The Effect of Whole-Body Radiation and Infection on Arterial Replacement *

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PRINCIPLES of vascular surgery were established at the turn of the century by Gluck, Carrel, and others.[2-4, 7, 14] Little progress was achieved in this field during the next 40 years, and until the middle of the Korean war, ligation, with the frequent sequellae of gangrene and amputation, remains the textbook treatment for acute, major, arterial injuries.

The nature of the medical support in the Korean War was such that military surgeons were presented with the problem of repair of considerable numbers of vascular injuries. By adoption of the proven but little-used technics of suture anastomosis, transverse repair and vein grafting, morbidity associated with vascular injuries was greatly reduced.[9-11]

Considering the recent rapid expansion of the field of vascular surgery and the possibility of large numbers of arterial injuries associated with mass casualties among civilians as well as soldiers in modern warfare, an experimental evaluation of the treatment of acute arterial injuries was designed to investigate the following problems:

1. The fate, and long-term results of vein grafts used for replacement of peripheral arterial segments.
2. The effect of infection on the implantation of vein grafts, homografts and plastic arterial prostheses.
3. The fate of arterial grafting for traumatic arterial injury with associated total body ionizing radiation.

Methods

In 34 adult mongrel dogs a 2.0- to 4.0-cm. segment of the proximal right superficial femoral artery was resected under sterile conditions and replaced with a 2.5- to 5.0-cm. segment of autogenous vein graft from the left superficial femoral vein.

In 50 dogs, 92 stretch dacron-teflon arterial prostheses † were inserted in defects of similar length in the aorta and the femoral, carotid, and iliac arteries, two to four prostheses being inserted in dogs receiving peripheral-artery grafting.

End-to-end anastomosis with an over-and-over 4-0 or 5-0 Dacron or silk suture was made in each instance. The grafts usually were iso-dimensional or slightly larger than the resected artery. The diameter of the artery at the site of resection was measured at the time of operation, and also by presacrifice arteriogram. Blood loss and occlusion time were noted. Heparin was not

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† Warp of Helanca dacron, 70-denier, 2-ply yarn, 62 threads/inch. Woof of untreated teflon, 400-denier, 1-ply yarn, 52 threads/inch.

