A further object is the provision of a prosthesis that is created from biological tissue which can be simply and effectively installed using the conventional techniques.

Still a further object of the invention is the provision of a method by which such a prosthesis on a basis of biological tissue can be formed.

The manner in which these and other objects of this invention are obtained will become apparent from the detailed description and the following drawings in which:

FIG. 1 is a longitudinal central section through an embodiment of a prosthesis in accordance with the invention:

FIG. 2 is a diagrammatic view illustrating the method of forming the prosthesis of FIG. 1; and

FIGS. 3 and 4 are diagrammatic perspective views illustrating two somewhat different forms of the prostheses embodying the invention.

According to the invention there is provided a prosthesis in tubular, sheet or strip form which comprises at least two layers of biological tissue intimately joined and dried. More specifically the prosthesis comprises alternating layers of biological tissue and collagen fibers intimately joined and dried.

According to the present invention, the biological prostheses are manufactured by placing over, i.e., applying onto the surface of a firm support a piece of tubular, sheet or strip form biological tissue, causing the exposed surface thereof to swell so as to produce thereon an adhesive or glue like effect and/or the exposed surface is coated with a binder or bonding agent as for example a collagen fiber paste, a second piece of biological tissue is then applied to the first and the procedure repeated until a multi-layered structure of the desired wall thickness is obtained. The prosthesis is then dried and removed from the support.

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As natural tissue for use in the manufacture of the prostheses of the invention are suitable in particular the submucosa, which can be obtained in pure form from the submucosa can be easily be removed by the process as conventionally used in the manufacture of catgut.

As the strength of a single layer of submucosa is far too inadequate, the same having a thickness of only about 15μ, it is advantageous to use a number of layers cemented together with a binder, as for example, a collagen fibre paste. The collagen fibre paste may be prepared, for example, by the process described in German patent specification No. 659,490. Furthermore, this layer of collagen fibres ensures that any holes, tears, and the like made in the tissue during the manufacture thereof, during the operation for installing the same, or a later time, will close easily. This can prevent hemorhage, which hitherto has been highly dangerous. The collagen fibre paste has a further advantage in that therapeutic substances may be incorporated therein. Thus, for example, heparin may be added to inhibit the clotting of blood, cartilage powder or chondroitin sulphate included to stimulate the formation of cartilage, or other collagen fibres for the vascular intima, as well as other therapeutic substances.

It is also possible to cause the individual layers of tissue to swell and to bond them together in the swollen state. Organic acids, especially dilute lactic acid, have been found to be particularly suitable for swelling the single layers. The use of highly diluting solutions of lactic acid is preferred in this connection as the same has the advantage that no acidic end products are formed.

In carrying out the process of the invention it is
possible to use, for example, a tubular core or a plate made of glass or a synthetic material as the firm, more or less rigid support. Instances of synthetic materials include polyelefin as for example polyethylene or polypropylene etc. However, any inert fairly firm material may be employed. Prior to use, it is advantageous to treat the surface or surfaces of the support with a lubricant, as for example, glycerol or a silicone oil. A thoroughly cleansed tubular or flat piece of biological tissue, for example, submucosa or serosa tissue, which may have been subjected to bleaching with hydrogen peroxide, is then placed onto the support. The tissue is then coated with a binder paste, preferably a collagen fibre paste, and, if necessary, the paste is allowed to dry slightly. Another piece of tissue is then applied, and the process is repeated until the desired thickness is obtained. The finished prosthesis may contain, for example, about eight layers of tissue. The number of layers is generally determined by the thickness of the composite layers and by the ultimate use.

The prosthesis made by the process of the invention may be subjected to a hardening process to prevent premature absorption by the body tissues. As hardening agents, there may be used physiologically acceptable vegetable or synthetic substances or, as for example, aldehydes. Instances of aldehydes that are suitable for this purpose are formaldehyde, glutaraldehyde and aldehydes of higher polyhydroxy compounds. The concentration of the hardening agent may be varied to produce the rate of absorption required.

The hardening process is preferably carried out after the final layer of tissue has been applied. However, it is possible to harden the single layers of tissue before they are applied. By adopting this latter procedure, the single layers of tissue may be hardened to varying degrees, thereby producing a prosthesis in which the single layers have different rates of absorption. For example, when using a tubular core as a support, the innermost layers may be hardened to a considerable degree to produce a tough, resistant core, and the outside layers may be only slightly hardened to ensure a specific rate of absorption.

After removal of the support and, if necessary, after the tube has been cut open, fascia prostheses are obtained which are generally known as "patchers" and which may be used to close defects in the tympanic membrane and the heart wall, for hollow-walled organs or as heart valves.

Furthermore, collagen patches in sheet form are also used to repair damage to parenchymatous soft tissue, for example, in the liver, kidney, spleen and pancreas. This can be effected in the following manner:

A so-called mattress suture is made, i.e., a largeatraumatic needle threaded with a soft suture is passed through the parenchymatous tissue on one side of the wound and out of the other side. The needle is then passed through a stiffened and perforated collagen patch from underneath. The needle is then passed back through an adjacent perforation in the collagen patch at an appropriate distance from the point at which it emerged, through the organ and out the other side. The length of the suture should be such that a second perforated collagen patch may be threaded onto the ends. When the needle has been removed, the two ends of the suture are knotted together over the collagen patch.

Strips for surgical purposes, as for example, for securing a kidney or for use in surgery of the incontinetia vesicae, may also be cut from sheets, i.e., membranes of the same material.

