PROGRESS IN CARDIOVASCULAR SURGERY

Materials for Repair of Vascular Defects

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Progress in Cardiovascular Surgery has been, and will continue to be, inextricably bound to the development of suitable materials for the closure of various cardiovascular defects. Such interdependence arises out of the technical requirements for mechanical closure of various defects in the cardiac, arterial and venous portions of the blood vascular wall. Listing of the common cardiovascular defects which may require the use of some type of graft material during surgical correction emphasizes this interdependence (Table 1). Mechanical closure of the vascular defect, while satisfying the immediate technical needs at operation, represents only half of the problem. In order to justify the operative procedure, the physiologic benefits accruing from the mechanics of closure must have sufficiently lasting benefits. In other words, the long-term biologic fate of the implanted material should be acceptable, the implant offering no source of difficulty throughout the remainder of the life of the recipient patient.

In the use of autologous tissue grafts in the vascular system, as elsewhere in the body, a short-term mechanically good result usually implies a favorable and lasting biologic result. However, when non-autologous materials, whether of tissue origin or of a prosthetic nature are used, an initially good mechanical result may bear no relationship to the ultimate biologic fate of the implant; that is, there may be wide divergence of the short-term and long-term results. Vascular materials of other than autologous tissue origin, therefore, must be carefully screened before such materials be recommended for widespread implantation into clinical patients. Practice, however, often mandates the implantation of less than an ideal type of vascular graft material because of the urgency of the clinical situation; e.g., where the surgeon unex-

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<table>
<thead>
<tr>
<th>TABLE I—CARDIOVASCULAR DEFECTS REQUIRING GRAFT MATERIAL FOR CLOSURE</th>
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<tr>
<td><strong>CARDIAC</strong></td>
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<tr>
<td>SEPTAL</td>
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<tr>
<td>A.S.D.—seldom requires graft for closure</td>
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<tr>
<td>V.S.D.—often requires graft for closure</td>
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<td>R.V. OUTFLOW TRACT—often requires graft for widening in Fallot type lesion.</td>
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<tr>
<td>VALVULAR—rarely requires graft for restoration of function.</td>
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<td><strong>ACQUIRED</strong></td>
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<tr>
<td>VALVULAR</td>
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<tr>
<td>Mitral—rarely requires implant for stenosis; often, for regurgitation</td>
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<tr>
<td>Aortic—often requires implant for stenosis and for regurgitation</td>
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<td>SEPTAL—rare lesion, requires implant</td>
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<td>ANEURYSM—rarely requires implant</td>
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<td><strong>ARTERIAL</strong></td>
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<td>COARCTATION OF AORTA—rarely requires graft for correction</td>
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<td>TRANSPOSITIONAL—developmental—graft will often be required.</td>
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<td><strong>ACQUIRED</strong></td>
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<tr>
<td>ARTERIOSCLEROSIS—obstruction and aneurysm—graft very often required</td>
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<tr>
<td>TRAUMATIC—obstruction, aneurysm, fistula—graft sometimes required</td>
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<tr>
<td>INFECTIOUS ANEURYSM—syphilitic, mycotic, etc., graft usually required</td>
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<tr>
<td><strong>VENOUS</strong></td>
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<td>Developmental—graft will often be required.</td>
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pectedly encounters a ruptured aneurysm and is faced with the stark reality of reconstituting flow through the abdominal aorta as a life-saving measure.

The vascular prostheses presently available do not satisfy the criteria for the ideal material for use in the surgical correction of all cardiovascular defects, but for all of the defects listed in Table 1 there are practical closure materials available. The adequacy of a material for a particular lesion must be considered in terms of not only the expected longevity of the implant per se, but also the requirements for longevity of the implant; i.e., the anticipated longevity of the patient. Certainly a graft required for the correction of coarctation of the aorta has a different longevity requirement than a graft used to bypass an abdominal aortic obstruction in an elderly arteriosclerotic. For this reason, a given vascular prosthesis which may be adequate in the elderly arteriosclerotic may be inadequate for implantation into the child.

