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Thromboatheromatous complications of umbilical arterial catheterization in the newborn period

Clinicopathological study

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Tyson, J. E., deSa, D. J., and Moore, S. (1976). *Archives of Disease in Childhood*, **51**, 744. **Thromboatheromatous complications of umbilical arterial catheterization in the newborn period: clinicopathological study.** Severe catheter-related thromboatheromatous lesions were found at necropsy in 33 of 56 infants who had umbilical arterial catheters passed during life. In infants dying within 8 days of insertion of the catheter, varying degrees of thrombosis of the aorta and its major branches were seen. With increasing thrombosis and aging of the thrombus, fatty deposits were seen first within the thrombus, and then in the intima and media. In addition there was evidence of proliferation of medial smooth muscle cells and of disruption of the medial architecture below the thrombus, characterized by the presence of abundant mucopolysaccharide. In infants who survived longer, varying degrees of organization of the thrombus could be traced, leading eventually to raised fibrous plaques with lipid and occasionally calcification. The lesions in the older infants were similar in many respects to experimental thromboatheromatous lesions produced in rabbits, and to some lesions of atheroma occurring spontaneously in humans.

A wide variety of embolic phenomena were found, with features suggesting asynchrony of embolic episodes. The presence of thrombotic lesions could not be related to birthweight, Apgar scores at 1 and 5 minutes, age at catheterization, duration of catheterization, underlying disease process, age at death or the presence of hypothermia, acidosis, or anomalies in coagulation tests. There is a need for less hazardous methods of monitoring arterial oxygen tension.

The insertion of a catheter into the aorta shortly after birth via an umbilical artery (Warley and Gairdner, 1962; Nelson *et al.*, 1962) has become a widely-used procedure in the care of the sick newborn infant. It is recognized that the procedure invariably carries certain risks, and a recent report by Neal *et al.* (1972) has highlighted many of the thromboembolic consequences of its use in the newborn period.

This report describes the vascular pathology associated with catheterization in necropsies of infants who died in a neonatal intensive care unit, and analyses some of the salient clinical features. In addition to the obvious clinical interest of thromboemboli complicating catheterization, the natural history of the thrombi throws an interesting light on problems of arterial wall repair in general.

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Materials and methods

The intensive care unit at McMaster University was opened in February 1973, and until 31 December 1974 had received 482 admission of sick newborn ininfants. In those infants requiring ventilation and oxygen therapy in a concentration of 40% or greater, a no. 3·5 or 5 polyvinyl catheter (Argyle Umbilical Artery Catheter) was inserted and placed so that the tip lay above the level of the diaphragm for oxygen tension and *p*H estimations; medications and fluids were infused through the catheter. Hypertonic bicarbonate solutions were given by slow infusions rather than as a

bolus. Heparin was not used in the infants or in the solutions used to flush the catheter.

There was a total of 95 deaths during the period and 85 of these infants had a full necropsy examination. In 56 of these infants an umbilical arterial catheter had been inserted. In all infants, irrespective of whether an umbilical arterial catheter had been inserted, a detailed examination of the aorta and its main branches was undertaken. Routine necropsy procedures were followed and in addition to the study of paraffin sections, lesions were studied for the presence of fat using Oil Red O staining of frozen sections. In some infants blocks of tissue obtained at necropsy were fixed in 3% glutaraldehyde, postfixed in osmium tetroxide, and embedded in epon. Sections were cut 0·5–1 μm thick and stained with toluidine blue and other routine stains after removing the plastic with potassium hydroxide. Thin sections were cut with an LKB ultramicrotome, stained with lead citrate and uranyl acetate and examined with a Phillips 300 electron microscope.

Results

Thirty-three infants were seen to have lesions of the aorta and its main branches that could be directly attributed to the passage of an umbilical arterial catheter. They were not seen in infants who had not had an arterial catheter.

Gestation, birthweight, and clinical status. A summary of some of the relevant data in infants with catheter-related thromboatheromatous lesions is given in an appendix which is available on request from the authors.

Gestation. 31 of the 33 affected infants had a gestational age less than 266 days (38 weeks), and of these 15 were less than 196 days (28 weeks).

Birthweight. 30 infants had a birthweight of 2500 g or less, 14 weighing 1000 g or less at birth.

Apgar scores. Apgar scores of 3 or less were present at 1 minute in 20 infants and in 19 infants were still depressed (6 or less) at 5 minutes.

Age at catheterization. With only two exceptions attempts at catheterization were made in the first 24 hours of life and usually shortly after birth. In 2 infants attempts at inserting an umbilical arterial catheter were unsuccessful.

Duration of catheterization. There was considerable variation in the length of time the cather was *in situ*, varying from 12 hours to 16 days. In 2 infants the duration of catheterization of the aorta was uncertain.

Survival after removal of catheter. In 14 infants, all aged 8 days or less, the catheter was in place up to the time of death. In the remaining infants there was considerable variation in the length of survival after the removal of the catheter, with many infants surviving for considerable lengths of time. In general terms, however, two broad categories of infants could be identified. There were 19 infants with a survival of 8 days or less, and in whom the catheter had been *in situ* for much of the infant's life. There were 12 aged 14 to 184 days where the infant survived several days after the catheter was removed.

