by these vessels.

Pathological considerations

In turning now to the application of these findings to the problem of cancer spread, and in attempting certain conclusions of surgical significance, it is necessary to enter the realm of hypothesis.

The distribution of blood-borne metastases is, as Willis (1953) remarks, subject to many vagaries, for which two main explanations exist. The first depends on the mechanics of the circulation, and the second on the differing biological properties of the various tissues; some inhibiting and others favouring the growth of cells arrested within them. There is, in addition, the question of the " dosage " of tumour cells to which a given tissue may be subjected. Coman, Eisenberg and McCutcheon (1949) believe that it is the availability of tumour cells and emboli that determines the anatomical distribution of metastases rather than local tissue factors. On this point Willis agrees that metastasis is the result of the dissemination of clumps of cells and tumour fragments rather than isolated cells.

These tumour emboli will be arrested in the first vascular bed they encounter. For systemic tumours this will of course occur in the lung and for portal system tumours in the liver. From the findings of this investigation it seems likely that tumour emboli in the systemic venous blood may also lodge in the bones of the axial skeleton before reaching the lung, just as Batson postulated. It is well recognized that some cells will pass through the capillary bed of the lung to be distributed widely throughout the body in the arterial circulation, as Schmidt (1903) and Zeidmann and Buss (1952) have demonstrated. However, the vast majority of tumour fragments and cell clumps will surely be arrested and only isolated cells will escape in this manner. If this supposition is correct, the incidence of metastases in general would be higher in the lungs, liver and axial skeleton than in any other tissue.

Willis's series of 500 autopsies on all types of malignant disease shows an incidence in the lung of 29 per cent., in the liver of 36 per cent. and in the bones of 14 per cent. In all other tissues the incidence varies from 9 per cent. in the adrenals to 1 per cent. in the skin and muscle. If on the other hand a particular tumour is considered, and one whose venous drainage might be expected to distribute tumour emboli to the vertebral venous system, the incidence of bone metastases increases. In 45 autopsies on cases of breast cancer there were 21 (47 per cent.) examples of skeletal deposits.

Autopsy figures are unsatisfactory in that they provide only a picture of the late stages of the disease, where repeated metastasis from one site to another has greatly complicated the pattern of distribution. Moreover, the skeletal incidence will tend to be artificially low due to the obvious impossibility of examining the entire skeleton. It is desirable, therefore, to know the pattern of metastasis in the earlier stages of dissemination if the mode of spread is to be more clearly understood. Such information as may be obtained from clinical studies tends to support the concept of a high skeletal incidence in the early stages of spread from breast cancer, for example. Thus Wheatley (1961), in a review of 194 cases of treated breast cancer followed up at King's College Hospital for a minimum of five years, found that no less than 38 per cent. showed radiological evidence of metastases in the axial skeleton as the first indication of recurrent disease.

Surgical application

In conclusion, what may be said of the surgical implications inherent in the concept of the dissemination of cancer cells through the vertebral venous system in the manner that has been outlined?

Half a century ago cancer was written of as an infective process, surgeons were as conscious of contaminating the wound and their instruments with cancer cells as they were of contamination by bacteria. This valuable analogy has only recently been rediscovered and written of by such authors as Crile (1956), but Sir Charles Ryall was writing in identical terms in 1908.

Moreover it is a sober thought that the use of cytotoxic agents at operation was current practice when Lister himself was first writing on antisepsis. In an address given in Glasgow in 1868, he speaks of carbolic acid as being but one of many antiseptic agents with similar beneficial properties and continues:

> " This statement is not made on theoretical grounds alone. About nine months after I had first treated compound fracture with carbolic acid, Mr. Campbell de Morgan published a paper on " The Use of Chloride of Zinc in Surgical Operations and Injuries " and was kind enough to send me a copy of it. By means of this salt he had obtained highly satisfactory results though led to employ it with a very different object in view. Mr. de Morgan used chloride of zinc in the first instance in cases of cancer upon the idea that the frequency of the return of the disease after operation might depend on the dissemination of its germs on the cut surface, and he hoped that by applying a strong solution of the chloride to the wound, so as to destroy any cancer germs that might be scattered over it, he might diminish the chance of recurrence."

To this risk of local contamination, to which some attention is once more being directed, must now be added the risk of systemic dissemination both at operation and in the course of our treatment of the patient in general.

Tyzzer (1913) showed that massage of tumours in mice increased the incidence of lung metastases by 80 per cent., an observation recently confirmed by Fisher and Turnbull (1955). Tyzzer himself warned surgeons of the risk of repeated physical examination of tumours and pleaded for the avoidance of manipulation at operation whenever possible.

