Normal wound healing compared to healing within porous Dacron implants

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This study examined the hypothesis that healing within porous implants differs from that in normal connective tissue. Special attention was given to extracellular components including collagen, reticular fibers, and ground substance, and to enzymes associated with activated macrophages. Using Dacron velour and the rabbit as host, the healing of normal connective tissue and that of the tissue/implant interface were histologically compared 10 and 28 days postimplantation. The results exhibited significant differences between connective tissue healing, implant capsule formation, and granulation tissue generation. The healing of connective tissue and implant capsule formation were essentially complete at 28 days. However, tissue inside the implant was qualitatively different and did not significantly change between 10 and 28 days. It was characterized by macrophages and giant cells, a predominantly acid mucopolysaccharide ground substance, and qualitatively fewer and less well defined collagen and reticular fibers were observed than in normal wound healing. Thus we conclude that the connective tissue inside Dacron velour does not resemble normal connective tissue after 10 or 28 days of healing. Furthermore, the collagen never fully matures into orderly bundles, a phenomenon which may be related to an altered mucopolysaccharide composition and a diminished reticular network. The lysosomal enzymatic activity of the macrophages and perhaps the giant cells at the tissue/implant interface may be linked to these differences.

INTRODUCTION

Dacron velour has been used in a variety of biomedical applications. These include use as fixation for percutaneous devices, tracheal and bronchial implants, ear implants, urethral prostheses, and eye reimplantations,[1] artificial heart linings, artificial skin, and vascular prostheses.[2] While the applications vary, the purposes for the use of the velour are the same. It reduces tissue bed/implant motion by connective tissue anchorage to the velour pores.[1] Achieving this goal requires a strong mechanical link between the collagen surrounding the implant and that within the implant, since collagen acts as the primary tensile element of the tissue. Research at this laboratory indicates that the connective tissue grown into the interstices of Dacron velour differs both in quantity and organization from that found in normal implant bed tissue or scar tissue.[3–6]

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Journal of Biomedical Materials Research, Vol. 22, 121–135 (1988)
 CCC 0021-9304/88/020121-15$04.00

In addition, tissue ingrowth into the velour has also been used to minimize undesirable response by the tissue surrounding the implant. It has been postulated that collagen formation within porous coatings surrounding percutaneous devices may play a major role in the inhibition of epithelial downgrowth, thereby preventing marsupialization of the implant.[7–9]

In vascular prostheses, the use of porous implants was originally intended to promote a well-anchored, viable internal lining.[2] Unfortunately the formation of a neointima occurs only when sufficient connective tissue and capillary networks exist to provide adequate nutrition for the neointima.[10] In humans, neointimal growth has not been found to occur more than a centimeter from the anastomosis. Such growth is similar, in extent, to that found in dogs with prostheses having an impervious external coating.[9] Seven days postimplantation one finds the growth of phagocytes, fibroblasts, and early giant cell formation within the velour and adjacent to the fibrin network formed by preclotting of the velour.[11]

In those cases where the porosity of the velour is sufficient to allow the ingrowth through the knitted outer segment of the prosthesis, after a few weeks granulation tissue grows in discrete tufts between the yarn bundles. This granulation tissue begins to organize the fibrin layer of the blood surface of the graft (usually called the pseudointima). Blood vessels then grow through these pores to vascularize the internal capsule. Unfortunately, with the passage of time, this vascular tissue is believed to be obliterated by contraction of the external scar tissue, beginning a process which eventually results in the degeneration, calcification, and necrosis of the inner capsule. This cycle from ingrowth to necrosis may be repeated many times. Increases in the porosity of the implant have been shown to decrease the levels of calcification.[12]

All of these applications eventually fail due to the inability of the healing interfacial tissue to convert or mature into connective or well-vascularized repair tissue. This failure appears in two different forms. Either the tissue fails to grow into the porosity of the velour or it is of a chronic inflammatory tissue type that lacks the mechanical strength to provide a good linkage free from permanent inflammation between the tissue and the implant.[1,5,8]