During recent years there has been a sufficient increase in variety and numbers of graft materials available as to confuse even the consumer vascular surgeon. In an effort to determine the acceptability of these materials there was established at the State University of New York Downstate Medical Center in Brooklyn, a Vascular Graft Material Screening Center. The aims of the Center since 1957 have been: (1) to compare the biologic fates of all materials available for closure of vascular defects, (2) to discover the principles which determine the biologic fates of various types of implants into the vascular system, (3) to establish scientific specifications for the ideal vascular prosthesis, and (4) to develop better materials for closure of vascular defects. In order to accomplish these aims during the life-span of a single investigator, an experimental animal preparation which would show acceleration of degenerative changes in implants and which would subject the implant to a test of growth within a short period of time was necessary. Previous investigations had established the validity of the preparation of the growing pig for these purposes.18

During the first three years of activity of the Screening Center, it was determined that the changes observed in vascular implants in the pig after six months were similar to changes in similar implants in dogs and humans after much longer periods of time (estimated two to 20 years).19

Vascular materials implanted into the cardiac, arterial and venous sites exhibit similar qualitative changes. Since the enormity of the effort dictated the adoption of a standard site of implantation for the screening of vascular materials, the site chosen was the upper descending thoracic aorta immediately distal to the subclavian artery (coarctation site) because a vascular implant at this site is subjected to significant stresses of growth and tension and has the opportunity to become vascularized.

The knowledge gained from aortic implantation can be applied to the cardiac and venous sites with certain stipulations. The cardiac septal and valvular sites provide less opportunity for vascularization of an implant while free grafts implanted onto the surface of the heart will be in contact with a ready vascular supply if the pericardium be left open. Implants into the venous system may require mechanical support of the wall of the implant under certain circumstances; support of the implant wall in the arterial tree derives from the blood pressure.

**Results**

Seventy-five vascular materials have thus far been screened at the Center.18-44 These materials fall into four general classes: (1) tissues of autologous origin, (2) tissues of non-autologous origin, (3) simple prosthetic materials and (4) compound prosthetic materials.

The present review will indicate the general results of the various classes of vascular materials, outline the principles which govern the biologic fates of the various types of materials, indicate the present
status of the specifications for the ideal simple and compound prosthetic materials, list the presently known vascular materials into a scale of long-term and short-term acceptability, indicate our present preference for the clinical application of certain vascular materials, and indicate certain promising leads for further development of materials for closure of vascular defects.  

I. Tissues of Autologous Origin

At the outset, the following two presently-applicable aphorisms should be stressed: "The best graft is no graft" and "There is no good substitute for autologous tissue."

When a graft is used, the ideal material is autologous tissue of the type indigenous to the area to be grafted. In terms of the cardiovascular tree, however, the availability of such material is limited because of the absolute or relative indispensibility of most of the mural tissue of the vascular system. Implants of indigenous autologous aortic tissue in the growing pig have shown persistent viability of all of the elements of the graft wall, normal growth characteristics, absence of degenerative changes and microscopic findings indistinguishable from the normal host aorta. The indigenous autologous material, therefore, represents the standard graft against which all other materials can, and should, be compared (Fig. 1).  

The materials whose fates most closely approximate these of indigenous autologous origin are those of autologous non-indigenous origin. For instance, grafts of central tendon of the diaphragm implanted into the aorta of the growing pig demonstrate persistent viability of the implanted tissue, normal growth characteristics, absence of