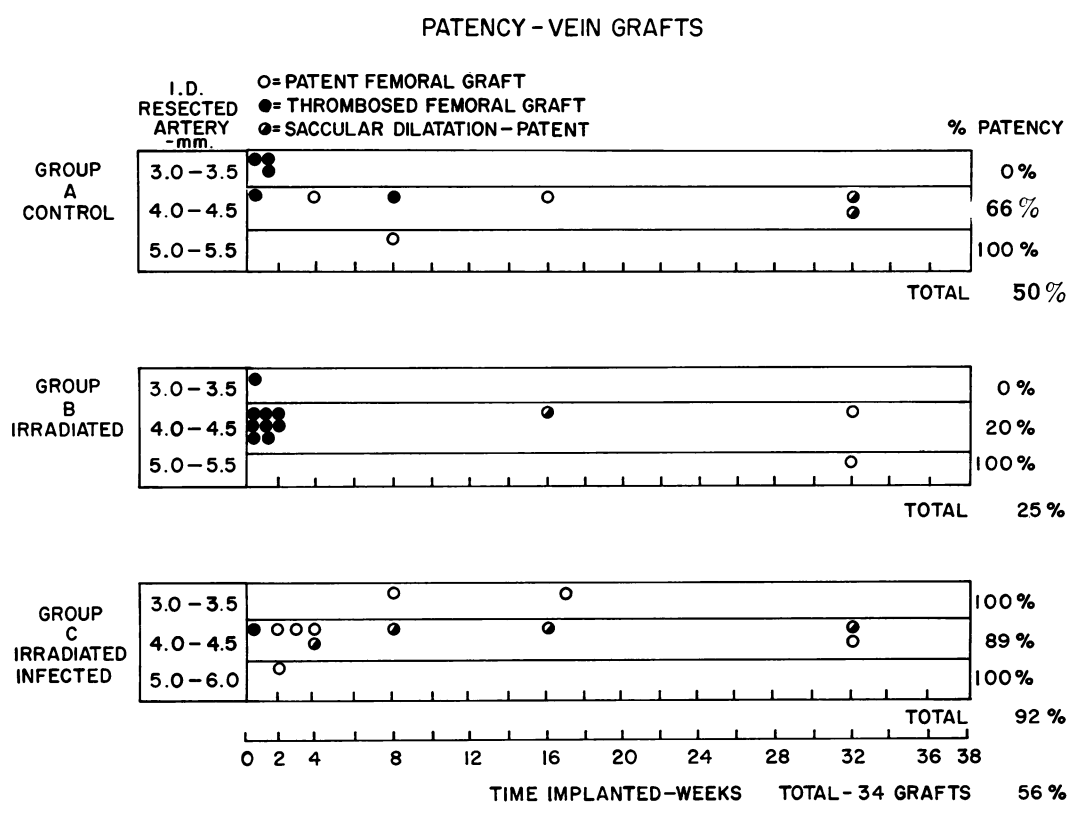

FIGURE 1.

used. The animals were divided into three groups.

Group A—Control. In 10 dogs, 10 autogenous vein grafts were inserted in femoral arterial defects and in 16 dogs, 24 plastic arterial prostheses were utilized, as outlined above.

Group B—Whole Body Ionizing Radiation. Autogenous vein grafts were inserted in the superficial femoral artery of 12 dogs and in 23 dogs, 42 plastic prostheses were used to replace a segment of major artery. Four to 28 hours prior to operation, animals in this group received 300 r. total body radiation (an estimated $LD_{10/30}$) [15] from a high intensity cobalt source. Other investigators have established sublethal radiation received up to 36 hours before injury as essentially a simultaneous challenge.[13]

Group C—Whole Body Ionizing Radiation Plus Induced Infection. Twelve autogenous vein grafts and 26 plastic prostheses were utilized in 23 dogs in this group. In addition to total body radiation as in Group B, the dogs received an injection into the periarterial tissues, at the time of operation, of 3 ml. of a mixed bacterial culture containing *Staphlococcus aureus, Streptococcus faecalis, Escherichia coli* and *Clostridium perfringens* in concentration of 10^8 bacteria per ml.

All animals in the three groups received 600,000 units procaine penicillin and 0.5 Gm. streptomycin I.M., b.i.d. for five days postoperatively. White blood cell counts were made at weekly intervals on all animals in the radiation groups to ascertain the intensity of the radiation response. That the radiation was effective was shown by a

drop in the white blood cell counts in the irradiated animals from the average control value of 15,000 to 18,000 to 3,000 to 4,000 after one to two weeks.

The dogs were sacrificed at one, two, four, eight, 16 or 32 weeks, respectively, after operation. Animals with manifest indications of graft occlusion were sacrificed when occlusion was observed. Occlusion of the aortic and femoral grafts was readily ascertained by femoral artery palpation. It was difficult to ascertain patency of the carotid grafts by palpation. An arteriogram was taken prior to sacrifice, at which time the patency of the graft was determined.

At necropsy the adjacent artery was resected in continuity with the arterial grafts for gross and microscopic examination. Tissues were fixed in 10 per cent buffered formalin for microscopic examination. Slides were prepared using routine histologic methods and stained with Harris' hematoxylin and alcoholic eosin, Weigert elastic tissue, and Rinehart modification of the Hale colloidal iron methods.

Results

1. **Graft Patency.** Only two grafts became occluded after two weeks of implantation (Fig. 1, 2). The majority of grafts found occluded were discovered at the time of the first postoperative examination for graft patency. These early graft occlusions (first to tenth day postoperative) were included in calculating results, it being believed that this would result in a more correct interpretation of the success of the grafts. Gross examination of the adjacent arteries revealed eight partial to complete thrombi at sites of arterial clamping.