PROCEDURE

Implant fabrication

The implants were manufactured from surgical grade Dacron velour* purchased as sheets 15 cm × 15 cm × 1 mm, having a woven and a plush side. These cloth sheets were then cut into 1 cm × 2 cm pledgets along the weave of the fabric to minimize raveling. The implants were cleaned in a low-residue detergent,† rinsed three times in fresh distilled water for 10 min each rinse and then refluxed for 24 hr in a Soxhlet column containing distilled

*Cat. no. 001642; U.S.C.I, Billerica, Massachusetts.
†Liquinox, Alconox, Inc., New York, New York.

water. The implants were dried in a vacuum desiccator and sterilized with ethylene oxide in groups of 6, followed by vacuum degassing for over 48 hr and storage in room air for at least 8 days.

Implantation procedure

Healthy New Zealand White Rabbits, from licensed dealers, with body weights of approximately 3 kg, were tranquilized with acetylpromazine maleate (1–2 mg/kg B. W.)[‡] and ketamine hydrochloride (55 mg/kg B. W.)[§] I. M. Two groups of 5 animals each (10- and 28-day) received a total of 8 subcutaneous implants, 4 on each side of the midline. Each site was numbered and randomly selected to receive either an implant into a surgically created connective tissue pocket (implantation site, I), a pocket without an implant (scar tissue, S), or no surgical manipulation at all (normal tissue sites, N). Tissue pockets were generated by blunt dissection of the subcutis from a midline incision. All surgical procedures were performed under strict sterile implantation protocols.[13] Each animal received 3–4 saline soaked implants, 2–3 sham implantation sites, leaving 2–3 unoperated sampling sites.

Subcutaneous closure was made with 4-0 polyethylene terephthalate green braided cardiovascular suture[#] in a simple continuous pattern. Final closure was made with skin staples.

Following surgery, the animal was placed in an intensive care unit (maintained at 26°C) for 3 to 4 hr to allow for recovery from surgery and then returned to a cage. Food and water were provided *ad libitum.* Animals were examined daily. In one animal, initial signs of infection were treated by IM injections of 25 mg gentamycin sulfate* twice daily for 3 consecutive days. When no signs of infection persisted, treatment was discontinued. In all animals, the surgical staples were removed on the eighth day postoperatively.

Implant retrieval

The animals were terminated at the predetermined times using an overdose (approximately 1,950 mg) of sodium pentobarbital[†] administered into the pleural cavity. Upon reaching a surgical level of anesthesia, pneumothorax was induced. A rectangular patch of the skin, encompassing all of the experimental sites, was removed and both its outer, epidermal, surface and subcutaneous aspect grossly examined for inflammation. From this integument section, tissue samples were retrieved from the incision site, a

[‡]Aveco Co., Inc., Fort Dodge, Iowa.
[§]Ketaset, Bristol Laboratories, Syracuse, New York.
[#]Ethiflex, Ethicon Inc., Somerville, New Jersey.
*Gentavet, Burns-Biotec Laboratories, Inc., Omaha, Nebraska.
[†]Socumb-6 GR, Butler, Co., Columbus, Ohio.

normal fascial tissue site (away from the surgical sites), tissue from the sham implantation sites, and implantation sites.

Histological techniques

The retrieval material was evaluated using both standard histological and enzyme histochemical techniques including hemotoxylin and eosin (H&E) (for routine observation), Gomori's one-step trichrome (for collagen organization observations), Gomori's reticular stain (for evaluation of the reticular networks), and alcian blue/periodic acid Schiff (AB/PAS) (for extracellular matrix observation) as well as leucyl aminopeptidase (LAP) and β-glucuronidase sensitive enzyme histochemical procedures. The tissues were fixed according to the methods described in Table I.

Histological specimens were prepared using standard techniques.[14–16]

Light Microscopic Evaluation Methods

Four groups of tissue samples were evaluated. The first group, the incision sites, was evaluated with H&E alone. The other three sets of tissue samples (normal tissue, scar tissue, and the implantation sites) were evaluated using all of the above staining techniques, unless otherwise specified. Implants were examined at three locations; the capsule surrounding the implant, the overall tissue characteristics within its porosity, and the tissue adjacent to the fibers within the porosity. Tissue was considered adjacent to a fiber if it was within one fiber diameter (approximately 20 μm) of the Dacron fiber.