![Image of Figure 1: Autologous tissue grafts six months after implantation in the thoracic aorta of the growing pig. Top (left): Gross photograph of open specimen of indigenous aortic graft. Note similarity of graft to host aorta; (right) photomicrograph of wall of same graft, H&E, x200, showing persistent viability of all elements of graft wall. Bottom (left): autologous central tendon of diaphragm showing normal growth and absence of degenerative changes (circular suture line is an artefact incident to gathering the mature specimen); (right) photomicrograph of same graft, H&E, x20, showing persistence of all elements of the implant and healthy inner and outer fibrous capsules.](Image)
degenerative changes and quite acceptable histologic findings (Fig. 1). Tissues of autologous veins implanted into the arterial tree show persistent viability and architectural integrity of the implants into peripheral vessels and into the thoracic aortic site in the mature dog. Sauvage has shown that such venous autografts into the thoracic aorta of the mature dog are acceptable after four years of implantation; whereas, Sako has less enthusiastic reports of calcification of venous grafts into the thoracic aorta of mature dogs after ten years of implantation. Further studies of implantation of venous autografts into the thoracic aorta of the growing pig are indicated.

II. Tissues of Non-autologous Origin

Such materials can be grouped into homologous tissues and heterologous tissues.

**Homologous Tissues:** Aortic homografts in the growing pig preparation demonstrate essentially no growth, loss of viability of the cellular elements of the wall with varying degrees of lysis of the elastic tissue elements, calcification of the wall, ulceration in regions of calcification attracting mural thrombus, and frequent full lumen thrombosis with graft obstruction (Fig. 2). These changes in the homograft vary with the method of preservation and/or storage. The descending order of acceptability of biologic fates of homografts according to the method of storage is: fresh, frozen, freeze-dried, alcohol or glycerine preserved, dried by evaporation and formalin fixed. Except for an occasional fresh homograft which exhibits persistent viability of its cellular elements and growth, homologous tissues cannot be considered to have a long-

**Figure 2:** Results of implantation of homologous aortic tissues into the thoracic aorta of the growing pig seven months after implantation. Top (left): Roentgenogram of air-inflated graft showing 2 1/2+ calcification; (right) photograph of open graft which had been freeze-dried. Note calcification, ulceration and mural thrombus formation. Bottom (left): Homograft preserved for five months in 70% alcohol. Note severe calcification, ulceration and mural thrombus formation; (right) photomicrograph of freeze-dried homograft, elastic tissue stain, x20, shows greatly thinned-out elastic tissue and a large calcium plaque in the elastic tissue layer.
Figure 3: Results of implantation of heterologous tissues into the thoracic aorta of the growing pig. Left (top): Fresh canine heterograft five minutes after implantation. Note minimal calcification and absence of aneurysm formation. Right: Photomicrograph of the same graft, H&E x110, showing the mild foreign body giant cell reaction.
term acceptability rating, but certainly are acceptable as short-term grafts. Properly prepared homografts cannot be considered, therefore, as an ideal graft for correction of coarctation of the aorta in an infant, but may be perfectly acceptable in the elderly atherosclerotic. There have been reports of early failure of homografts secondary to an accelerated "immune response." In the experience of the author, these early failures have been attributable either to necrosis of the recipient host aorta at the host-graft junction (probably secondary to devascularization of the end of the host aorta resulting from assiduous cleaning of the adventitia bearing the only blood supply to the atherosclerotic host aorta) or to grafts which had been improperly gathered, prepared or stored. In homografts which have been properly gathered, prepared and stored, we have observed none of these early deleterious changes. There have been reports of late changes after eight to ten years of implantation with homograft rupture, but in no apparently greater incidence than the late failures secondary to anastomotic rupture with fistulization, graft rupture and graft obstruction observed with prosthetic grafts. Gross has noted none of these complications of homografts in the coarctation site after ten years of implantation, although he has reported calcification. Homografts properly processed are, therefore, considered to be the equivalent of the clinically-available simple prosthetic materials.

Heterologous Tissues: Fresh or freeze-dried heterologous aortic grafts exhibit severe calcification and accelerated lysis of the graft wall with a high incidence of aneurysm formation and rupture. The enzyme-digested heterograft artery of Rosenberg exhibits a qualitatively different biologic fate. This graft consists essentially of heterologous collagen fibers. The present product does not form aneurysms and exhibits little or no calcification in the growing pig. Such material may prove acceptable for at least short term results in the femoro-popliteal site in the clinical patient (Fig. 3).