Effects of unsuccessful catheterization attempts. In one infant a false passage parallel to the left umbilical artery had been created and this extended from 1 cm beyond the umbilicus to the common iliac artery. Here it re-entered the vascular lumen, just proximal to the bifurcation of the common iliac artery. At the point of re-entry an obliterating thrombus which could be traced down the external and internal iliac vessels for a distance of approximately 0·5 cm was found. Histologically the thrombus was an unremarkable platelet-fibrin thrombus with marginal organization at the base. The infant's left foot was blue with evidence of frank tissue necrosis and gangrene of the tips of the toes. At necropsy, wedges of gangrenous skin and subcutaneous tissue from the distal phalanges of the feet were studied and emboli could be shown in numerous small dermal arterial and arteriolar channels.

In the second case attempts at catheterization had been unsuccessful and were abandoned. The infant had a blue right foot for 4 days after the attempts, but this finally cleared completely by the tenth day of life. The infant died at 32 days of age with bronchopulmonary dysplasia associated Gram-negative septicaemia, thrombocytopenia, and disseminated capillary thrombi. A raised organizing thrombus was present in the right common iliac artery at necropsy. The thrombus could be traced back into a severely torn and thrombosed right umbilical artery.

Pathological findings.

Genesis of thrombosis. The earliest changes within the aorta and umbilical artery were fine platelet-fibrin thrombi (Fig. 1) in relation to areas of abrasion of the vascular endothelium, caused presumably by contact with the catheter. In the infant aged 12 hours the aorta looked surprisingly clean on macroscopical examination, but histologically there was no difficulty in identifying these

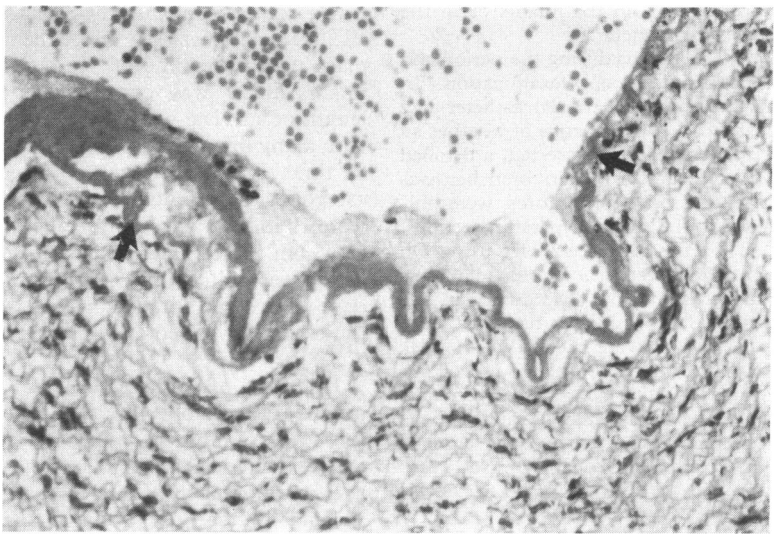

FIG. 1.—*Early platelet-fibrin thrombus deposited on abraded aortic wall (Case 4). Arrows indicate internal elastic lamina covered by thrombus. In central segment of figure even the internal elastic lamina has been destroyed. (H. & E. ×288.)* (Note: *All cases mentioned in legends refer to appendix which is available from authors.*)

very early lesions. Characteristically these lesions were multiple and distributed irregularly along both anterior and posterior aortic walls. As the age of the infants increased, progressively more thrombus could be detected leading eventually to extensive thrombosis of the aorta (Fig. 2).

Other changes in fresh thrombi. Intracellular deposits of neutral fat in macrophage-like cells were first seen in an infant aged 22 hours (Fig. 3).

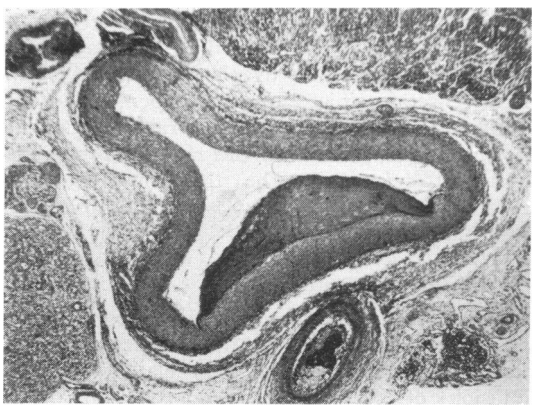

FIG. 2.—*Low power view of a well developed aortic thrombus. Note propagation of thrombus into a major branch in lower central area (Case 7). (Picromallory stain ×20.)*

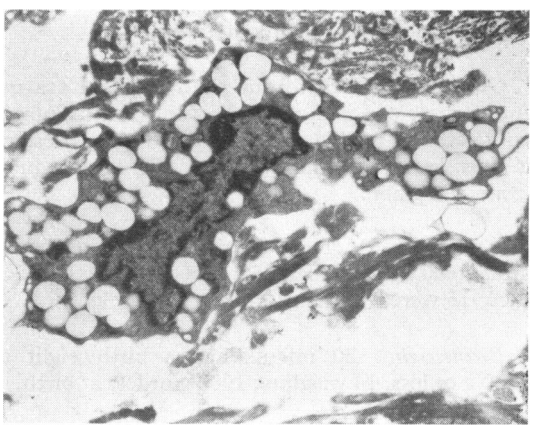

FIG. 3.—*Ultrastructural photomicrograph of a 'macrophage' in a thrombus. Note the abundant rounded, cytoplasmic lipid vacuoles (Case 3) (×6000.)*