The evaluations were semiquantitative with the exception of those sections stained for the presence of leucyl aminopeptidase. These were examined qualitatively. In general the semiquantitative evaluations consisted of numerically rating the tissue on the basis of organization and stain color. The use of tint and color density was avoided since these qualities are subject to variations in staining technique. Where two or more distinctly different types of tissue existed within an evaluation area, they were given equal weight and an average value recorded. These values were normalized to from 0.0 to 1.0, where 0.0 represented an absence of the evaluated quality and 1.0 a maximum of the quality.

TABLE I
Fixation Used for the Staining Techniques

Fixation Method	Stain
Neutral buffered formalin	HE, AB/PAS
Bouin's fluid	Gomori's trichrome
Carnoy's fluid	Gomori's reticular
Liquid nitrogen Immersion	β-Glucuronidase, leucyl aminopeptidase

Hematoxylin and eosin

Three different methods were used in the evaluation of each slides stained with H&E. After inspection of the entire specimen under low magnification, the semiquantitative measurements were made using a 320X magnification which allowed the best cellular differentiation and interpretation of extracellular matrix. No normalization was necessary.

The slides stained with H&E were first examined for variations in the wound healing processes surrounding the implant. The slides made from the tissue recovered from the incision sites were used to determine the presence of infection.

The second method determined the fraction of the Dacron fibers with associated multinucleate giant cells (MNGCs). This was evaluated by counting the number of Dacron fibers within three 0.32 mm × 0.32 mm fields and the number of these fibers which had MNGCs associated with them. The fraction of fibers with associated MNGCs was the ratio of these values.

The third method determined the area fraction of the various components within the velour's porosity. Four components were arbitrarily considered. They included Dacron fibers, MNGCs, vascular tissues and the remaining "other" cells. The latter cells were distinct from either the vasculature or MNGCs. Care was taken in the choice of the observation areas in order to ensure that no obvious cutting or section processing artifacts were included.

The numerical value of each fraction was determined using the grid intersection method.[17] In this method, sections were evaluated using an eyepiece containing a grid of 11 equally spaced vertical and 11 equally spaced horizontal lines covering an area 0.32 mm × 0.32 mm on the microscope slide. The grid was superimposed over the porosity of the implant with one edge of the grid adjacent to the implant capsule. The intersections of the line were designated potential hits. There were a total of 121 potential hits per full grid. Since it was not always possible to lay a full grid within the porosity of the velour, fractional grids were used, as necessary, to create between 330 and 363 potential hits per microscope slide. A hit was defined as a component over which a potential hit was superimposed. The fraction of a particular component was the number of hits divided by the number of potential hits.

Gomori's trichrome

Slides stained with Gomori's trichrome were evaluated upon the basis of the structural organization of the collagen strands at a magnification of 320X. The rating scale was adapted from that of Feldman[3] as follows:

0 = densely assembled collagen bundles with directionally oriented long fibers (fascia);
1 = dense long strands without directional orientation (e.g., dermis);
2 = short well defined strands;
3 = fluffy cloudlike appearance;
4 = fluffy cloudlike appearance with large numbers of voids;

5 = no organization of visible structure;
6 = faint spider's web of collagen;
7 = no collagen present;

The ratings were normalized by subtracting them from 7, to reverse the scale, and dividing the result by 7.

Gomori's reticular stain

These slides were evaluated only within the porosity of the velour due to the interference of the collagen in the differentiation of reticulum in other collagen dense tissue areas. The evaluations were made using the scale below at a magnification of 200X and was based upon the amount and degree of organization of the reticulum.

0 = no reticulum;
1 = sparse faint network of reticulum;
2 = moderately dense network of reticulum;
3 = dense organized network of reticulum.

Data gained using this evaluation scheme were normalized by dividing the determined value by 3.

Alcian blue/periodic acid Schiff

Slides stained with AB/PAS were evaluated upon the basis of dominant color using a red to blue scale at a magnification of 200X. The evaluation scale ranged from 1 to 5 and was:

1 = pure red (neutral polysaccharides);
2 = red dominant;
3 = approximately equal levels of red and blue;
4 = blue dominant;
5 = pure blue (acid mucopolysaccharides).