III. Simple Prosthetic Materials

We have screened 35 simple prosthetic materials composed of Vinvon-N, Nylon, Orlon, Ivalon, Dacron, Teflon, Fiberglass and metallic lead. It is clear that a solid-walled plastic material sutured into the place of an aortic defect exhibits excessive mural thrombosis which rapidly progresses to full-lumen thrombosis with or without distal arterial embolization.18 Porous prostheses of identical materials (Vinyl, Teflon, glass, lead) exhibit controlled deposition of fibrin upon the inner surface of the implanted prosthesis. The thickness of this fibrin mat is rarely in excess of 1 millimeter and is independent of the type of material. In the case of the plastic substances, the prosthetic tubes are manufactured in the form of fabrics which can be woven, braided or knitted. In the case of metallic lead tubes, multiple pin perforations are made in the wall.

The changes with all vascular prosthetic materials tested are similar, but may vary in degree. The healing pattern shortly following implantation has been established by careful histologic survey as follows: the inner fibrin layer becomes organized through the interstices of the mesh. The organizational tissue is granulation which matures in a manner similar to any cicatricular tissue in the body. The inner layer assumes the gross and microscopic appearance of an inner capsule. The latter term is preferred to neo- or pseudo-intima because these vascular prostheses behave as foreign bodies which the host attempts to reject. If a foreign body cannot be rejected by extrusion, the host attempts to exclude it by encapsulation with cicatrix. Encapsulation of a cylindric foreign body involves the formation with two concentric cylinders of scar tissue, one within and the other without, the lumen of the implanted cylinder. Since the host completely encapsulates the vascular prosthesis, it would appear appropriate to name the inner and outer layers of the prosthesis, the inner
fibrous capsule and the outer fibrous capsule respectively.

The inner fibrous capsule exhibits normal cicatricial contracture. Contracture effectively obliterates the blood vessels nourishing the inner fibrous capsule within the interstices of the implant. The resulting ischemia to the inner fibrous capsule becomes manifest as varying degrees of tissue death (necrosis) inasmuch as the dying inner fibrous capsule cannot easily be absorbed. Histologically the changes vary from local hyalinization to frank necrosis with slough depending upon the extent of the devascularization at a given time.

In the grafts of high porosity, reorganization with new granulation tissue arising from the outer fibrous capsule can occur easily. If the graft wall is of low porosity, there is a significant delay in reorganization of the ischemic inner fibrous capsule; under these conditions the degenerate inner capsule attracts calcium salts which are grossly, roentgenologically and histologically identifiable. Indeed, there is a good inverse relationship between the degree of porosity and the degree of calcification (Fig. 4).

During the degenerative phase of the inner fibrous capsule, secondary deposits of fibrin can occur upon the inner surface of graft, causing a gross septum and further narrowing of the internal diameter. Reorganization of the entire mass of inner fibrous capsule can occur with some thickening. Repeated cycles of degeneration and reorganization can lead to full lumen thrombosis. Occasional prostheses exhibit pedunculated thrombi which theoretically could break away to embolize distally.

The ultimate biologic fate of the simple vascular prostheses that are available commercially for clinical implantation exhibit a significant incidence of late graft obstruction and bear the potential to cause distal arterial embolization from slough of degenerate inner capsule and/or slough of sessile or pedunculated mural thrombi. In our experience, the ultimate biologic fates of the simple prosthetic materials are of the same order of acceptability as homograft tissue properly gathered, processed and stored. It is clear from our studies, furthermore, that the biologic reactivity of the prosthetic material per se is not an important limiting factor (Fig. 5).14

IV. Compound Prosthetic Materials

During the study of simple prosthetic materials, we have not been able to correlate the incidence of septum formation with porosity. The fact that the more porous materials exhibit less calcification and on the possibility that high orders of porosity that might prevent septum formation, we developed materials consisting of both non-absorbable and absorbable components in the fabricated prosthetic wall. We have termed such materials compound prosthetic materials and to date have screened approximately two dozen of these (Fig. 6).15-18