In older infants fat could be shown in the intima around the internal elastic lamina and in the media below the thrombus. The presence of fat within the thrombus also helped to explain the appearance of foam cells at the base of a well established thrombus in an infant of 4 days (Fig. 4). In these thrombi there was disruption of the medial architecture immediately below the thrombus, and these irregularities (Fig. 4) of arrangement of medial smooth muscle cells could be explained, in part, by the presence of excess acid mucopolysaccharide

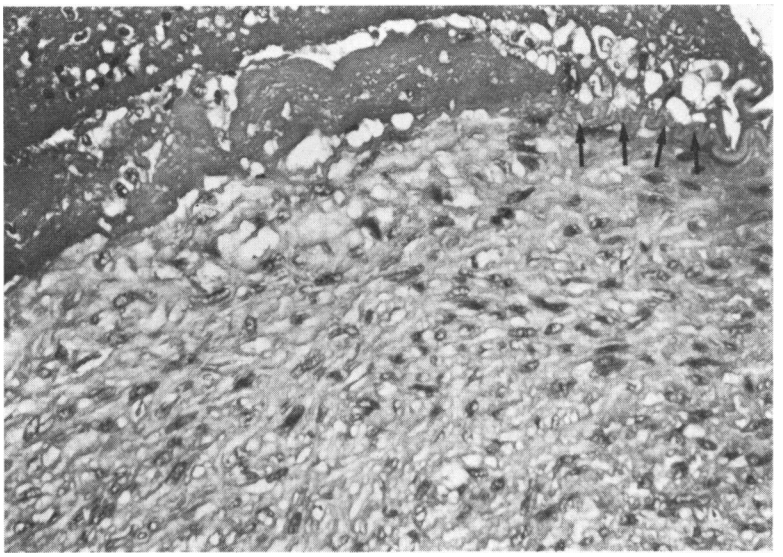

FIG. 4.—*Base of a well established thrombus. Arrows (upper right) outline internal elastic lamina, above which numerous foam cells can be seen within the thrombus. Note gross disorganizations of the media below thrombus, and variation in nuclear size of smooth muscle cells. (H. & E. ×256.)*

between the cells. There was also considerable variation in the nuclear size of the medial smooth muscle cells (Fig. 4), interpreted as possibly representing a premitotic phase before the start of organization of the thrombus.

Organization of thrombi in the older infants.

Early stages. In the older infants fresh thrombi were not seen, but varying stages of organization were present. In the earliest stages, mitotic activity was seen in medial cells and the intima on the edges of a thrombus appeared oedematous, loose, and friable. It was possible to see smooth muscle cells passing through defects of the internal elastic lamina into the media (Fig. 5) and many of the intimal cells appeared laden with deposits of stainable lipid. Ultrastructurally, the smooth muscle nature of such lipid-containing cells was not in doubt (Fig. 6).

Polypoidal lesions. In 2 of the older infants the organized thrombus had a polypoid appearance presumably reflecting the volume and shape of the thrombus that had been replaced (Fig. 7). Haemosiderin-containing macrophages were present within such lesions and there was a progressive replacement of fibrin strands by loose myxoid tissue, rich in mucopolysaccharide. The intima adjacent to such

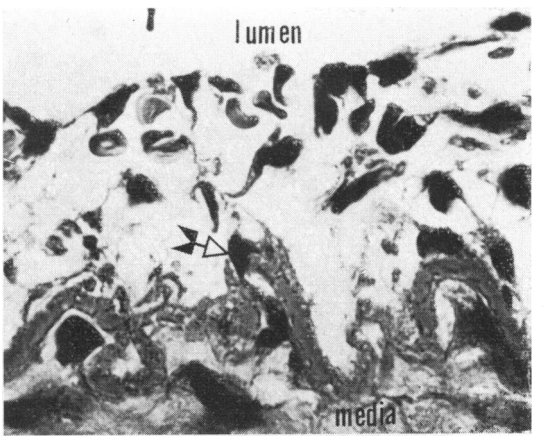

FIG. 5.—*Early stage of organization in a 14-day-old infant (Case 9). Arrow indicates a smooth muscle cell in transit through a gap in the internal elastic lamina. Note the loose friable texture of the intimal structures and presence of red cells among proliferating smooth muscle cells. (H. & E. ×700.)*

lesions showed a marked increase in thickness with excessive mucopolysaccharide and stainable fat.

Nodular lesions. In 2 infants the organizing thrombi had a nodular outline. In such lesions only minute amounts of fibrin strands were present, the nodule being composed of an exuberant,

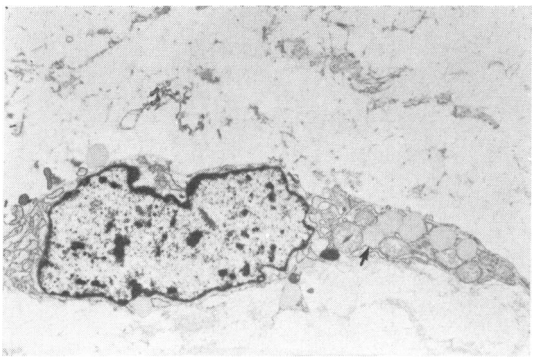

FIG. 6.—*Ultrastructural photomicrograph of lesion shown in Fig. 5. A smooth muscle cell filled with lipid vacuoles (arrow) is seen. Note also wide separation between other structures presumably representing the oedematous nature of lesion.* (×*5280.*)

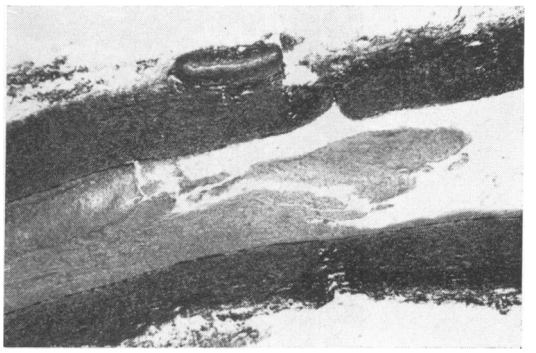

FIG. 7.—*Polypoidal organizing thrombus in an infant aged 40 days (Case 23). (Haematoxylin; Alcian Green; Elastic-Van Gieson.* (×*73.*)

irregular proliferation of smooth muscle cells. With Oil Red O staining of frozen sections abundant extracellular and intracellular deposits of lipid were present (Fig. 8).