These values were normalized to a scale of from 0.2 to 1.0 by dividing by the determined values by 5.

Beta-glucuronidase

Slides treated for the presence of β-glucuronidase (lysosomal activity) were evaluated on the basis of the approximate fraction (0.0, 0.2, 0.4, 0.6, 0.8, and 1.0) of the cells staining positively for the presence of the enzyme at a magnification of 200X. No differentiation was made based upon the intensity or definition of the stain boundaries.

Leucyl aminopeptidase

The slides stained for the presence of leucyl aminopeptidase were qualitatively evaluated based upon the overall level and location of the stain within the implant, since the stain was somewhat diffuse and adequate definition of stained cells was not possible.

Statistics

The statistical procedures and computations involved used the Statistical Analysis System (SAS Institute, Inc. Cary, North Carolina) computer system for data analysis. Two methods were used to evaluate the numerical data. The first of these consisted of comparing the results of the histological analyses for the different implantation durations. The second method involved determination of the relationships between the tissue at the various locations. The results are presented in terms of their means and standard deviations and compared using a *t*-test (significance level 0.05). It should be noted that the form of the *t*-test was altered if the variances were statistically different. However a significance level of 0.05 was maintained. Due to a paucity of data, the data were evaluated using small number statistics and may lack some of the strength of a larger data set.

RESULTS AND DISCUSSION

This section contains three major segments: a segment examining the samples taken after 10 days, a segment examining those taken after 28 days, and a segment comparing the 10- and 28-day data.

Ten-day implants

Examination of hematoxylin and eosin stained sections of the 10-day tissue samples revealed various stages of wound healing and documented the absence of infection, hematomas inflicted during implantation, seromas, neoplastic growth, or other pathological conditions interfering with normal wound healing. Results are compared graphically in Figures 1, 2, and 3.

The area fraction of the components within the porosity of the velour were: Dacron fibers 0.22 ± 0.04, multinucleate giant cells 0.19 ± 0.12, fraction of vascular material 0.01 ± 0.04, and fraction of remaining other cells 0.23 ± 0.10. The latter group primarily consisted of fibroblasts, fibrocytes, macrophages, and other cells of the chronic inflammatory type. The fraction of the Dacron fiber segments with closely associated multinucleate giant cells was also determined (0.52 ± 0.28).

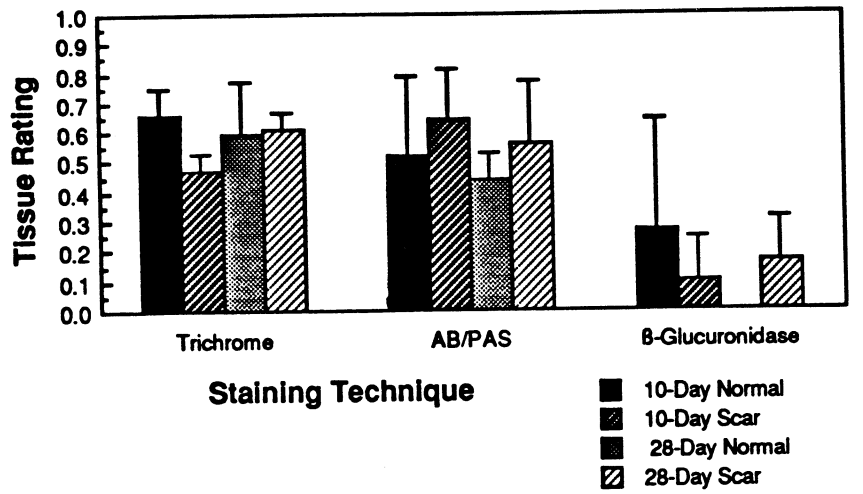

Figure 1. Comparison of normal and scar tissue.