Compound prosthetic materials are of three classes: those consisting of a non-
MATERIALS FOR REPAIR OF VASCULAR DEFECTS

Figure 5. Results of implantation of various vascular prostheses six months after implantation into the thoracic site. (Top left): A graft of Teflon from the growing pig inflated with polyethylene (iodoprene) solution. Note the gross serpentine formation immediately distal to the center of the graft. (Top right): Aoecroplasty of a thoracic aortic arch with permanent artificial knitted metallic lead in the thorax. (Bottom left): An aortic arch with permanent artificial knitted metallic lead in the thorax. (Bottom right): An aortic arch with permanent artificial knitted metallic lead in the thorax.
absorbable open mesh which has been coated with some type of collagen derivative, those consisting of alternating strands of multifilament Dacron and monofilament collagen derivative and those consisting of multifilament Dacron in the warp with a filling of compound yarn whose core is a monofilament collagen derivative around which is wound a Dacron multifilament yarn. We have termed the latter class the "core-wound yarn compound prosthetic material." Compound materials have the following porosity characteristics. At the time of implantation, the porosity is very low, less than 50 ml. water/sq. cm.-min. at a pressure of 120 millimeters of mercury. At this porosity a prosthetic graft can be implanted into a heparinized subject. When the absorbable component is digested chemically, the porosity is very high and varies with the specific fabrication between 5,000 and 20,000 ml. water/sq. cm.-min. at a pressure head of 120 mm. Hg. Materials of this order of porosity cannot be safely implanted in the non-heparinized subject, even following repeated external and internal preclotting maneuvers.

Materials of each of the classes of compound materials were implanted into the growing pigs and dogs. From observation of the calcification index we have determined the biologic or healing porosity as summarized in Fig. 7. It can be noted that the biologic porosities are intermediate between the initial and chemically-digested porosities of most of the materials plotted in Fig. 7. Materials 52 and 53 are in the class of coated materials. Materials 55 through 61 are in the multifilament Dacron-monofilament collagen derivative class, while materials 68 through 71 are in the core wound yarn class of compound pros-

**FIGURE 6:** Photomicrographs of two different compound vascular prostheses, x22. Left (top): Initial, and; Bottom—chemically-digested material consisting of a mixture of multifilament Dacron yarn and monofilament collagen derivative yarn. Right (top): Initial, and; Bottom—chemically-digested compound vascular prosthetic material of the core wound yarn type. Note the dramatic increase in interstice size upon chemical digestion in both types.
the results of these particular compound prosthetic grafts are not dramatically better than the more porous simple prosthetic grafts, the data indicate that the concept of the compound prosthetic graft is valid. We are presently developing a series of compound prosthetic grafts with biologic porosities more closely approximating the chemically digested porosities.\textsuperscript{13}

**Acceptability Rating of Presently Available Vascular Materials**

The various vascular materials are listed in descending order of preference in Fig. 8. The order is divided into thirds: long-term acceptability, short-term acceptability and not acceptable. In general, autologous tissue materials are the only materials which are acceptable on a long-term basis; homologous tissue and most of the synthetic fabric prostheses fall jointly into the acceptable short-term category. Those materials listed as unacceptable are generally agreed upon by all. Controversy regarding the illustrated order of acceptability is concerned mainly with those materials that are listed as acceptable on a short-term basis. Detailed reporting of the long-term results of human implantation of these same materials will settle any such controversy.

Further development of materials for repair of vascular defects centers around four types of materials. There is a pressing need for developing the application of non-vascular autologous tissues to the repair of various cardiac, arterial and, perhaps, venous defects.