Older lesions. In the oldest infants oedematous, raised, fibrous aortic plaques were present, associated in one instance with calcium deposits (Fig. 9). Near the surface of such plaques the smooth muscle cells were compactly arranged between horizontal lamellae of collagen and elastic tissue, but in the deeper layers of such plaques, irregular whorls and masses of smooth muscle cells were seen. All such lesions contained stainable fat but the amount

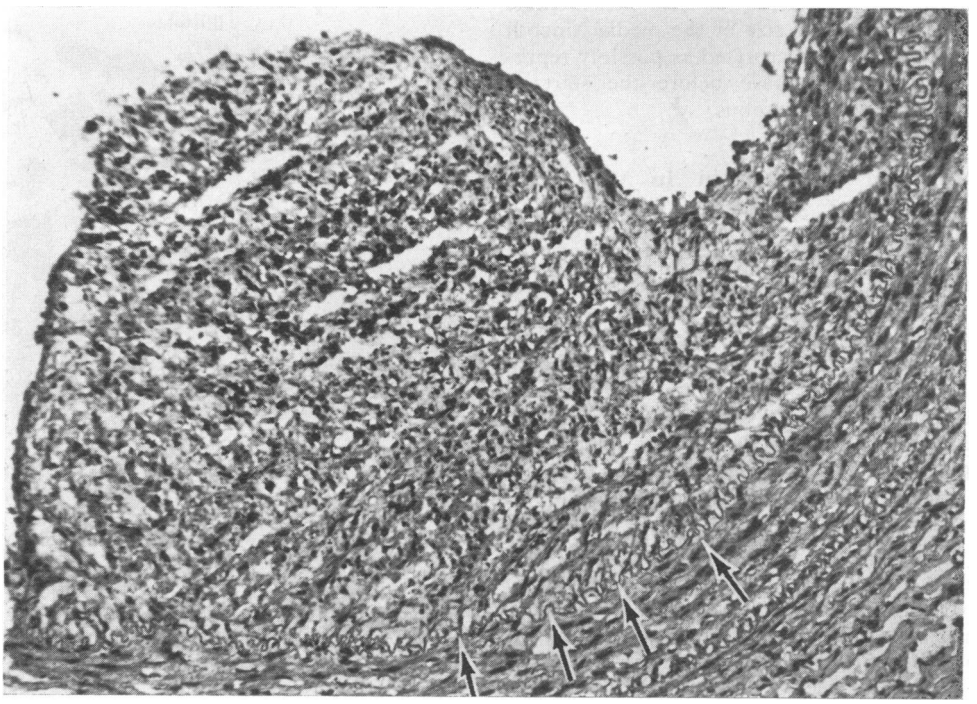

FIG. 8.—*Nodular aortic lesion in an infant aged 46 days (Case 2), showing irregular proliferation of smooth muscle cells containing globules of darkly staining intracellular and extracellular lipid. Arrows indicate internal elastic lamina. (Frozen section, Oil Red O Staining.* ×*133.*)

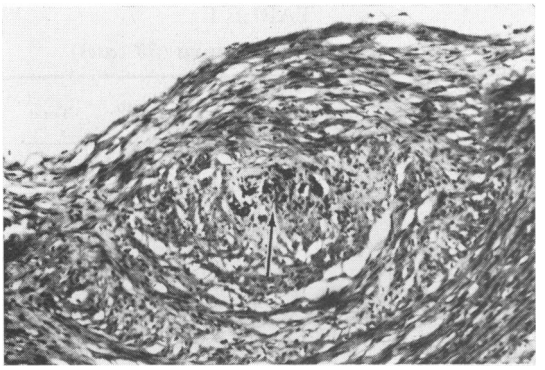

FIG. 9.—*Calcified raised fibrous plaque in aorta of infant of 162 days (Case 8). Superficial smooth muscle cells are arranged in horizontal fashion parallel to main medial musculature. The cells comprising the core of plaque are arranged in an irregular, haphazard fashion, with darkly staining (arrow) calcific deposits (H. & E. ×30.)*

present was extremely variable and in most cases only small deposits were present. Ultrastructurally smooth muscle cells were intimately admixed with bundles of collagen and elastic tissue, and occasional cells in the lesions examined contained deposits of intracellular fat (Fig. 10).

Special lesions. In 2 infants special catheter-related lesions of the aorta were present. In an infant aged 8 days in addition to the more usual variety of thrombus, a cylindrical thrombus loosely tethered to the aortic wall at two points was seen. Since it was obviously formed by a concentric deposition of thrombus around the catheter, this was called a 'tunnel lesion' (Fig. 11a). In one infant aged 179 days a fibrous cord, overlying but not occluding the orifice of the inferior mesenteric artery, was present (Fig. 11b). Clearly this was derived from organization of a 'tunnel lesion', a point borne out by its structure (Fig. 12) where the former position of the catheter is obvious.