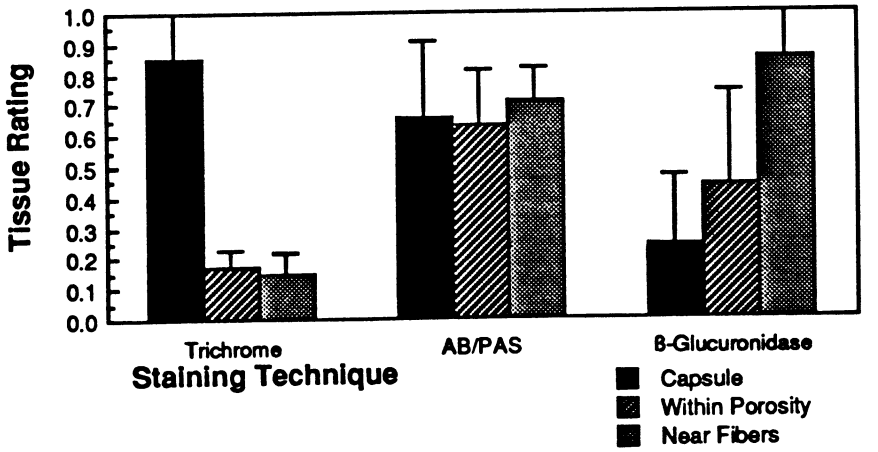

Figure 2. Rating near implants (10-day).

The collagen fiber distribution, as demonstrated by Gomori's trichrome, and found within the scar tissue (0.47 ± 0.06) was significantly less ordered than observed within the normal subcutaneous tissue (0.66 ± 0.09). While the collagen within the porosity (0.17 ± 0.06) was not significantly different from that adjacent to the individual Dacron fibers (0.15 ± 0.07), both of these locations showed significantly lower ratings than all other sample locations. Collagen in all of the sample locations was directionally oriented significantly less than that found in the capsule surrounding the implant (0.85 ± 0.03).

If the increases in the length and order of the collagen bundles connoted increases in collagen maturity, then these results indicate that the collagen found in the 10-day scar tissue was less mature than that within undamaged

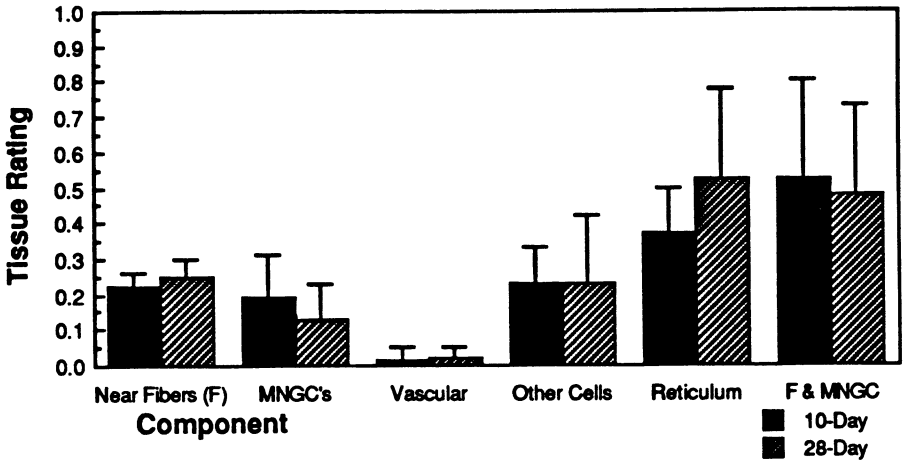

Figure 3. Ratings of components in porosity.

tissue, least mature inside the pores of the implant, and most mature in the capsule surrounding the implant.

The reticulum rating within the pores of the velour was 0.37 ± 0.13. Actually, the reticulum ratings for the implants retrieved from the animals were all 0.33 with one exception which was 0.67. This lack of variation may be indicative of either a truly uniform reticulum development within the implants or a rating scheme not significantly sensitive to detect the differences present.

The AB/PAS staining technique was used to examine the composition of the extracellular matrix. While the rating for normal tissue (0.52 ± 0.27) showed a tendency to be more red (PAS positive) than blue (alcian blue stained) in color and the tissue surrounding the Dacron fibers (0.71 ± 0.11) showed the opposite tendency, there were no significant differences between the values measured at the various locations including scar (0.64 ± 0.17), capsule (0.66 ± 0.25), and tissue within the porosity (0.63 ± 0.18).

