sealed, although it seemed to be so on casual inspection. This difficulty was eliminated by painting the skin around the wound with the methacrylate polymer before the saline or test solution was applied. Following this procedure none of the wounds became infected. There was no evidence of irritation or inflammation following the application of the chromatin fraction.

For the first two series the following results were observed on the fifth postoperative day:

Granulation Tissue on the Fifth Post-Operative Day.

	Control	Experimental
Granulation Absent	12	3*
Present	3 (<1/10 wound area)	13 (1/4 to 2/3 wound area)

*Wounds badly infected.

Of 15 controls only 3 showed any granulation on the fifth day. It appeared as a band 1 mm or less in width, about the periphery of the wound. On the other hand, only 3 of the 16 chromatin-treated wounds failed to show granulation tissue covering at least 1/4 of the wound, and these 3 were badly infected.

In the third series in which none of the wounds became infected, no granulation appeared in the 4 control wounds until the fifth day. Of the 5 experimental animals, small islands af granulation appeared in 2 of them as early as the second day, in another on the third day, and by the fourth day all had granulation tissue over 1/4 to 2/3 of the wound area. The granulation tissue in the experimental animals was bright red as compared with the pale red or pink of the controls and in microscopic section was clearly more vascular. Although the granulation tissue appears earlier in the treated wounds, the amount of such tissue formed is no greater than in the controls. After epithelialization was complete, the elevation of the treated wounds above the surrounding skin was no greater than in the controls.

Circumstances made it impossible to continue these experiments. However, the results obtained seem sufficiently promising to warrant further study.

We are indebted to Dr. E. L. Howes for testing the effect of whole chromatin on rabbit wounds and tissue cultures. In a personal communication he has reported that following intravenous administration of the chromatin, there was an optimum rate of healing of wounds of the rabbit's ear. This substance also increased the rate of growth of fibroblasts in tissue culture.

Summary. Following the application of a chromatin fraction to skin wounds of the rat, granulation tissue appeared one to three days earlier than in the controls. On the fifth postoperative day, several times as much of the surface of treated wounds was covered with granulation tissue as in the controls. There was no evidence of inflammation or irritation, and an excess of granulation tissue was not found.

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Healing of Experimental Skin Wounds.

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In the methods for the study of wound healing which have previously been described, there are inadequacies and sources of error which limit the usefulness of the procedures used. Carrel[1,2] used the rate of closure of square skin defects as an index of healing,

* The work described in this paper was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the University of California.

1 Carrel, A., *J. Exp. Med.*, 1913, **17**, 14.

2 Carrel, A., and Hartman, A., *J. Exp. Med.*, 1916, **24**, 429.

and by mathematical analysis, du Noüy[3,4] extended the method to apply to wounds of irregular shape. However there was no experimental segregation of two processes involved in wound closure, *i.e.*, contraction and proliferation. As a consequence, on the basis of du Noüy's equation for normal healing, a small wound would be expected to heal instantaneously which of course is not in accord with observation. Howes, Sooy, and Harvey[5,6,7,8] determined rate of healing by measuring the tensile strength of linear wounds. Although they mention the desirability of an experimental separation of the "contraction and epidermization processes," their method yields little or no information on changes occurring in the first 5 days of healing. More recently, Howes[9] used the rate of extension of a small island of epithelium in a large, square skin defect as an index of healing rate. This method assumed that contraction would not affect the rate of epithelial extension but did not provide a means for controlling or analyzing such contraction. In studying the effect of various substances on wounds, it was necessary in all of these methods to incorporate the agent in an ointment which introduced further complications. Since gauze bandage dressings were used, it was difficult or impossible to keep the wound aseptic, especially when repeated inspection and measurement were necessary. In an effort to avoid these difficulties the following technic was devised.

A stainless steel tube was ground at one end to make a circular cutting edge 6.6 mm in diameter.† With it a depression was made in the skin of the back of the neck of the anesthetized rat, and along this line the skin was cut with a pair of iridectomy scissors through the dense connective tissue of the dermis, but not through the loose connective tissue of the hypodermis. The skin thus circumscribed was then lifted off without any dissection. With care and practice the thickness of the connective tissue left in place was surprisingly uniform. There was usually no bleeding and when it did occur it was easily controlled with small swabs so that the wound contained no blood clots. A thick solution of methacrylate polymer‡ dissolved in toluene was then dropped onto the wound from a small brush and the adjacent skin painted with the same solution to make a coat completely covering the wound and extending 3 to 5 mm beyond it. In 15 minutes the coat had dried sufficiently so that the animal could be returned to its cage. No contraction occurred on drying as was the case with collodion or some other plastics. To keep the animal from pulling the coat off, its hind paws were covered with adhesive tape.