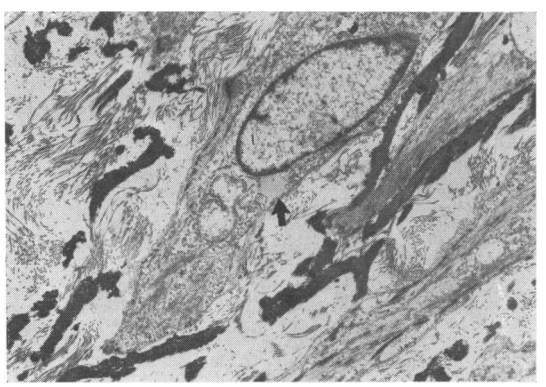

FIG. 10—*Ultrastructural photomicrograph of same lesion as Fig. 9, showing smooth muscle cells packed between lamellae of collagen and elastic tissue. Note lipid vacuole in the cytoplasm. (×5500.)*

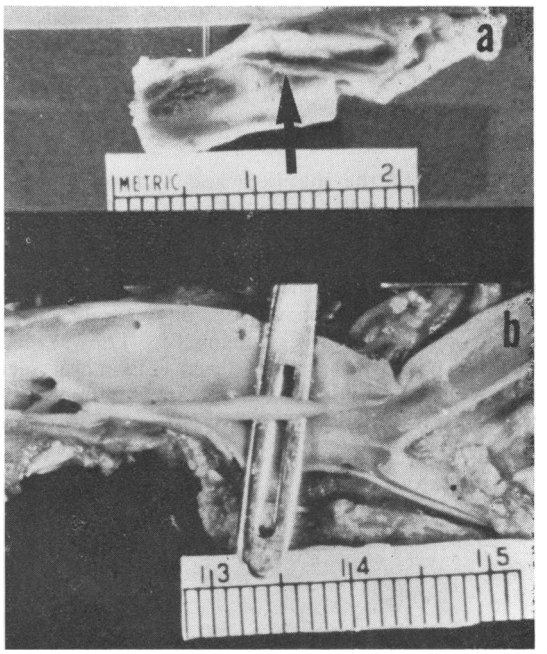

FIG. 11.—*'Tunnel lesions'. (a) Early variant (Case 1). (b) Late, organized variant (Case 20).*

Embolic lesions. A wide range of embolic lesions was noted in our series. Certain histological features deserve special mention.

Possible asynchrony of emboli. It was not unusual to find slight discrepancies in the histological appearances of different emboli in the same case (Fig. 13). Variations of this degree were interpreted as being due, in part at least, to possible asynchrony in the timing of embolic episodes.

Aging and organization of emboli. A feature of considerable histological interest is shown in Fig. 14, where it can be seen that the emboli undergo progressive organization in parallel with the state of development of the parent aortic thrombus. The recognition of the fact that emboli show similar changes to the aortic lesion allowed a more accurate

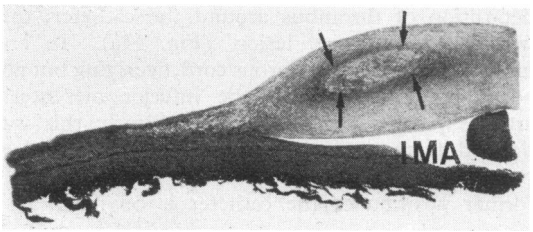

FIG. 12.—*Structure of fibrous variant of the 'tunnel lesion' (Fig. 11b). It merges on the left with the greatly thickened intima and overlies the orifice of the inferior mesenteric artery (IMA). Arrows outline site where the catheter once lay. (Haematoxylin; Alcian green; Elastic-van Gieson. ×26.)*

TABLE I

Summary of embolic lesions (33 cases)

	Emboli only	Embolus with infarction	Total
Liver	8	10	18
Kidney	4	7	11
Adrenals	9	11	20
Intestine (small & large)	8	15	23
Stomach	1	1	2
Spleen	3	5	8
Pancreas	12	—	12
Spinal cord	4	—	4
Lower limbs	10	3	13
Upper limbs	1	—	1
Bronchus	1	—	1

assessment of the numbers and a distribution of emboli in our cases, as attested by the wide spectrum of the embolic phenomena seen in Table I.

Infarcts of organs were attributed to emboli only if the emboli (or their effects on the arterial wall in the older infants) could be convincingly shown in the appropriate arterial channels. Thus adrenal necrosis without capsular arterial emboli was seen in 3 of the 23 catheterized infants in whom no aortic thrombus was found at necropsy. These cases were not attributed to the insertion of a catheter. In a similar fashion there were 4 cases of bowel infarction ('necrotizing enterocolitis') among this same group of 23 infants who had been catheterized but did not have demonstrable thrombus at necropsy. The need for adopting strict histological criteria is obvious, and the importance of the 'aging' and organization of the emboli is stressed.

