

# INFLUENCE OF VITAMIN B COMPLEX DEFICIENCY AND PARTIAL STARVATION ON WOUND HEALING

EXPERIMENTAL RESEARCH WITH RATS

JANET C. HOLDEN, M.D.

AND

GEORGE CRILE JR., M.D.

CLEVELAND

The literature on the effect of the vitamin B complex on wound healing is confined to observations on surface healing and is summarized by Arey<sup>1</sup> in his article on wound healing. Saitta<sup>2</sup> found that a deficiency in the vitamin B complex resulted in diminished power of cicatrization in wounds of the skin, the subcutaneous tissue and the muscles. Oral administration of extract of cereals prevented these changes, and direct treatment of the wounds with the vitamin B complex produced normal activation of the cellular repair. Lauber<sup>3</sup> emphasized the unreliability of results obtained with the vitamin B complex and attributed this to a lack of standardization of the exact amounts of the vitamin in vitamin B-rich diets. He found no difference in wound healing between control animals and animals fed with yeast. Larcher<sup>4</sup> found that wounds in pigeons suffering from a deficiency of the vitamin B complex healed with equal rapidity or faster than similar wounds in a control series. Padula<sup>5</sup> found that the local application of vitamin B complex to a wound slowed the rate of healing in normal animals but increased it in animals maintained on a diet low in vitamins. Healing was found to be still faster when the deficient animals were subsequently given a normal diet to which vitamins were added. Howes, Briggs and Harvey<sup>6</sup> found that in partially starved adult rats the curve of fibroplasia was not markedly changed from normal.

- 
1. Arey, L. B.: *Physiol. Rev.* **16**:327-406 (July) 1936.
  2. Saitta, S.: *Scritti biol.* **5**:273-283, 1930.
  3. Lauber, H. J.: *Beitr. z. klin. Chir.* **158**:293-302, 1934.
  4. Larcher, A.: *Arch. di fisiol.* **25**:348-360 (July-Sept.) 1927.
  5. Padula, A.: *Arch. ital. di chir.* **42**:627, 1936; abstracted, *Internat. Abstr. Surg.* **63**:288, 1936; in *Surg., Gynec. & Obst.*, September 1936.
  6. Howes, E. L.; Briggs, H.; Shea, R., and Harvey, S. C.: *Effect of Complete and Partial Starvation on Rate of Fibroplasia in Healing Wound*, *Arch. Surg.* **27**:846 (Nov.) 1933.

EXPERIMENTS TO DETERMINE EFFECT OF A DEFICIENCY OF THE  
VITAMIN B COMPLEX ON WOUND HEALING

A series of experiments were carried out on the albino male rat to determine the effect of vitamin B complex deficiency on wound healing.

Two groups of rats were observed; there were 14 rats in each group.

Group 1—Normal adult controls

Group 2—Rats maintained on a diet deficient in the vitamin B complex

Group 1 was given the following normal diet:

Casein .....	400 Gm.
Osborne-Mendel salt mixture.....	80 Gm.
Corn starch.....	1,320 Gm.
Cottonseed oil.....	160 Gm.
Cod liver oil.....	40 Gm.
Yeast .....	200 Gm.

Group 2 was given the following diet deficient in vitamin B complex:

Purified casein (heated in an oven at 212 F. for forty-eight hours).....	400 Gm.
Osborne-Mendel salt mixture.....	80 Gm.
Corn starch.....	1,320 Gm.
Cottonseed oil.....	160 Gm.
Cod liver oil.....	40 Gm.

Wound healing in the rats was tested by the method of Harvey.<sup>7</sup> An experimental wound 2 cm. long was placed in the midline of the wall of the abdomen and was closed with a through and through running suture of black silk. The operation was performed with aseptic technic. The suture was removed one week after operation. The tensile strength of the wound was tested on the eighth and the tenth postoperative day by inflating the abdomen with air injected into the peritoneal cavity through a lumbar puncture needle. The breaking point of the incision was measured on a mercury sphygmomanometer. The appearance of the wound and the presence or absence of peritonitis were noted. The manometer measured only to 300 mm. of mercury, and figures above this level are recorded as 300.

In each group 6 animals were killed on the eighth postoperative day (subdivision A), and 6 animals were killed on the tenth postoperative day (subdivision B).

The seventh animal in each division was used for histologic studies. Each group of rats was kept on its respective diet an equivalent length of time. The rats were weighed once a week. When the vitamin-deficient rats had lost about 30 per cent of their original weight, they were subjected to operation.