The coat formed did not adhere to the wound tissue but did cling to the surrounding normal skin so that a completely protective covering was provided which at the same time eliminated tissue damage due to adhesion and friction. If, before the plastic was applied the surface of the wound was allowed to dry, adhesion did occur, and if there was moisture on the adjacent normal skin, the plastic did not adhere. There was no vascular reaction

3 du Noüy, P. L., *J. Exp. Med.*, 1916, **24**, 451.

4 du Noüy, P. L., *J. Exp. Med.*, 1919, **29**, 329.

5 Howes, E. L., Sooy, J. W., and Harvey, S. C., *J. A. M. A.*, 1929, **92**, 42.

6 Howes, E. L., and Harvey, S. C., *New England J. Med.*, 1929, **200**, 1285.

7 Howes, E. L., and Harvey, S. C., *Yale J. Biol. and Med.*, 1930, **2**, 285.

8 Harvey, S. C., and Howes, E. L., *Ann. Surg.*, 1930, **91**, 641.

9 Howes, E. L., *Surg., Gyn., and Obst.*, 1943, **76**, 738.

† A more complicated instrument was constructed in which the cutting tool protected by a guard of lucite could be rotated by means of a flexible shaft connected to a motor. The depth of the cut could be regulated by adjusting a vernier scale on the hand piece of the tool. It was not used in these experiments since it offered no advantages over the simple tube in the excision of the cervical skin of the rat. It is mentioned, however, since it did prove to be more useful in the excision of portions of skin from the abdomen or back which is much more firmly attached to the hypodermis.

‡ When isobutyl methacrylate polymer was used, it was found necessary to apply a second coat on the day following the operation to prevent its cracking. This was not necessary when a mixture of equal parts of the isobutyl polymer and interpolymer of normal and isobutyl methacrylate was used. We are indebted to the E. I. du Pont de Nemours Company for supplying us with these materials.

and no visible exudate. By the fourth or fifth day following the operation some of the plastic coats began to come loose along the edges. These edges were then repainted with the same solution of the plastic and allowed to dry before the animal was returned to the cage. In this way, with relatively little attention, the wounds were kept sealed and protected until they were completely epithelialized. The changes which took place could be observed and measurements made without disturbing them in any way.

The plastic acted as a splint which prevented contraction of the wound. The marked contraction which occurs in unsplinted wounds[1,2,6] was not observed under these conditions. That contraction can occur after the wound is completely filled with granulation tissue may be demonstrated by removing the plastic coat at that time (8th day post-op.). On the following day, the diameter of the wound is reduced and a papilla of granulation tissue 2 to 4 mm high appears in the center of it.

A further advantage of the method is that the effect of aqueous solutions may be determined without having to incorporate the solution into an ointment which would complicate interpretation of the results observed. An example is given in the preceding paper on the effects of a derivative of chromatin.

The use of the plastic dressing made it possible to study the uptake of radioactive phosphorus (P^{32}) and radioactive sulfur (S^{35}) by the wound during the healing process. The data obtained in these experiments will not be presented here but are mentioned as an additional example of the usefulness of the plastic dressing.

Although the plastic solution produces no reaction in skin wounds of the rat and rabbit, it was found unsuited to the study of human skin wounds since it stimulated the formation of copious amounts of serosanguinous exudate. It may have some practical use, however, since it has been found that when applied to cuts, bruises, and small burns of the hand on the second or third day there is no exudation. Since the plastic does not contract, as does collodion for example, an entire finger may be coated. It has been found to adhere and protect the wound for 3 to 4 days under conditions (K.P. duty) where a bandage dressing was of little value. By the proper combination of normal and isobutyl polymers almost any degree of flexibility may be obtained.

Summary. The use of methacrylate polymers as a wound dressing in rodents is described and its advantage in the experimental study of wound healing indicated.

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Origin of Cardiac Disorders in Thiamine-Deficient Cats.

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Some of the cardiac disorders reported in thiamine deficiency may be neurogenic rather than myogenic in origin.[1,2] The following observations suggest a dual origin of the electrocardiographic signs in the thiamine-deficient cat.

Method. The method used for producing specific thiamine deficiency in cats has been reported previously in connection with a study of the neurological findings.[3] During the development of the deficiency and during the recovery period, limb lead electrocardiograms were taken in 37 unanesthetized animals. The electrocardiograms were recorded with an ink-

[1] McEachern, D., and Brophy, D., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 75.

[2] Weiss, S., and Wilkins, R. W., *Ann. Int. Med.*, 1937, **11**, 104.

[3] Everett, G. M., *Am. J. Physiol.*, 1944, **141**, 439.