The number and severity of embolic lesions varied widely from case to case. In many instances

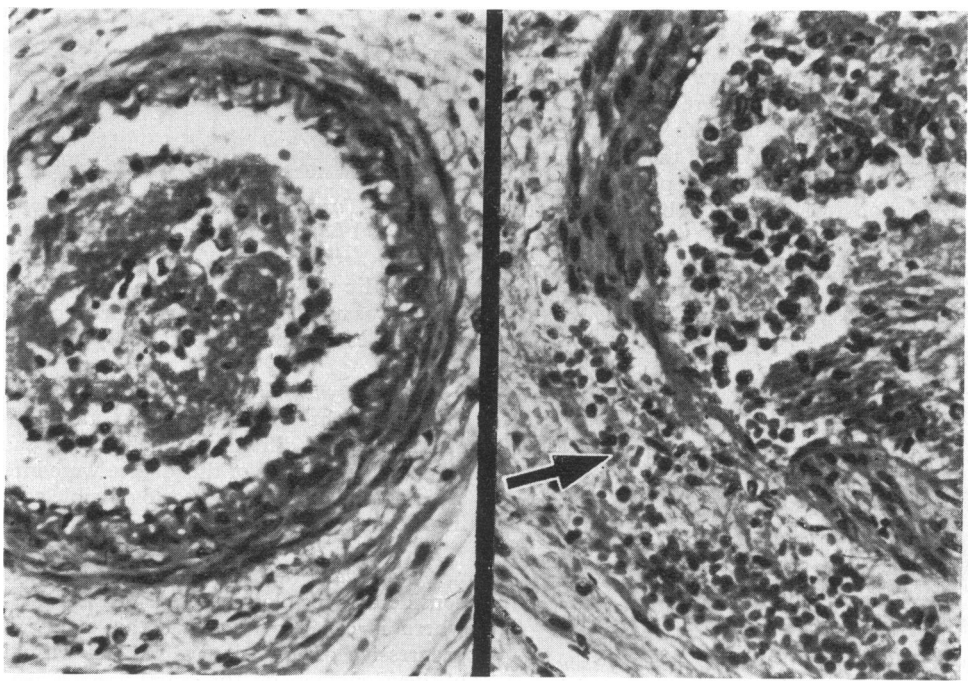

FIG. 13.—*Two emboli from the same patient (Case 26) showing an apparently bland embolus on the left, while on the right embolism has led to imminent rupture (arrow) of the wall. (H. & E. ×307.)*

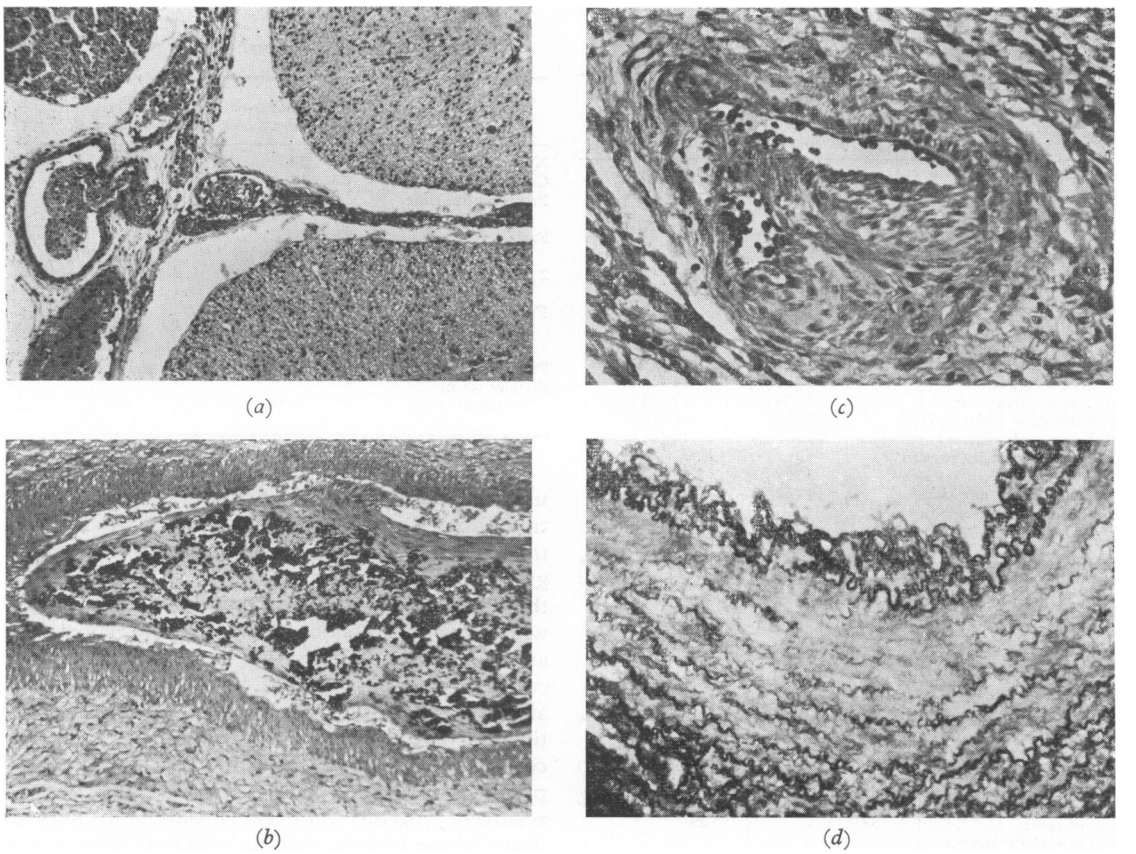

FIG. 14.—*Composite illustrations depicting the organization of emboli. (a) Spinal cord embolus, Case 9, 7 days (Picromallory ×84); (b) calcified mesenteric embolus, Case 5, 46 days (H. & E. ×84); (c) recanalized vessel in submucosa of small bowel, Case 8, 162 days (Gomori's trichrome, ×169); (d) scarring of intima and media and duplication of intimal elastica in superior mesenteric artery, Case 10, 184 days (Haematoxylin; Alcian green; Elastic-van Gieson. ×169)*

emboli were associated with extensive infarction, while in others numerous emboli were found without definite evidence of tissue necrosis. This variability in the effects of emboli was seen in all the major organs. It is obvious, furthermore, that in some instances (e.g. bowel lesions in 3 cases) infarcts may not have overt clinical manifestations in these very sick babies.