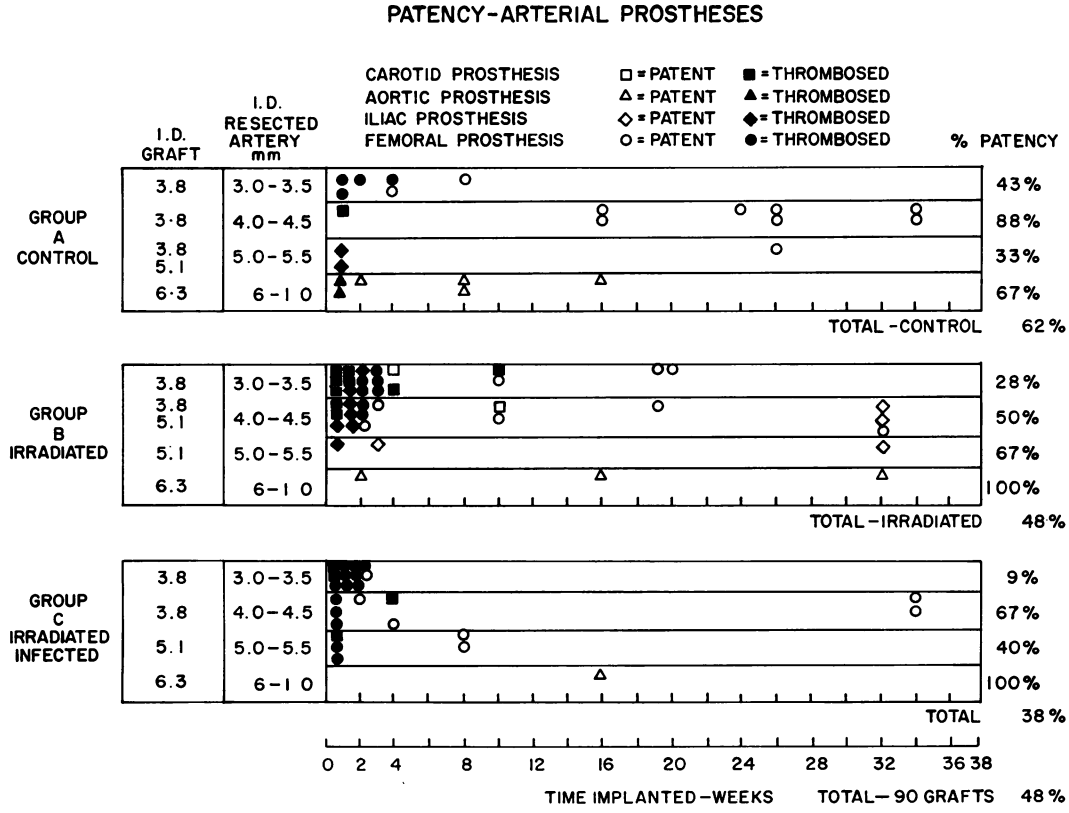

FIGURE 2.

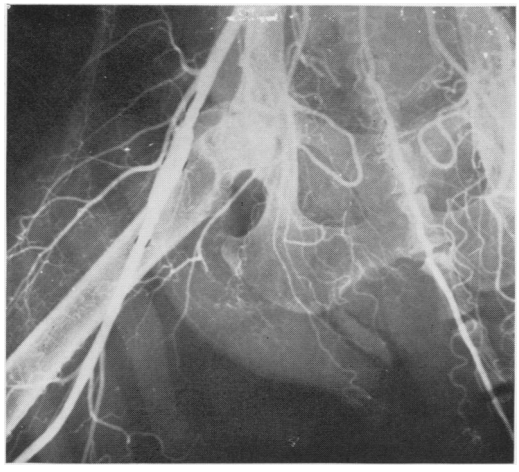

FIG. 3A. Femoral arteriogram of vein graft after 16-week implantation. Resected graft is shown in Fig. 3B.

Five additional arteries showed microscopic arterial damage due to clamping.* In two animals, the "clamp" thrombus was the direct cause of failure of the prostheses.

The percentage of arterial grafts that were patent was proportionate to the size of the graft or resected artery. Irradiation alone and irradiation with contamination under these experimental conditions has no significant effect on the patency of the grafts of greater than 3.5 mm. internal diameter. However, thickening of the intimal reaction in contaminated wounds may cause significant reduction of the lumen to cause thrombosis in the smaller grafts.

* Pott's coarctation clamps.

2. Graft Pathology. Gross examination revealed no marked difference in the grafts of Group A, B, or C. Microscopic examination at the line of anastomosis of artery wall adjacent both vein graft and plastic prosthesis showed subintimal fibrous proliferation of minimal to severe degree in all cases. This subintimal proliferation greatly compromised the lumen of the artery in some of the experiments, reducing the diameter by more than one-half.

