United States Patent [19]

Reick

[11] **3,914,802**

[45] **Oct. 28, 1975**

[54] **NON-THROMBOGENIC PROSTHETIC MATERIAL**

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[73] Assignee: **Michael Ebert,** Mamaroneck, N.Y. ; a part interest

[22] Filed: **May 23, 1974**

[21] Appl. No.: **472,677**

[52] **U.S. Cl.** **3/1.4;** 3/1; 128/DIG. 21

[51] **Int. Cl.²** **A61F 1/24**

[58] **Field of Search** ..... 3/1, DIG. 1–3, 3/1.4, 1.7; 128/334 R, 1 R, 1 D, DIG. 21

[56] **References Cited**

UNITED STATES PATENTS

3,609,768	10/1971	Ayres	3/1
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OTHER PUBLICATIONS

"Artificial Organs" by Howard J. Sanders, Chemical & Engineering News, April 5, 1971, p. 49 relied upon under heading Polypropylene fibers.

"An External Velour Surface for Porous Arterial Prosthesis" by Lester R. Sauvage et al., Surgery, Vol. 70, No. 6, pp. 940–953, Dec. 1971.

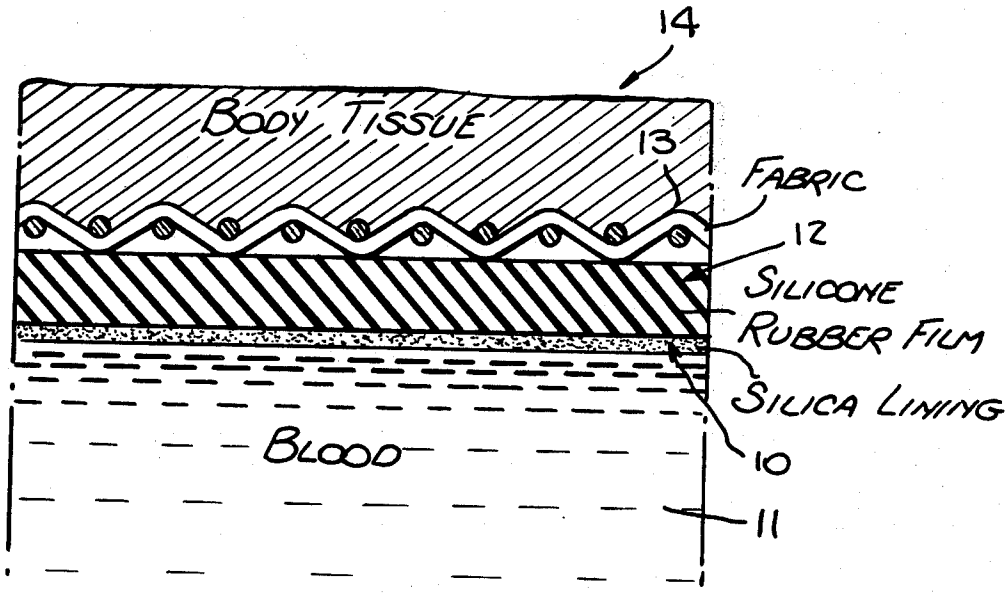
"The Coating of Intravascular Plastic Protheses with Colloidal Graphite" by V. L. Gott et al., Surgery, Vol. 50, No. 2, Aug. 1961, pp. 382–389.

Primary Examiner—Ronald L. Frinks

[57] **ABSTRACT**

A non-thrombogenic material possessing mechanical, chemical, biological and electrical properties that render the material acceptable for a broad range of prosthetic applications. The material is provided with a hydrophilic inner lining formed primarily of a sintered network of colloidal silica bonded onto a thin layer of oxygen-diffusing elastomeric material, reinforced by a porous fabric backing. The silica imparts a net negative charge to the lining which repels negatively-charged blood platelets in contact therewith. The silica network acts as a matrix to promote the growth of neo-intima.