Assuming the reliability of the staining method, the large variability and lack of significant differences with the AB/PAS preparations may be due to considerable variation in ground substance composition or perhaps indicates high ground substance turnover in both sulfated polysaccharides and glycoproteins as the wounds healed, coupled with variations in both the healing rates of the individual rabbits and the amount of trauma caused by the surgery.

An examination of the fraction of cells staining positive for the presence of β-glucuronidase revealed that scar tissue (0.10 ± 0.14) showed slightly, but not significantly, fewer cells containing β-glucuronidase than did normal tissue (0.27 ± 0.38) and that the level present in the capsule (0.24 ± 0.23) was virtually identical to that found in normal tissue. The level of β-glucoronidase was significantly higher within the porosity of the velour

(0.44 ± 0.30) than in scar tissue but the variation from the normal tissue was not meaningful. The highest levels of β-glucuronidase were found within one fiber diameter of a Dacron fiber (0.86 ± 0.24), where giant cells and macrophages are primarily located, and were found to be significantly higher than in any other location.

Evaluation of the sections stained for the presence of LAP was difficult primarily due to lack of uniform staining density and the extreme thermal sensitivity of the enzyme which limited recutting and restaining coupled with damage to the fragile tissue within the porosity of the velour.

The level of LAP staining (usually indicative of protein restructuring) in normal tissue was uniformly low to nonexistent. However, in scar tissue the LAP level was highly variable and almost uniformly higher than that found in the surgically undisturbed tissue. Staining for the presence of LAP around the implant showed two divergent results. Three of the five samples showed more accumulation in the capsule than in the porosity. The remaining sections showed higher levels in the porosity than in the capsule. This higher level of staining, whether in the capsule or in the porosity, was usually above that demonstrated in the scar tissue. If the degree of staining for LAP is interpreted as correlating with connective tissue restructuring, then at 10 days postsurgery, there was collagen generation within the scar tissue. Furthermore, one of two processes was occurring. Either there was collagen formation surrounding the implant but not inside it or the collagen was forming within the implant but not surrounding it.

Twenty-eight day implants

Tissue samples gathered from the five animals 28 days postimplantation were evaluated using the same locations, techniques, and stains as those taken after 10 days. Results are compared graphically in Figures 1, 3, and 4.

As with the 10-day rabbits, infection or other factors retarding healing were not evident. The area fraction of Dacron within the porosity of the velour was 0.25 ± 0.05. The fraction of giant cells was 0.13 ± 0.10. The fraction of other cells was 0.23 ± 0.19. The fraction of vascular material within the porosity of the velour was 0.02 ± 0.03. The fraction of the fibers with associated multinucleate giant cells was 0.48 ± 0.25.

The trichrome ratings were: surgically undisturbed tissue (0.59 ± 0.18), scar tissue (0.61 ± 0.06), implant capsule (0.84 ± 0.06), implant porosity (0.18 ± 0.07), and adjacent to the fibers within the porosity (0.14 ± 0.08). Examination of the means indicated that the scar tissue was not significantly different from the normal tissue and that the tissue within the velour's porosity was similar to that directly adjacent to the fibers. The capsules collagen was significantly more directionally arranged than in any other tissue. Both the normal tissue and the scar tissue were significantly more ordered than any tissue within the velour.

This implies that the scar tissue had returned to approximately the same histological state as the surrounding normal tissue. The collagen close to the

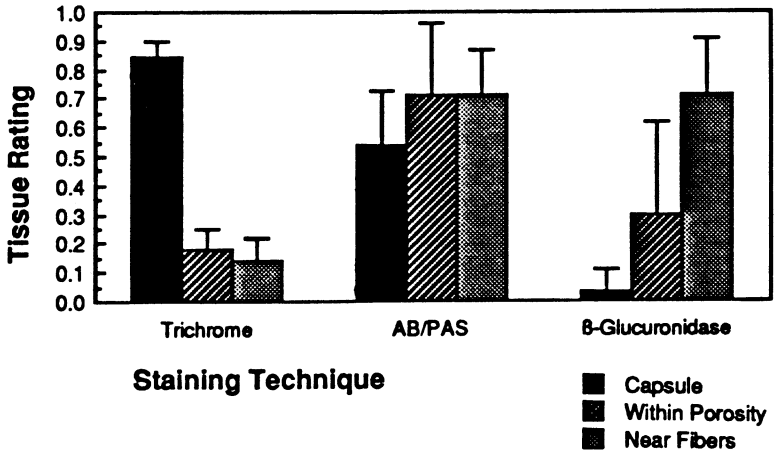

Figure 4. Ratings near implants (28-day).