Crile (1956), quoting Tyzzer's paper, remarks that the high incidence of liver metastases two years after operations for cancer of the colon and the frequency of blood-borne metastases after operations on angio-invasive thyroid tumours, raises the question of the part played by manipulation. Now in addition it is clear that circulatory mechanisms themselves may be of equal significance, and moreover there is some experimental evidence to support this contention. Coman and de Long (1951) showed that if, during the injection of living tumour cells into the femoral vein of the rat, the animal's abdomen was momentarily compressed, 12 out of 14 animals developed tumours in the vertebral column; of the 16 control animals only one developed growth in this situation. It may well be that in terms of spread at operation, positive pressure respiration, posture, shock and local tissue factors, all combine in the presence of showers of tumour emboli to dictate the site of metastasis.

CONCLUSION

It is therefore submitted for your consideration that whilst undeniably many factors are involved in the dissemination of cancer, mechanical factors play an all-important role. The so-called vagaries of the circulation tend to-day to be discounted in favour of the more fashionable biochemical considerations, but it is just these mechanical factors which lie to a far greater extent within our control than any of the other agencies at work.

A section of the body of a dorsal vertebra, from a patient who died with skeletal metastases from breast cancer and who had no evidence whatever of tumour deposits in the lung, serves to emphasize this point (Fig. 14). The azygos vein was injected with a gelatin Prussian blue solution prior to cutting the sections in order to demonstrate the vertebral system. Here may be seen, side by side, deposits of tumour and a large venous canal within the bone, from which an emissary vessel passes to join the posterior intercostal vein on the surface of the vertebral body; sections at other levels show the expected junction of this venous canal with the vertebral veins and the intercostal vein on the other side. It seems reasonable in the light of the evidence presented to ask whether the two are not in any way related to one another and to suggest that patterns of blood flow in the venous circulation as a whole, and in the vertebral veins in particular, offer a satisfactory explanation for much that is otherwise credited to hypothetical biochemistry.

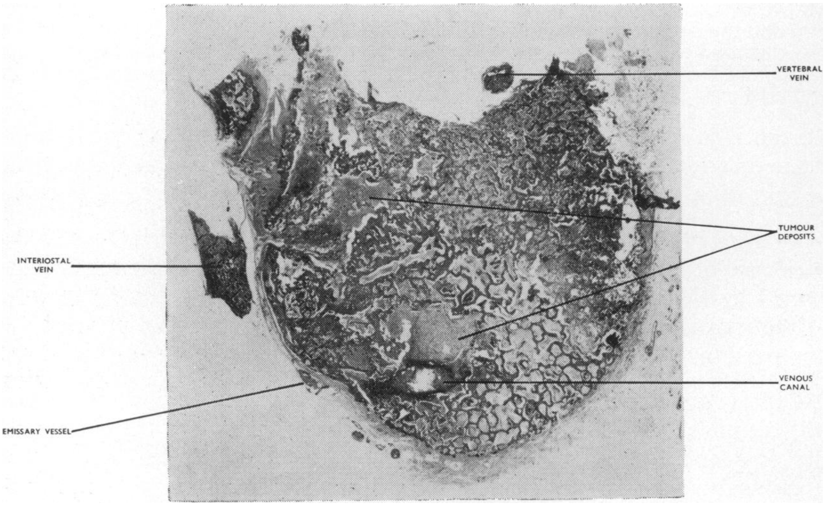

Fig. 14. Cross-section of the body of a dorsal vertebra containing metastatic growth from cancer of the breast and demonstrating a venous canal within the bone which communicates by an emissary vessel with the intercostal vein.

By keeping the number of circulating tumour cells to the minimum; by securing the main venous drainage of a tumour at the outset of an operation and not diverting the drainage to other channels; by avoiding vena caval obstruction through intermittent positive pressure respiration in anaesthesia; by awareness of the effect of posture on venous flow, we may reduce the risk of bombarding a susceptible target tissue with such a number of tumour emboli that metastasis becomes inevitable.

John Hunter shall have the final word in this lecture which bears his name; on those who commit their ideas to paper he makes this pungent comment which, though true of any topic in medicine, is particularly so of the subject presented and which it has been my endeavour constantly to bear in mind:

"No man should write a book without taking every circumstance of the disease into consideration; he should not write from a single idea, which many circumstances may render futile."

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HONOURS CONFERRED ON FELLOWS AND MEMBERS

In the Birthday Honours List, the following Fellows and Members of the College were graciously honoured by Her Majesty The Queen:

William Robert Silvester Panckridge, C.B., M.R.C.S.	K.B.E.
Theodore Fortescue Fox, M.R.C.S.	Knighthood
John Mansel Reese, O.B.E., M.R.C.S.	C.B. (Military)
James Percival Ainslie, F.R.C.S.	C.M.G.
Caleb William Davies, M.R.C.S.	„
MacDonald Critchley, M.R.C.S.	C.B.E. (Civil)
Alastair Campbell Frazer, M.R.C.S.	„ „
George Frederick Gibberd, F.R.C.S.	„ „
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