11 Claims, 3 Drawing Figures



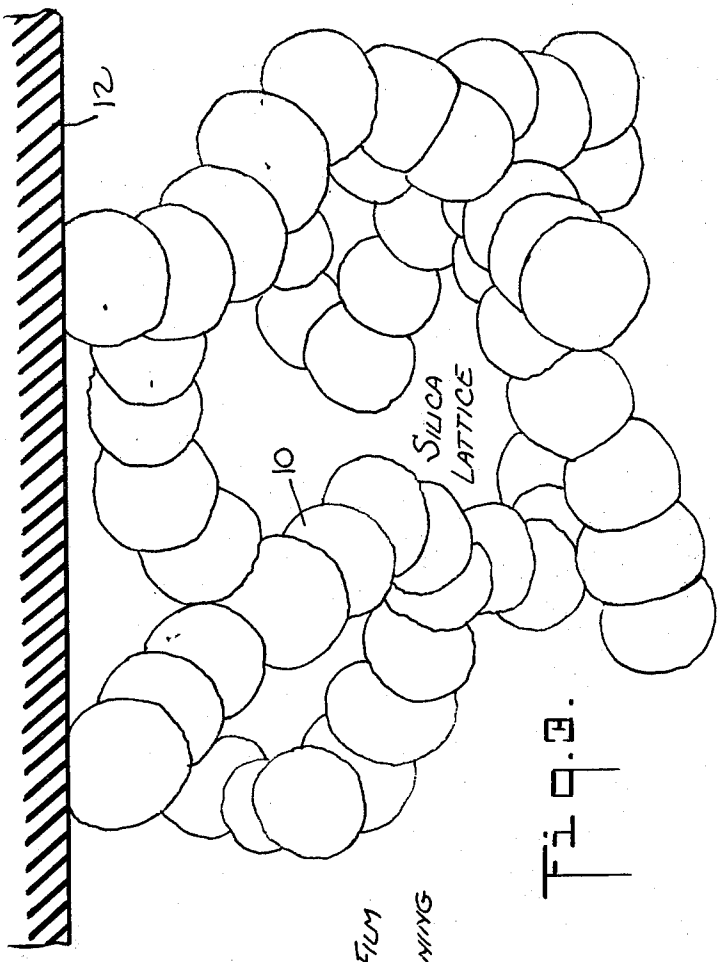


Fig. 3.

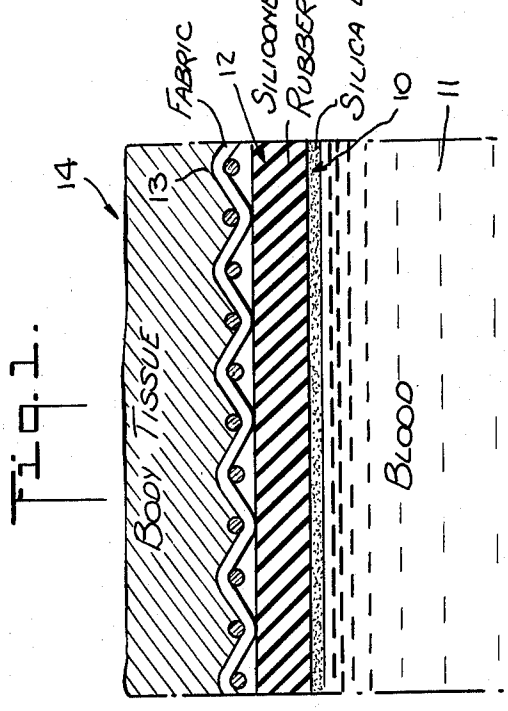


Fig. 1.