Vein grafts generally showed ingrowth of fibrous tissue throughout the wall of the graft, with resultant fragmentation and disorganization of collagenous and elastic tissue fibers. In some cases, the collagenous fibers had lost their staining characteristics and fibrous detail. Saccular dilatation in the vein wall secondary to the above change was noted in seven of the 20 patent vein grafts (35%) (Fig. 3A, 3B, 3C). Within the original vein wall of all patent vein grafts was a sleeve of new connective tissue which contained abundant ground substance and a few pink collagen fibers. This connective tissue sleeve had an average thickness equal to or greater than that of the vein wall (Fig. 4A, 4B). The inner

FIG. 3B. Femoral vein graft after 16-week implantation. Although the arteriogram shows a functioning normal-appearing vein graft at time of sacrifice, the graft when removed was found to have undergone saccular dilatation with beginning thrombus formation.

sleeve was increased in thickness in the majority of the contaminated vein grafts (Group C). Aside from the increased thickness of the connective-tissue sleeve in the infected grafts, the pathological changes were the same for all three groups of vein grafts.

A slight to moderate cellular reaction to the dacron-teflon prosthetic material was noted with fibroblasts, macrophages, lymphocytes, plasma cells, foreign body giant cells and an occasional polymorphonuclear leukocyte, but this cellular reaction was qualitatively and quantitatively slightly less than the reaction to silk suture material. In infected grafts the total cellular reaction was greater and qualitatively characterized by an increase in polymorphonuclear leukocytes. An occasional pocket of bacteria was found adjacent the prostheses in some of the infected cases. The grafts, when patent, were surrounded by a narrow rim of loose, well-vascularized, connective tissue and were lined with a sheath of connective tissue. The inner luminal surface of this sheath was smooth and well endothelialized, this endothelialization being complete in all grafts after 24 weeks of implantation and in most grafts after eight weeks. The average thickness of the endothelialized sheath was approximately 340μ with a range of 50μ to 1,000μ, the thicker lining being located in post stenotic areas of the graft.

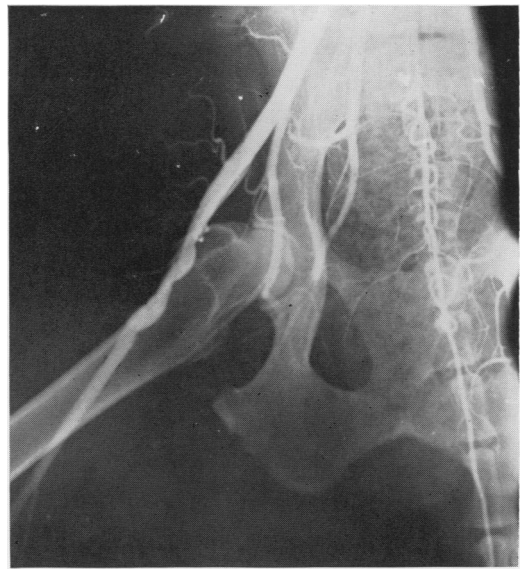

FIG. 3C. Femoral arteriogram showing dilated, irregular-walled, vein graft after 32-week implantation. Saccular dilatation was noted in the gross specimen.

The general tissue reaction to the prosthesis was increased in the infected Group C and the inner sheath was thicker in these grafts (500μ to 1000μ) (Fig. 5).

The majority of the thrombosed prostheses were found to have a wrinkle type thrombosis. Irradiation did not alter the process of lining a newly inserted woven plastic prosthesis with fibrin, and eventual replacement of the fibrin by connective tissue pseudointima (Fig. 6).

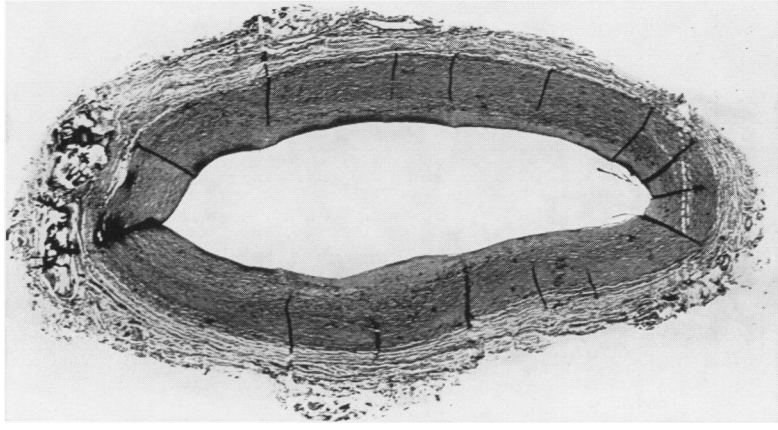

FIG. 4A. Vein graft removed from attachment to femoral artery at 17 weeks. The inner fibrous sheath is clearly visible. Remnant of original vein is shown in higher magnification in Fig. 4B. (Rinehart, × 4.25).