implant, however, was quite different. Collagen organization within the porosity of the velour was less advanced and the implant capsule showed collagen of significantly greater directionality than the collagen of the normal fascia.

The reticulum rating within the porosity of the velour was 0.52 ± 0.26. The means of the AB/PAS ratings were: normal tissue 0.44 ± 0.09, scar tissue 0.56 ± 0.22, capsule surrounding the implant 0.54 ± 0.19, the tissue within the velour's porosity 0.71 ± 0.16. The variation between the normal tissue and the tissue adjacent to the fibers and that between the normal tissue and that within the porosity were the only comparisons which showed significant differences. This indicates that significant differences exist between the interior and the exterior of the implant.

The mean fraction of the cells staining positively for the presence of β-glucuronidase were: normal tissue 0.00 ± 0.00, scar tissue 0.16 ± 0.15, the implant capsule 0.03 ± 0.08, the tissue associated with the fibers of the velour 0.71 ± 0.20, and the tissue within the velour 0.30 ± 0.32. An examination of the means indicated that no significant differences existed between the levels of β-glucuronidase within the normal tissue, the scar tissue, and the capsule surrounding the implant. The levels found in the tissue surrounding the implant were shown to be significantly higher than in any other 28-day tissue, including the bulk of the tissue within the porosity of the velour. The tissue within the porosity was shown to differ significantly from both the normal tissue and the capsule surrounding the implant. No significant difference was demonstrated between the scar tissue and the tissue within the implant's porosity.

Demonstrating the presence of LAP in the 28-day samples involved the same difficulties as in the 10-day samples. The normal tissue samples from both implantation periods showed virtually no positive staining for the presence of LAP. The scar tissue showed slightly higher levels of activity. After 28 days the capsule surrounding the implant showed a moderate to

low level of activity. However, within the pores of the implant one of two states occurred. It was either high or low with no intermediate level.

Comparison of the implantation periods

This was primarily done by comparing the means and applying a *t*-test with a significance level of 0.05 to determine if significant changes occurred between the implantation periods. Other relationships between the data sets were also examined.

A comparison of the pores of the implants in the 10- and 28-day samples using H&E showed that the means of the fractions of giant cells, Dacron fibers, fibers with associated giant cells, vascular material, and other cells demonstrated no significant differences when compared using the *t*-test. This appears to indicate that the condition of healing reached at 10 days is not significantly changed over the following 18 days.

Similarly, the trichrome ratings for the normal tissue sampled after 10 days (mean = 0.66) was not significantly different from that of the tissue taken after 28 days (mean = 0.59). However, the scar tissue taken after 10 days (mean = 0.47) was dissimilar to that taken after 28 days (mean = 0.61). This supports the applicability of the technique, since normal tissue can be expected to be in steady state in both sets of samples but the tissue damaged 10 days prior to sampling should be in the midst of its healing period while after 28 days it should be near or at the end of its healing period. None of the trichrome ratings involving the implant's porosity or capsule showed any significant variations between the 10- and 28-day samples.

No significant differences in the reticular fiber content were demonstrated between the 10- and 28-day samples at any location that measurements were taken. This lack of variation is probably the result of wide variations between the animals.

While the means of the 10-day samples were higher than those of the 28-day samples in all cases except one, no significant differences in the amounts of β-glucuronidase were demonstrated between the two sets of data. The exception to this was the levels found within the scar tissue where the 28-day samples had a slightly, but not significantly, higher level of β-glucuronidase than the 10-day samples.