Tubular, flat or fluted prostheses may also be made by the process of the invention in addition to membranes and strips. The tubular prostheses may be of uniform diameter throughout the length of their diameter may be in the form of or narrowed conically.

Referring to the drawing a tube made of synthetic material as, for example, a tube made of polyethylene or polypropylene and which has been provided with a plurality of threads 2 is thoroughly cleaned and, if necessary, treated with a silicone oil. A tube of tissue 3, preferably submucosa, which has been thoroughly cleansed and, if necessary, bleached with hydrogen peroxide, is drawn over the tube. The tube is then coated with a binder paste, preferably a collagen fibre paste, the paste is allowed to dry slightly, and then another tube of tissue is drawn over the first one. A synthetic filament is wound round it as before and the tissue is dried. This procedure may be repeated until the desired thickness of wall is obtained. The multiple layers of tissue are firmly cemented together by the binder. When the single layers of tissue are to be united by swelling it is possible either first to swell the single layers of tissue and to draw them onto the tube or core in the swollen state or to swell them on the core. To form a tube a tube formed by these layers of tissue from the supporting tube or core, warm air is passed through the tube or core in this case a plastic tube, to soften it slightly, whereupon both ends of the tube are pulled until it stretches and detaches from the tissue at the beginning of the thread section. This can then be pulled outwards with the screw-threaded form of a plastic filament without the submucosa tube adhering to it or being damaged. Prostheses suitable for various purposes may be produced by varying the pitch of the thread, the depth of the thread and the number of turns.

The threaded tube of tissue so obtained has the necessary strength, density and elasticity required of vascular prostheses, and it can be sutured and is puncture-proof. The thread with which it is provided prevents it from kinking when it is moved after implantation in the host, thereby permitting an unhindered flow of blood. It is also extensible.

On the other hand, if a smooth tubular prosthesis is required, that is to say, without any thread or fluting, for example, as used for prosthetic repair of the cystic duct, the ureter, the esophagus or, in special cases, blood vessels, the same procedure as for the plastic tube may be followed, but without winding a filament round the tissue or allowing it to conform to the shape of the thread. The elastic tube of tissue is drawn over the plastic tube and held taut over it by tying the tissue tube at both ends and allowing it to conform to the outer circumference of the plastic tube without complementing the shape of the thread. Alternatively, a smooth plastic tube may be used as a support, for the layers of tissue.

Prostheses, for example, for the esophagus, trachea and intestine, can be made by the process described above, with due regard to anatomical requirements, diameter and thickness of wall. The strength of such prostheses can be considerably increased by placing layers of synthetic or natural tissue or even metallic clasps or spirals between the layers making up the actual prosthesis. The synthetic tissue used may be made, for example, from polypyrrole or polyurethane fibres. The natural tissue may be, for example, biological tissue, for example, serosa tissue, or material made from natural fibres. The serosa tissue may be wound round the prosthesis diagonally, first from left to right and then from right to left. If necessary, these layers of tissue may be pre-treated, as for example, by stretching.

It is also possible to bond the layers of tissue by swelling the tubular or flat pieces in an acidic or alkaline medium. In this process the upper layers of collagen fibres are slightly hydrolyzed and converted into tropocollagen which, on drying, has a glue-like adhesive effect.
The process has a negative effect on the physical properties of the collagen fibre and neutralization is generally necessary afterwards, followed by washing out of the salts formed during neutralization.

Sterilization of the prostheses so obtained may be effected by gamma-radiation, which process also reduces the antigenic properties of the collagen.

In FIGS. 3 and 4 there are shown two somewhat different forms of the prostheses in accordance with the invention. In FIG. 3 the embodiment comprising alternating layers of biological tissue 7 bonded together with a bonding agent 8 is shown and in FIG. 4 the embodiment wherein the bonding is effected by swelling the layers 7 is set out.

The prostheses in accordance with the invention has been subjected to trial and has been observed and evaluated as a suitability, production of toxic symptoms, decomposition, detachment, secondary reactions such as abnormal tissue growth, etc. The trials consisted in surgical implantation of the prostheses in otherwise normal animals, i.e., the requirement for the prostheses was surgically induced, observation of the thusly treated animals during the recovery period and for varying periods thereafter. During this time, numerous test procedures were carried out, the same including chemical, X-ray, electrocardiographic, etc., procedures. At the end of various predetermined time intervals certain of the animals were sacrificed and any of the animal’s possibly involved organs examined both microscopically and macroscopically. In every instance, the results of procedures and tests in both the living and sacrificed animals established the safety and suitability of the prosthetic devices for replacement and repair of damaged organs. It is to be noted that as experimental animals, there were employed cats, dogs and monkeys.

The device has been surgically implanted in human subjects, in each case where the subject’s condition was indicative of such treatment. Almost all of the subjects are still under observation and to date there have not been observed any untoward results or happenings directly associated with the use of the herein disclosed prosthetic devices.

What is claimed is:

1. A tubular prosthetic device on a basis of biological tissue comprising at least two superimposed layers consisting of tubes of natural tissue applied in their natural tubular form prepared from the submucous layers of intestines of mammals, and said layers being bonded together by means of collagen fibers.

2. A prosthetic device according to claim 1 wherein said collagen fibres consist of a collagen fiber paste.

3. A prosthetic device according to claim 1 wherein at least one of said layers is a prehardened layer which has been prehardened by contacting the same with a hardening agent.

4. A prosthetic device according to claim 3 wherein said hardening agent is an aldehyde.

5. A hardened prosthetic device according to claim 1 wherein said prosthetic device has been hardened by treatment thereof with a hardening agent.

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DALTON L. TRULUCK, Primary Examiner
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