It is worth noting that in the older infants 'atheromatous' lesions were seen in infants who who did not receive intravenous fat emulsions (Intralipid), as well as in some infants who did. Structurally no differences other than those attributable to aging of the lesion, were seen in the thromboatheromatous lesions in the two groups.

Catheterized infants with and without thrombus. 23 infants who had been catheterized but did not have any thrombus or thrombus-related lesions were also studied. Detailed analysis of the clinical features and laboratory investigations in *all* catheterized infants studied at necropsy was undertaken in an attempt to see whether or not it was possible to identify any particular differences between the infants with and without thrombus-related lesions. The results are shown in Tables II, III, and IV. In these tables 'infants with thrombus at necropsy', refers to infants with any of the range of thromboatheromatous lesions described.

In Table II the clinical status of the two groups of infants is compared and it is clear that they are very similar. There is an indication that more infants of 1000 g birthweight or less are represented

TABLE II

Clinical status of catheterized infants

	(A) with thrombus at necropsy	(B) without thrombus at necropsy
No. of infants	33	23
Median gestation (w)	29	29
Median birthweight (g)	1165	1260
Age at death (median)	3 d 23 h	1 d 23 h
Age at catheter insertion (median) (h)	6	4
Median *p*H at admission	7·17	7·18
Median lowest *p*H*	7·02	7·01
Infants with:		
(a) Birthweight <1000 g	14 (42%)	5 (22%)
(b) Small for gestational age	5 (15%)	2 (9%)
(c) 1-min Apgar <3	20 (61%)	14 (61%)
(d) 5-min Apgar <6	19 (58%)	12 (52%)
(e) Admission temp <35°C	9 (27%)	6 (26%)
(f) Respiratory distress syndrome	20 (61%)	14 (61%)
(g) Bacteriologically proven sepsis	3 (9%)	4 (17%)
(h) *p*H <7·0 at any time*	14 (42%)	10 (44%)
(i) *p*H <7·0 recurrent or* persisting more than 6 h	6 (18%)	2 (9%)

*Includes only those measurements made with catheter in place and excludes those in the last 2 hours of life.

TABLE III

Catheter usage data

	Infants with thrombus at necropsy	Infants without thrombus at necropsy
No. of cases	33	23
Age at catheterization (median) (h)	6	4
Duration of catheterization (h)		
<24	9 (27%)	8 (35%)
25–72	8 (24%)	9 (39%)
>72	14 (42%)	5 (22%)
Uncertain*	2 (7%)	1 (4%)

*Umbilical catheter inserted elsewhere by referring physician.

in the group of infants developing catheter-related thromboatheromatous lesions. The difference, however, is nonsignificant. Similarly, in Table III the suggestion that infants with catheter-related thromboathermomatous lesions include more infants with a duration of catheterization of more than 72 hours, is nonsignificant. The standard studies on the coagulation status in infants with an arterial catheter *in situ* (Table IV) appear to be of little value in predicting catheter-related thrombosis.

Discussion

The incidence of thrombosis after umbilical artery catheterization in this study was considerably greater than in previous studies, irrespective of the usage of heparin or the position of the catheter tip (Table V). Routine placement of the catheter tip above the diaphragm was associated with a much greater risk of embolic damage to abdominal organs than has previously been noted. In the 2 infants with thromboembolic lesions of the subclavian artery and bronchial arterial tree, umbilical arterial catheters had been passed in other hospitals and after *x*-ray examination in our unit were repositioned. Factors which may relate to the increased complications noted in this study include the large proportion of very low birthweight infants, the relatively long interval between catheterization and death in our infants, and the attention given to the detection of gross and histological lesions. The large number of lesions noted in 12 infants older than 14 days also contributes to our higher incidence.

The high incidence of catheter-related thrombus formation in this post-mortem study may nevertheless be an underestimate of the incidence in life. Experimental studies show that damaged endothelium with adherent platelets may be found within minutes after catheter insertion (Jorgensen *et al.*, 1974). Clinical studies of indwelling arterial catheters show very rapid thrombus formation (Formanek, Frech, and Amplatz, 1970; Jorgensen *et al.*, 1974) and a high incidence of sleeve thrombus surrounding the catheter even when heparin is added to the infusate (Krist, Rosenberg, and Engel, 1974; Neal *et al.*, 1972). The sleeve thrombus and loosely attached friable thrombus may be dislodged or removed when the catheter is removed (Formanek *et al.*, 1970; Neal *et al.*, 1972). Attention has already been drawn to the relatively normal appearance of an aorta that may have extensive but superficial platelet-fibrin adherent

TABLE IV

Coagulation studies with catheter in situ

	Infants with thrombus	Infants without thrombus
No. of cases in group	33	23
Coagulation studies	17	17
Prothrombin time >18 s	7 (41%)	9 (53%)
Partial thromboplastin time >90 s	5 (29%)	5 (29%)
2 unit thrombin time >30 s	4 (24%)	3 (18%)
Fibrin degradation products >40 µg/ml	4 (24%)	3 (18%)
	—	—
Platelet counts available	29	19
Platelet count <100 000/mm³	13 (45%)	8 (42%)