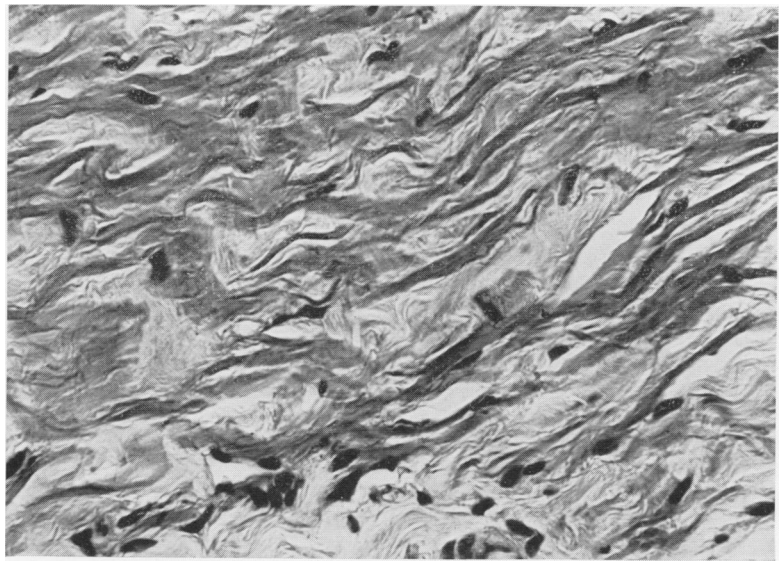

FIG. 4B. Outer media and adventitia of vein graft. Smooth muscle elements are separated and segmented by ingrowing fibrous tissue. (H & E, × 198)

Six dogs died of the effects of irradiation, but even in these cases of severe pancytopenia, the graft healing at time of death was not altered significantly.

3. Local Response to Contamination (Group C). Induration with rubor and calor was noted in all contaminated wounds. Several dogs developed cyanosis and edema of the entire extremity. Three dogs developed superficial wound dehiscence requiring secondary closure. Transient drainage was noted in five dogs but this responded to the antibiotic therapy. At sacrifice, three superficial stitch abscesses were observed

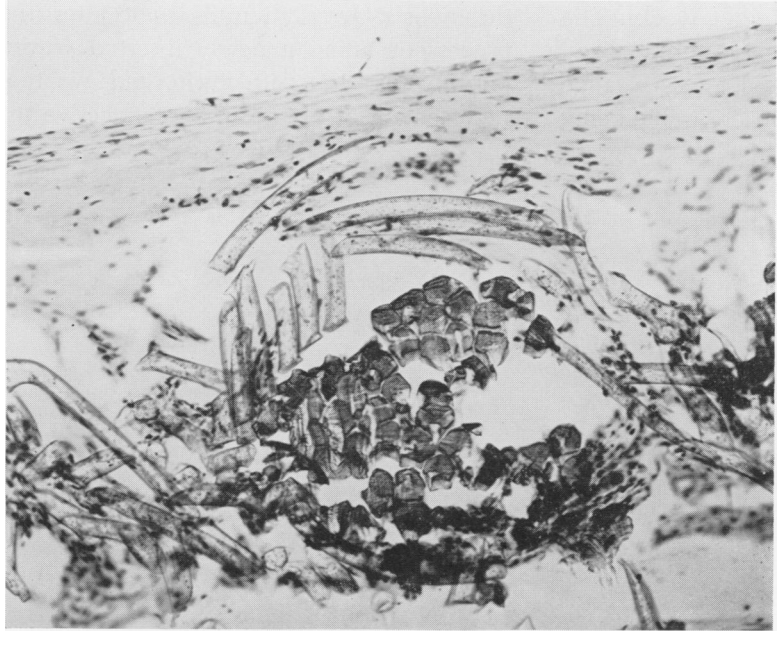

FIG. 5. Dacron-teflon arterial prosthesis removed from femoral artery at 10 weeks. Lumen at top of photograph. Dog received 300 r. total body radiation ($LD_{10/30}$) at time of insertion of prosthesis. Intimization is apparent with cellular ingrowth and orientation in parallel rows. (Rinehart, × 87.5)