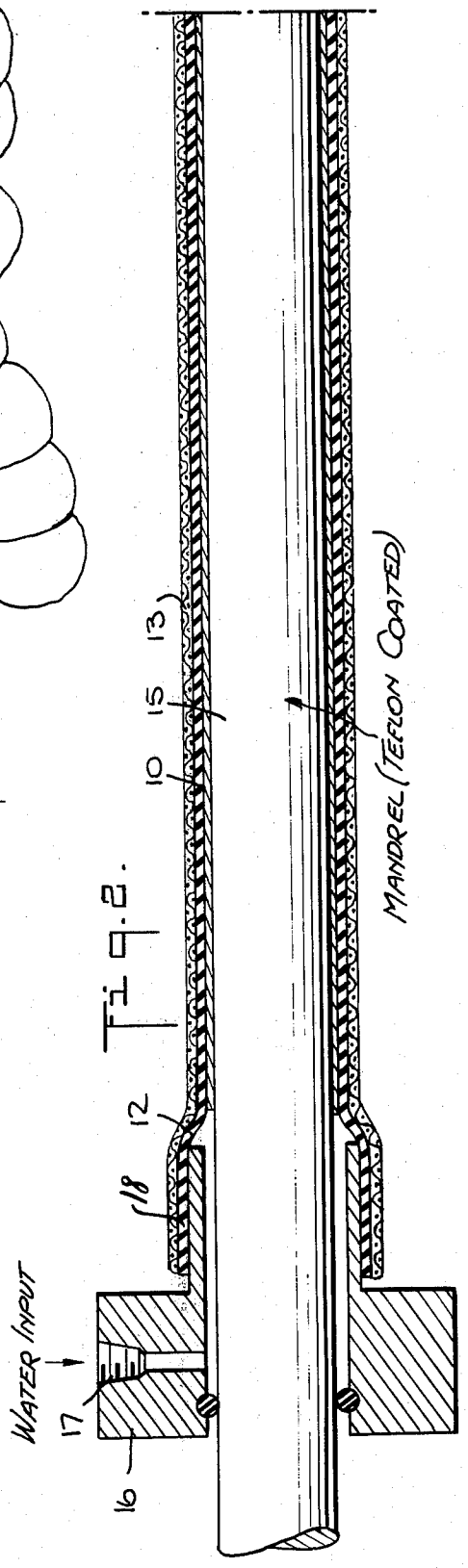


Fig. 2.

NON-THROMBOGENIC PROSTHETIC MATERIAL

BACKGROUND OF THE INVENTION

This invention relates generally to prosthetic materials, and more particularly to prosthetic tubing adapted to replace veins and arteries.

Prosthesis refers to the surgical practice of replacing defective or missing parts of the human body with artificial devices. As noted in the articles on "Artificial Organs" (Parts 1 and 2) which appear in the Apr. 5, 1971 issue of Chemical and Engineering News, the main problem encountered in connection with artifical hearts and other organs as well as in human implants such as finger joints and in synthetic plastic tubing serving as blood vessels, is the incompatibility of the prosthetic material with human blood.

In order to be compatible with blood, it is vital that the prosthetic material not cause blood clotting or bring about the destruction of red blood cells. The material must not alter blood proteins, cause damage to blood platelets, or produce other deleterious blood changes.

According to the above-identified articles, all presently available synthetic material without exception, when immersed in blood for substantial periods of time, cause blood clotting. They can also damage red blood cells, blood platelets and blood proteins. Although artificial materials in contact with blood can give rise to many adverse reactions, of greatest medical concern is the tendency of known materials to cause blood clots or thrombi. If the material has a marked tendency to induce clotting, it is referred to as highly thrombogenic.

The reason why a thrombogenic material is unacceptable is that clots forming on the surface thereof may dislodge and be carried along in the blood stream until they completely block a blood vessel, thereby inducing a heart attack or a stroke. In those instances where the clot remains at its formation site in a narrow organ such as a blood vessel, it can dangerously constrict the vessel.

The mere fact that a given material does not promote clotting does not automatically render it acceptable for prosthetic applications, in that the same material can also bring about destruction of red blood cells or damage blood proteins. Or its mechanical properties may be unsatisfactory. To be acceptable in all respects, a prosthetic material must satisfy a large number of critical requirements, for in addition to those already mentioned, the material must not damage adjacent tissue, it must be free of carcinogenic or toxic agents, and it must not induce allergic reactions or interfere with the normal immunological mechanism of the body.

One widely used prosthetic material is silicone rubber. This material is employed for implants and for various types of tubing to drain fluid from the brain, the chest cavity, the bladder and other organs. Silicone rubber, because of its flexibility, softness and other mechanical, biological and chemical properties, has distinct advantages. But though relatively compatible with blood, silicone rubber, under some circumstances, such as when the blood is not flowing fast enough, can promote clotting. Moreover, this material does not possess sufficient strength when continuously flexed for protracted periods.