TABLE V

Incidence of thrombosis after umbilical artery catherization at necropsy

Authors	Position of catheter tip	Heparin usage	Thrombus detected at necropsy* (%)
Cochran, Davis, and Smith (1968)	Unspecified	Variable	18 of 86 (21)
Erkan, Blankenship, and Stahlman (1968)	Abdominal aorta	Unspecified	6 of 152 (4)
Gupta, Roberton, and Wigglesworth (1968)	Thoracic aorta	Within catheter	5 of 144 (3)
Wigger, Bransilver, and Blanc (1970)	Variable	Unspecified	Unspecified †
Egan and Eitzmann (1971)	Variable	Unspecified	6 of 65 (9)
Symanski and Fox (1972)	Thoracic aorta	Infusion after sampling	4 of 48 (8)
Tooley (1972)	Lower abdominal aorta	Continuous infusion	27 of 123 (22)
Present series	Thoracic aorta	Not used	33 of 56 (59)

*Excludes lesions of umbilical artery only.
†Patients who had thrombus detected at necropsy between 1967 and 1968 comprised 12% of all patients (including survivors) who had either umbilical venous or arterial catheters.

thrombus (Fig. 1). It is likely that with increasing duration of catheterization, more time is available for the sleeve thrombus to become adherent to intimal thrombus to form larger thrombi and 'tunnel lesions'. Equally, a small platelet fibrin thrombus is likely to enlarge with prolonged catheterization, due to the prolonged thrombogenic stimulus afforded by repeated contact between the aortic wall and catheter.

Considerable attention has been paid to assessing the different factors that may help to predict the likelihood of any infant developing a thrombus after umbilical arterial catheterization. Despite a detailed analysis (Tables II-IV), no significant differences can be seen in the two groups analysed. There was the suggestion, as might be expected, that thrombi adherent to the arterial wall would occur more commonly with increasing duration of catheterization (Table III). The question of an increased frequency of thromboembolic lesions in infants under 1000 g birthweight may relate to many factors including the likelihood of prolonged catheter use in the smaller infant. It is clear, however, from the analysis given in Tables II-IV that any infant is at risk when an arterial catheter is inserted and that it is difficult to predict which infant will develop aortic thrombosis and/or embolic lesions.

It is disappointing that the standard coagulation studies provide little help in predicting, diagnosing, and monitoring the development of arterial thrombosis. This relative lack of correlation between coagulation studies and the development of thrombi reflects to some extent the relative insensitivity of these methods. Platelet adhesiveness and aggregation tests are of little value in detecting arterial thrombi (Hirsh, 1975). It appears that perhaps a more appropriate screening test might be the estimation of platelet survival and turnover (Genton and Steele, 1974), and within our centre these methods are being modified and developed for application to microsamples (S. Scott and A. Zipursky, unpublished). Hopefully, this may be of use in monitoring the development of thrombi in catheterized infants.

Our results outline an additional feature of considerable interest and possible importance. Moore (1973) used indwelling aortic catheters in normolipidaemic rabbits to produce thromboatheromatous lesions. The raised thromboatheromatous lesions contained considerably more cholesterol and cholesteryl ester than adjacent normal intima (Day *et al.*, 1974). The histology of the lesions is very similar to those reported in the present paper, but in the experimental model the raised atheromatous lesions contain considerably more stainable lipid than is seen in the neonatal human counterpart. In the rabbits, however, the catheter was *in situ* for much longer periods of time than in any of the newborn infants and the damage to the endothelium was prolonged and continuous. But there is good agreement between the experimental and human results with respect to the sequence of events within the vessel wall and lumen, and even in the somewhat unpredictable nature of the extent of vascular injury in any one particular case. The natural history of aortic thrombi that we have observed and described may, therefore, be of considerable relevance in discussion of arterial wall damage and repair in general terms and the genesis of atheroma in particular.

Using the catheter injury model, Moore, Friedman, and Gent (1975) have shown that even raised lipid-rich plaques may undergo spontaneous regression after removal of the catheter and all that may remain is a small area of fibromuscular scarring of the aortic wall. We have had the opportunity to examine the aorta of a 7-year-old child who had had

an umbilical arterial catheter inserted at birth. Minute scars were seen in the aorta involving focal destruction of the internal elastic lamina with slight intimal fibromuscular proliferation over and around these damaged areas. The lumen was not compromized. It is conceivable that these scars represent regressed raised fibrous plaques. It is possible that many surviving infants may have such scars in their aorta and other major vessels, and be quite asymptomatic. Equally, small scars in or near the renal artery and its origin could produce renal artery stenosis, and vascular scarring of the lower limb vessels could interfere with growth.

Although monitoring of arterial oxygen tension has contributed significantly to the reduction in incidence of retrolental fibroplasia and of neonatal mortality from respiratory disorders, methods to reduce or avoid the risk of umbilical artery catheterization deserve thorough study. Placement of the catheter tip above the diaphragm imposes substantial risk of embolic damage to abdominal organs and the optimal site for the catheter tip needs to be determined. Neither the benefits nor the risks of heparin administration to the newborn have been carefully studied, and as shown by Neal *et al.* (1972), heparin does not prevent thrombi from forming around the catheter. Silastic catheters may prove less thrombogenic than the usual polyvinyl catheters (Boros *et al.*, 1975), while cutaneous sensors (Huch, Lubbers, and Huch, *et al.*, 1974) may provide a noninvasive method to monitor oxygen therapy.

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