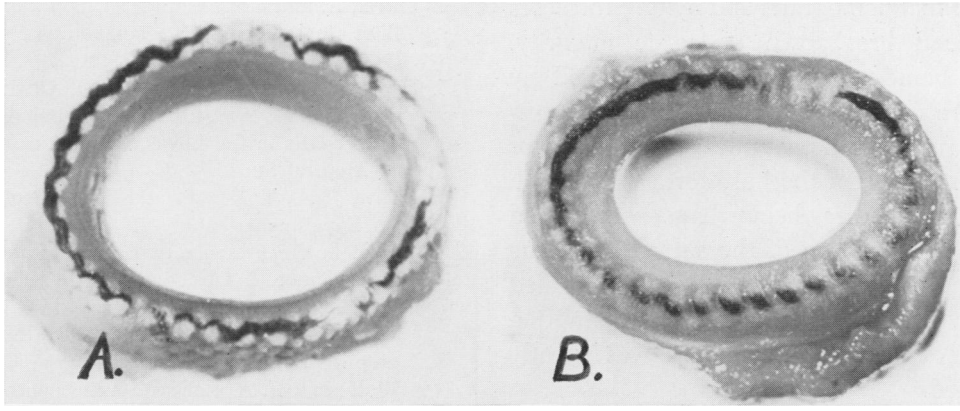

FIG. 6. A. Cross-section of dacron-teflon femoral-artery prosthesis (3.8 mm. I.D.) from irradiated dog showing ingrowth and intimal lining. B. Cross-section of dacron-teflon femoral-artery prosthesis from dog receiving irradiation and infection in the graft area at time of insertion of the prosthesis. The intimal lining is thickened in comparison with that of dog receiving irradiation only.

in infected dogs. There was no rupture of a graft nor breakdown of an anastomosis as a result of infection.

Discussion

Contrary to reports by several other investigators,[12, 16] our findings revealed that vein grafts did not remain viable. There was failure to retain original architecture in the autogenous vein grafts with degeneration and replacement by an ingrowth of fibrous tissue. This resulted in the reduction in the already marginal capacity of the venous autograft to carry arterial pressures. Dilatation is prone to follow with the possible sequelae of rupture or thrombosis. Dilatation of peripheral vein grafts has been reported in the clinical literature in one of the few follow up articles available.[5] The dilatation may become increasingly significant as the duration of implantation increases.

Sublethal whole body ionizing radiation produced no significant effect on the ultimate outcome of either vein grafts or plastic arterial prostheses in the dogs studied. Although there was a reduction in circulating blood cellular elements in radiated dogs, the process of fibrin deposition lining the arterial prosthesis with eventual replacement by ingrowth of fibrous tissue was not altered. It is surmised that ionizing radiation received at the time of wounding will not significantly affect the healing of arterial injuries, a conclusion which is in keeping with the effects of sublethal radiation at the time of wounding on wound healing in other systems.[1, 13]

Under the experimental conditions of this study, bacterial inoculation of the wound at the time of operation did not significantly affect the fate of vein grafts or of arterial prostheses. It is realized that technics which would result in failure in human cases can often be used with success in the dog and that inference concerning the effect of bacterial contamination on arterial grafting in humans should not be made on the basis of this study.

Humphries recently reported 11 clinical cases of rupture of homografts owing to infection and suggests that "When a homograft becomes infected, the only safe course to follow is to remove the entire graft." [8] This corroborates the experimental work of Foster, Berzins and Scott in which, in the presence of frank peritonitis and/or retroperitoneal infection, a large percentage of

abdominal homografts and nylon prostheses sustained breakdown of aortic integrity. With homografts breakdown occurred by rupture of the graft, disruption of the sutures from the homograft, or disruption of the sutures from the host aorta, while with nylon prostheses, hemorrhage was caused only by disruption of the sutures from the host aorta. Where infection was controlled with vigorous antibiotic therapy, disruption of the grafts or suture lines was greatly reduced.[6]

Summary

The use of autogenous vein grafts and plastic arterial prostheses is not contraindicated in wounding with concomitant sublethal radiation under the conditions of this study. Their use in contaminated wounds may be acceptable if thorough debridement and active treatment of infection is done.

The long-term fate of vein grafts is such that they are not the arterial replacement of choice but are to be used when suitable plastic prosthetic material is not available.

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