The average tensile strength of the wounds was lower in the vitamin B-deficient rats tested on the eighth postoperative day than in the controls, but by the tenth postoperative day the average tensile strength of the wounds of the vitamin B-deficient group was actually a little higher than that of the control group. In this experiment, however, the average tensile strength is perhaps not so significant a figure as the number of rats whose wounds withstood a pressure of 300 mm. of mercury. Since the manometer registered nothing higher than 300, a single low figure, such as the 120 recorded for rat 1 of group 1 A, tends to make a consid-

7. Harvey, S. C.: The Velocity of the Growth of Fibroblasts in the Healing Wound, *Arch. Surg.* **18**:1227 (April) 1929.

erable difference in the average tensile strength. Actually the wounds of 7 rats in the vitamin B-deficient group and of 7 rats in the control group withstood a pressure of 300 mm. of mercury, indicating that a deficiency of vitamin B complex

TABLE 1.—*Gain or Loss of Body Weight and Tensile Strength of Wound in Normal Adult Control Animals*

Rat	Percentage of Total Body Weight Gained or Lost During Experiment	Tensile Strength of Wound, Mm. of Mercury
Group 1A.—Killed on the Eighth Postoperative Day		
1.....	— 1	300
2.....	+ 1	300
3.....	— 1	240
4.....	+ 1	300
5.....	— 2	260
6.....	— 2	300
Group 1B.—Killed on the Tenth Postoperative Day		
1.....	+ 2	300
2.....	— 3	270
3.....	+ 5	300
4.....	— 1	270
5.....	+ 4	300
6.....	+ 4	270
Average.....	+ 1	285

TABLE 2.—*Gain or Loss of Body Weight and Tensile Strength of Wound in Adult Rats Given a Diet Deficient in Vitamin B*

Rat	Percentage of Total Body Weight Gained or Lost During Experiment	Tensile Strength of Wound, Mm. of Mercury
Group 2A.—Killed on the Eighth Postoperative Day		
1.....	—36	120
2.....	—46	200
3.....	—19	300
4.....	—35	220
5.....	—27	300
6.....	—34	210
Average.....	—33	225
Group 2A.—Killed on the Tenth Postoperative Day		
1.....	—41	300
2.....	—23	300
3.....	—43	280
4.....	—41	300
5.....	—13	300
6.....	—42	300
Average.....	—34	296

has little if any effect on wound healing if the results from the animals tested on the eighth day and on the tenth day are averaged together as though for a single group.

It is interesting to note that the number of wounds attaining strength enough to resist a pressure of 300 mm. of mercury was less and that the average breaking

point of the wounds was at a lower pressure in the rats on a vitamin B-deficient diet killed on the eighth postoperative day than in the control group. These figures, however, are not sufficiently striking to be outside the range of experimental error.

#### EXPERIMENTS TO DETERMINE EFFECT OF A LOW CALORIC DIET ON WOUND HEALING

Although we did not believe that it would be fair to conclude from the figures just given that a deficiency of vitamin B retarded the early stages of wound healing, we were unable to exclude this possibility and therefore undertook the study of a second control group. The animals in this group were given a low caloric diet designed to effect a loss of weight equivalent to the weight lost by the vitamin B-deficient rats in group 2. This diet consisted of one half of the diet used in the normal controls (group 1) and contained adequate vitamins to prevent deficiency.

TABLE 3.—*Gain or Loss of Body Weight and Tensile Strength of Wound in Adult Rats Given a Low Caloric Diet*

Rat	Percentage of Total Body Weight Gained or Lost During Experiment	Tensile Strength of Wound, Mm. of Mercury
Group 3A.—Killed on the Eighth Postoperative Day		
1.....	—26	300
2.....	—48	300
3.....	—31	240
4.....	—37	180
5.....	—32	200
6.....	—37	270
Average.....	—35	248
Group 3B.—Killed on the Tenth Postoperative Day		
1.....	—32	180
2.....	—34	200
3.....	—43	270
4.....	—31	300
5.....	—33	300
6.....	—48	170
Average.....	—36	236

In this group the wounds were less solidly healed on both the eighth and the tenth postoperative day than in the control group. Moreover, the number of wounds which resisted a pressure of 300 in the rats killed on the eighth postoperative day was exactly equal to that in the vitamin B-deficient group on the same day. These findings indicate that if a deficiency of vitamin B complex has any deleterious effect on wound healing, this effect is probably associated with the loss of weight which accompanies the deficiency rather than the result of the vitamin B deficiency itself. In short, loss of weight, whether due to vitamin deficiency or to deficiency in caloric intake, appears to cause some delay in wound healing.

#### COMMENT

Abdominal wounds in normal adult control rats were healed with equal strength on the eighth and the tenth postoperative day. The rats neither gained nor lost weight during the experiment.

Rats maintained on a diet deficient in vitamin B complex lost 33 to 34 per cent of their original weight, and on the eighth postoperative day their wounds were not as well healed as those of the controls. On the tenth postoperative day, however, these wounds were healed as solidly as the wounds of the animals in the control group.

Rats maintained on a low caloric diet lost 35 to 36 per cent of their original weight, and on both the eighth and the tenth postoperative day their wounds had failed to heal as well as those of the controls.

On the eighth postoperative day the strength of the wounds was practically the same in the vitamin B-deficient group and in the group maintained on a low caloric diet.

There seemed to be no correlation between the appearance of the wound and its tensile strength. No peritonitis was noted in any of the rats. Histologic examination of the wounds showed only the presence or the absence of surface infection and failed to reveal any apparent cause for the difference in tensile strength of the wounds in the different groups.

#### CONCLUSIONS

In adult albino rats a deficiency in vitamin B complex has little effect on wound healing.

The slight diminution in the tensile strength of the wounds in vitamin B-deficient rats killed on the eighth postoperative day is probably explained by factors associated with their loss of weight rather than by any specific effect of the vitamin deficiency.

Wound healing in the albino rat appears to be more closely related to changes in body weight than to deficiencies of the vitamin B complex.