The level of aminopeptidase within the surgically undisturbed tissue appears to be unaffected by the time period. However, the level of LAP in 10-day scar tissue was appreciably higher than that found within the 28-day scar tissue. This may imply that after 10 days there is still a high level of enzymatic activity possibly related to collagen turnover. After 28 days the capsule enzymatic activity has returned to that of normal tissue. The LAP level in the capsule showed a similar trend, except that some of the capsules had already low levels after 10 days.

CONCLUSIONS

After 10 days healing, the tissue external and internal to the velour implant appeared significantly different. Even after 28 days healing time, the tissue within the pores of the Dacron velour exhibited substantial differences in the composition of the cells and extracellular matrix compared to normal healing. These differences indicated that two completely different healing processes were being observed.

Normal wound healing

The wound healing process in the subcutaneous tissue of the rabbit was evaluated by comparing 10- and 28-day old scar tissue with normal, surgically undisturbed, tissue. This examination revealed that the tissue had healed to a great extent after only 10 days, and that the extracellular matrix had returned to its normal state with respect to the acid mucopolysaccharides. The only difference from normal tissue was that the collagen had not reached full maturity as shown both by active collagen synthesis and a lack of mature organization and structure. After 28 days the tissue had completed its maturation process and was virtually indistinguishable from normal connective tissue (Fig. 1). These results compare well with the processes described by Hunt and Dunphy.[18]

Healing inside an implant

After 10 days a normal host response was evident with the formation of a connective tissue capsule surrounding the implant. This capsule was virtually identical in composition to the normal connective tissue with the exception that the collagen was substantially more organized and had longer fibers (Fig. 2). However, the tissue within the velour was comparatively sparse and of a chronic inflammatory type with a large fraction of multinucleate giant cells and very little collagen or reticulum evident. While the composition of the extracellular matrix appeared to be similar to the tissue outside of the velour, the presence of large quantities of β-glucuronidase may indicate the presence of activated macrophages (Fig. 3).[19]

To our surprise, the condition of the elements of the extracellular matrix at 28 days did not differ significantly from that found after 10 days (Figs. 2, 3, and 4), indicating that, on a light microscopic level, within the interstices of the velour a balanced condition may have been achieved after 10 days and that no significant changes had occurred 18 days later.

The question then arises whether the fibroblasts alter the composition of the acid mucopolysaccharides, collagen, and reticulum in response to the presence of the polymeric implant material or the spatial conditions in the

pores or the macrophages and giant cells, or whether the macrophages and giant cells alter these tissue components after normal production by the fibroblasts. Since no significant changes in the collagen occurred after 10 days, collagen turnover without increased maturation was implied.

Conditions for ingrowth

If one assumes that the wound healing rates in the scar tissue are typical of connective tissue growth rates, then connective tissue formation within the velour should have begun after 10 days and certainly been visible after 28 days. While significant differences have been demonstrated between normal wound healing and ingrowth into the velour, examples exist at both 10 and 28 days to indicate that tissue formation is indeed possible. However, examples of implants from the same animals also exist where almost no ingrowth occurred even after 28 days. These variations may allow the determination of the optimal conditions for both cellular components and reticular fibers but their cause remains unclear. In spite of the fact that the surgical techniques were kept constant for all of the animals and the implants were manufactured from the same lot of Dacron velour and cleaned and sterilized according to the same procedure, significant differences were found between the implants within the same animal. One important factor may be variations in tissue oxygen tension and cellular lactate and lactate dehydrogenase levels, shown to have considerable influence by Hunt et. al.[20] Known variables include biological variations between individuals, implantation techniques, and variations in the implant material.

The second consideration may be the differences that exist between the surface porosity of the plush side of the velour, where the fibers are horizontal and, therefore, have a large cross-sectional area, and its interior, where they are vertical and have a much smaller cross-sectional area. Blood vessels may simply not be able to grow past this barrier, especially if the implant is bent. If this was true, then it would imply that the cellularity within the implant would decrease as the distances from the vascularity of the capsule increased. This decreasing cellularity was, in fact, observed in many specimens. However, the analytical techniques used in this research did not examine this phenomenon.

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Accepted July 29, 1987