Also in common use as a prosthetic material are synthetic polymers, such as "Dacron" polyester fiber. Woven into a tight fabric, Dacron has found its greatest

surgical use as artificial blood vessels and as patches for arteries and other human organs. While Dacron has good tensile and flexural strength and a high degree of compatibility with tissue, it can cause blood clotting. This tendency toward clotting is also characteristic of Teflon (polytetrafluoroethylene).

It is generally agreed that the manner in which blood flows greatly affects its tendency to clot. It has been found that clotting is more likely to occur when the flow rate of blood is too slow or even worse, becomes stagnant. Turbulent flow also promotes clotting. Hence if the interface between the blood and the prosthetic device is not smooth, turbulence is produced which may give rise to clotting. In general, the problem of thrombosis is not a serious problem in the grafting of medium and large sized vessels. But heretofore it has been a major deterent to small vessel venous repair where the hemodynamics are usually unfavorable.

A significant factor which influences thrombogenicity is the electrical charge appearing on the surface of the prosthetic material. It is known that a negatively-charged or anionic substance is less prone to induce clotting than one which is positively-charged. The lining of natural blood vessels has a negative charge which is as high as 5 m V. This negative charge causes the lining to repel blood platelets and red blood cells whose surfaces are negatively-charged.

The reason this charge repulsion is believed to inhibit blood clotting is that it prevents the attachment of platelets to the wall of the blood vessel. Such adhesion causes the platelet membrane to rupture and triggers off an intricate chain of enzyme-activated steps that lead ultimately to the conversion of fibrinogen to fibrin. Fibrin is an insoluble protein that forms the matrix of a blood clot made up chiefly of fibrin, platelets and red blood cells.

In an attempt to impart a negative charge to the surface of a prosthetic material in contact with blood so as to repel negatively-charged blood platelets, treated polymers have been developed, these being called electrets. The polymers, after being heated to slightly below their melting point, are exposed to a strong electrical field. When the polymer cools, one side has a negative surface charge and the opposite side a positive charge. The difficulty with electrets is that they are not only costly and difficult to fabricate, but their electrical charge may decay, disappear or even reverse itself.

SUMMARY OF THE INVENTION

In view of the foregoing, it is an object of this invention to provide a non-thrombogenic material possessing mechanical, chemical, biological and electrical properties that render the material acceptable for the full range of prosthetic applications.

More particularly, it is an object of this invention to provide a prosthetic tubing whose inner lining has a permanent negative charge to prevent the formation of deleterious blood clots, the structure of the lining encouraging the formation of self-renewing living tissue (neo-intima or pseudo-intima) which is highly compatible with the flowing blood in contact therewith.

Also an object of the invention is to provide a method for fabricating small bore flexible tubing which is non-thrombogenic and has other excellent prosthetic properties.

It is still another object of this invention to provide a technique for forming an inner lining on a prosthetic

material whose net electrical charge may be preset to conform to blood requirements.

Briefly stated, these objects are attained in a prosthetic material having an inner surface or lining formed primarily by a fine layer of sintered colloidal silica bonded to a thin film of elastomeric material, such as silicone rubber, reinforced by a porous fabric backing formed of synthetic yarn such as Dacron.

The porous fabric backing is conducive to external cellular diffusion to lock the prosthetic material in place after implantation. The lining has a net negative charge which repels negatively-charged blood platelets, the lining surface being micro-reticulated to provide a matrix encouraging the growth of living tissue. The thin silicone rubber layer permits oxygen to diffuse readily therethrough so that the support cells remain healthy.

OUTLINE OF DRAWINGS

For a better understanding of the invention as well as other objects and further features thereof, reference is made to the following detailed description to be read in conjunction with the accompanying drawing, wherein:

FIG. 1 schematically illustrates the structure of a prosthetic material in accordance with the invention;

FIG. 2 shows the mandrel on which the material is fabricated, and

FIG. 3 is a highly magnified view of the lattice network formed by the sintered silica particles in the inner lining of the prosthetic material.