Further development of homologous tissues rests with the solution of the problem of homograft incompatibility. Solution of this problem would result in the conversion of fresh homologous tissue into the equivalent of autologous tissue. Further development of despeciated heterologous artery holds certain promise in providing a scaffolding to allow the host to lay down an acceptable autologous tissue replacement.\textsuperscript{9}

Further development of prosthetic materials can be in two directions: the first approach is the development of a flexible non-porous prosthesis which would repel fibrin deposition upon its inner surface; i.e., a prosthesis with an "artificial intima." The work of Sawyer and his associates\textsuperscript{11} concerning the electrical phenomena of blood vessel wall metabolism and its relationship to intravascular thrombosis presents intriguing possibilities in this connection. The second approach, mentioned above, is further development of the compound prosthetic material to allow for a low initial porosity and a biologic porosity which would approach a very high chemically-digested porosity.

**Specifications for Prosthetic Vascular Materials**

It is appropriate to conclude this review with our interpretation of the specifications for the ideal prosthetic material.
Figure 8: Schema illustrating the acceptability rating of the presently-available vascular materials. (see text)

Specifications for the Simple Vascular Prosthesis

1. No toxicity, no allergenic potential, "biologic reactivity" not an important limiting factor.
2. No deterioration of the synthetic fiber upon biologic implantation for prolonged periods of time.
3. Certain desirable mechanical handling properties.
   A. Scrunchable—ability of the material to readjust its wall configuration to make a good fit at anastomoses.
   B. Crimped — allowing graceful accommodation across flexion creases and during shortening without causing kinking or decrease in porosity respectively.
   C. Twistable—allowing latitude in making anastomoses, in placement of the graft through tunnels and in flexion and rotary movements of the extremities following implantation.
4. Low implantation porosity to minimize hemorrhage at operation.
5. High biologic porosity, or fibroblastic permeability, for more favorable biologic fate.

Added Specifications for the Compound Vascular Prosthesis

6. The absorbable component should have a large surface-mass ratio.
7. The organization time of the absorbable component should be the order of that of autologous fibrin.
8. The residual wall should have an interstice size that will not allow for frank hemorrhage.
9. The residual pattern should be stable.
10. The residual wall should have a certain amount of stiffness to prevent subsequent stricture formation.

Acknowledgment: Figures 4 and 8 are modified from Wesolowski and Figures 6 and 7 are modified from Wesolowski et al.
REFERENCES


LESIONS OF CORONARY ARTERIES OF SURGICAL INTEREST

Several years ago, 5,000 consecutive necropsies were reviewed. One or more infarcts were found in 11.7 per cent. an incidence much higher than any other reported series. Of the persons with infarcts, the average age was 68 years: less than one-fourth had recent infarcts and over three-fourths had old infarcts; and in 30 per cent. the condition was entirely unsuspected. The high incidence of unsuspected infarcts seemed to be significant in that it represented a favorable aspect of myocardial infarction. At necropsy, it is sometimes astonishing to see, as much as 50 per cent. of the substance of the left ventricle destroyed by infarction and replaced by scar tissue. Occasionally in such cases there is no history or suspicion of heart disease. A frequent finding at necropsy is the association of a fresh apical infarct with an old posterior infarct or of a fresh posterior infarct with an old apical infarct. The reason is that atherosclerotic disease involves both coronary arteries simultaneously to a variable degree, is usually progressive, and both vessels may become occluded at different times. A finding frequently encountered at necropsy is fresh patchy infarction which is superimposed upon old patchy fibrosis of the left ventricle. This indicates that a person with an old or recent infarct may be subject to recurrent damage at the same site, whether by insufficiency of the arterial supply to the area or as the result of progressive or recurrent occlusion of the vessel.


RECOGNITION AND TREATMENT OF POTENTIALLY FATAL ASTHMA

Bronchial asthma terminates in a fatal paroxysm in 1 to 3 per cent. of hospitalized cases. The pathologic picture is unique and suggests that death results from bronchial obstruction by mucus plugs. Measurement of the arterial carbon dioxide tension may serve to predict the potentially fatal paroxysm, and tracheostomy may be a lifesaving procedure in patients with progressive hypercapnea.