DESCRIPTION OF THE INVENTION

A prosthetic tubing or other device in accordance with the invention is constituted by an inner layer of a non-thrombogenic substance which is bonded to and lines the face of a thin layer of oxygen-diffusing elastomeric material such as silicone or urethane rubber, the elastomeric layer being reinforced by a woven fabric backing made of synthetic plastic yarns of high-strength and acceptable chemical and biological properties. The resultant structure is similar in some respects to that of a fire hose in that the thin layer of rubber is externally-supported by an exceptionally strong fabric to provide a high-strength, burst-resistant tubing. This prosthetic tubing may be sutured, glued or otherwise connected to a vein or artery stub.

Various surgical techniques for grafting prosthetic tubing to small vessel stumps and for implanting prosthetic devices are disclosed in the following references:

1. Jacobson and Suarez, Surgical Forum, 11,243 (1960)
2. MaCaffrey, Australian and New Zealand Journal of Surgery, 37,398 (1968)
3. Salmon, British Journal of Surgery, 55 (1), 58 (1968)
4. Strauch & Murray, Plastic & Reconstructive Surgery, 40 (4) 325 (1967)
5. Bellman, Acta Chir. Scand., 128,509 (1964)

The fabric backing is preferably woven of Dacron yarn, a polyester fiber made from polyethylene terephthalate. The porous Dacron permits diffusion to lock it into place after implantation. It is soft and flexible and easily inflated by blood pressure. Dacron is not adversely affected by aging or body fluids. Also suitable as a backing is woven Lycra, made of a spandex fiber in the form of continuous monofilaments.

As noted previously, blood platelets carry a negative charge, the platelets being repelled by the negatively-charged surfaces of healthy veins and arteries. This mutual repulsion prevents damage to the extremely fragile platelets as they travel through an elaborate venous network whose conduits are in various diameters. Normal veins and arteries are extremely hydrophylic with respect to blood plasma, the fluid wetting the vessel.

The lining of a prosthetic material in accordance with the invention makes it possible to alter the inner surface of the prosthetic so that no discontinuity of any sort is introduced into the system. That is to say, the electrical charge of the lining is essentially equivalent to that encountered in the natural artery or vein in which the prosthetic tubing is interposed, hence there is no charge discontinuity therebetween; the lining has hydrophylic properties comparable to that of natural venous tubing, hence there is no wetting discontinuity; and the surface of the lining has physical properties comparable to that of natural venous tubing, hence there is no conductivity discontinuity.

The inner lining of the prosthetic tube is formed primarily of dispersed Cab-O-Sil, (the trademark for colloidal silica particles sintered together in chain-like formations), or particulate material having equivalent properties. This product is formed in a high temperature vapor phase flame hydrolysis process producing extremely fine particles of a diameter of about 15 millimicrons. One gram of Cab-O-Sil contains over 11 million billion particles and covers an area of about 200 square meters.

A typical Cab-O-Sil surface contains covalently bonded hydroxyl and siloxane groups. When Cab-O-Sil particles are dispersed in liquid and allowed to stand, they develop, as shown in FIG. 3, a loosely-woven lattice-like, three-dimensional network as a result of hydrogen bonding between particles. Cab-O-Sil, in water (or blood), as indicated in the descriptive booklet published by the White Pigment Division of Godfrey L. Cabot, Inc. of Boston, Mass., is normally negatively-charged.

Thus, when a fine Cab-O-Sil coating is formed on the inner surface of a prosthetic device, the resultant lining exhibits a negative charge which repels negatively-charged blood platelets and prevents the formation of blood clots. The lining is therefore inherently non-thrombogenic. Nevertheless the lining is synthetic in nature, whereas the best approach to making a foreign material fully compatible with blood is to allow the material to become covered with a layer of living tissue whereby the blood does not come in direct contact with a foreign substance but with living tissue similar to that of normal body organs. Such living tissue or neo-intima causes little damage to blood cells and blood proteins, and since neo-intima is self-renewing, it can repair itself.

A serious difficulty heretofore experienced in making a surface non-thrombogenic by growing living tissue over it, is that if the tissue layer continues to grow and becomes too thick, the tissue cannot survive. The reason for this is that the cells in the neo-intima depend on blood for nutrition, and unless the neo-intima is extremely thin, blood cannot reach all of the cells.

The extraordinary advantage of the microscale three-dimensional Cab-O-Sil network lining is that it affords a nearly ideal matrix or scaffolding for growing a thin neo-intimal layer that remains fully intact because it

enables all of the cells to receive an adequate supply of blood.

It is also to be noted that attempts have heretofore been made to provide a growth matrix for a neo-intimal layer by means of a gossamer-like polypropylene fiber web bonded to a substrate. In this web arrangement, should the neo-intimal layer grow too thick so that the blood is unable to reach the innermost cells, the resultant death of these cells cause the neo-intima to come loose from the web and to be sloughed off into the blood stream, as a result of which the exposed underlying web may cause clotting. But in the present invention, even should some of the neo-intima peel off the lining network, the negative charge on the exposed area would prevent the formation of blood clots.

Thus as shown in FIG. **1**, the prosthetic material is constituted by a thin, gossamer-like lining **10** of sintered silica particles in a lattice-like formation which has a negative charge and is in contact with the flowing blood **11**, making possible the growth of a thin layer of neo-intima. Lining **10** is firmly anchored on the face of a silicone rubber film **12** which permits the diffusion of oxygen therethrough, the film being bonded to the inner surface of a woven Dacron fabric backing **13** whose interstices facilitate cell growth and bonding of the material to the body tissue **14** in contact therewith. When the sintered silica three-dimensional network comes in contact with blood, minute blood clots form in the interstices of the network and are held therein. In time, these minute clots coalesce, and a layer of cells forms over them, so that eventually, the clots are replaced by a layer of living tissue.

METHOD OF FABRICATION:

As illustrated in FIG. **2**, the prosthetic tubing in accordance with the invention is made from the inside out on a Teflon-coated mandrel **15.** Teflon which is the trademark for tetraflouroethylene (TFE) flourocarbon polymers, has useful no-stick properties. We shall now describe the sequence of steps to be carried out in making prosthetic tubing.

1. The first step in the manufacturing procedure is to cover the mandrel with a release agent. Preferably, this agent has non-thrombogenic properties, so that should any trace thereof remain on the inner surface of the tubing, it will not impair the non-thrombogenic characteristic of this surface. Suitable for this purpose is Pluronic-**F68.** Pluronic is a trademark for polyoxyakylene derivatives of propylene glycol. Also acceptable as a release agent is Ethomid (polyethoxylated highmolecular-weight amides).

2. The second step is to spray a dispersion of Cab-O-Sil particles over the release agent coating to form an extremely fine layer thereover. The solvent for this dispersion is preferably hexane, for this solvent does not interact with the release agent and does wick up through the particles.

An ideal lining is one having a net negative charge comparable to that found in a natural blood vessel and similarly hydrophylic. In order to obtain these characteristics, it may be necessary to intermingle the Cab-O-Sil particles with Alon, which is a positively-charged fine-particle gamma alumina (also hydrophylic), made by the flame hydrolysis of aluminum chloride. By varying the ratio between the intermixed Alon and Cab-O-Sil particles, one may obtain the desired net negative charge and the desired hydrophylic lining characteristics. To adjust the hydrophylic properties, some Silanox or other hydrophobic colloidal particles may be added to the Cab-O-Sil particles.

It also may be desirable to add small amounts of colloidal graphite to the mixture to impart semiconductive electrical properties to the lining. In effect, therefore, the surface in contact with the blood can be "tuned" to attain optimum charge-carrying and wetting properties.

3. The third step is to spray over the lining layer a thin layer of silicone rubber to anchor the Cab-O-Sil particles therein without however encapsulating the particles or fully covering the surface thereof. Electrostatic spraying in a hexane solvent is preferred to create a thin elastomeric film whose thickness lies in a range of about **0.0005** to **0.005** inches, the film being readily diffused by oxygen. As an alternative to silicone rubber, one may use Silastic which has characteristics similar to unvulcanized rubber and contains organo-silicon polymers. The silicone rubber layer, after spraying, is permitted to air cure for about an hour.

4. The fourth step is to cover the silicone rubber layer on the mandrel with a long sleeve of woven Dacron fabric. To facilitate this operation, the sleeve is first wet down with water which acts as a lubricant, after which the sleeve is gently pulled over the mandrel. The sleeve is then smoothed down to squeeze out the water. After the sleeve is fully dry, the sleeve is dipcoated in highly dilute silicone rubber hexane solution (RTV) in order to bond the Dacron fabric sleeve to the silicone rubber underlayer without however filling and plugging the interstices of the fabric. It is important to maintain porosity of the sleeve. The sleeve is now permitted to air cure for several hours.

5. The fifth step involves removing the long prosthetic tube from the mandrel **15.** For this purpose, a ring **16** having a lateral water inlet **17** is fitted over one end of the mandrel, the ring having a hub extension **18** which is inserted under one end of the expansible tube. By forcing water or other lubricating fluid through inlet **17,** the long tube is dilated, thereby making it possible to withdraw the tube from the mandrel.

6. The sixth step involves the careful cleaning of the tube. This is done with hot water under high pressure to produce a highly turbulent stream which rinses loosely-bonded particles from the tube lining and removes whatever release agents remain therein. Finally, the tube is sterilized in preparation for use.

If desired, the inner lining may be coated with blood, a cell dispersion, Heparin, Pluronic **F68,** hydrogel or any other material heretofore used to enhance the performance characteristics of a prosthetic tubing.

KNEE JOINT SUPPORT

The fire hose construction described herein is satisfactory under body conditions where gentle deflection is encountered, for the tube will remain cylindrical when inflated with blood. But in high flex areas such as bone joints, there is a risk of creasing. This is undesireable, for creasing introduces a flow discontinuity which may promote the formation of clots.

If an area of high flex is anticipated, one may construct the prosthetic tubing in the manner previously described on the mandrel, and add to the long Dacron sleeve a shorter concentric sleeve of woven Dacron felt at a position corresponding to the flex area. This short sleeve may then be cemented in place. The sleeve acts

to resist creasing and to maintain a smooth blood flow through the high flex area.

While there have been shown and described preferred embodiments of the invention, it will be appreciated that many changes may be made therein without departing from the essential spirit of invention.

I claim:

1. A non-thrombogenic prosthetic material comprising:

A. an elastomeric layer capable of oxygen-diffusion, the outer face of the layer being bonded to a fabric backing acting to reinforce the layer, the interstices of the fabric permitting cellular diffusion to lock the material in place after implantation, and

B. a lining bonded to the inner face of said layer and formed primarily of colloidal, negatively-charged silica particles to repel negatively-charged blood platelets in contact therewith, said particles being sintered to define a three-dimensional micro-lattice acting as a matrix to promote the growth of neo-intima.

2. A prosthetic material as set forth in claim **1**, wherein said elastomeric material is silicone rubber.

3. A prosthetic material as set forth in claim **1**, wherein said elastomeric material is urethane rubber.

4. A prosthetic material as set forth in claim **1**, wherein said fabric is formed of woven polyester yarns.

5. A prosthetic material as set forth in claim **3**, wherein said yarns are formed of polyethylene terephthalate.

6. A prosthetic material as set forth in claim **1**, wherein said material is in tubular form and said fabric backing is constituted by a sleeve bonded to a tubular layer of elastomeric material whose inner face has said lining bonded thereto.

7. A prosthetic material as set forth in claim **1**, wherein said lining further includes positively-charged fumed alumina particles in a ratio to said negatively charged particles to provide a desired net negative charge.

8. A prosthetic material as set forth in claim **1**, wherein said lining further includes colloidal graphite to render the lining semi-conductive.

9. A prosthetic material as set forth in claim **1**, wherein said elastomeric layer has a thickness in the range of **0.0005** to **0.005** inches.

10. A material as set forth in claim **1** wherein said particles are hydrophilic.

11. A material as set forth in claim **10** further including hydrophobic particles in a ratio relative to said hydrophilic particles to impart a desired wetting characteristic to said material.

* * * * *

UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 3,914,802
DATED : October 28, 1975
INVENTOR(S) : Franklin G. Reick

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

Column 5, line 50 "highmolecu-" should have read -- high-molecu- --

Column 5, line 56 "does wick" should have read -- does not wick --

Signed and Sealed this

twentieth Day of *January 1976*

[SEAL]

Attest:

RUTH C. MASON
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents and Trademarks