REFRIGERATION IN CLINICAL SURGERY*

ALFRED LARGE, M.D., AND PETER HEINBECKER, M.D.

ST. LOUIS, MO.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, THE BARNES HOSPITAL AND THE HOMER PHILLIPS HOSPITAL, ST. LOUIS, MO.

DURING RECENT YEARS refrigeration has been employed increasingly in the surgical treatment of gangrenous limbs. Its value remains in dispute chiefly because of a lack of satisfactory information regarding the effect of cooling on the healing of the wounds and on the progress of infection.

Enough general knowledge pertaining to the effect of cold has accumulated to warrant its analysis to determine, if possible, the advantages and disadvantages which might be expected to follow from prolonged cooling of tissues. Such knowledge should serve as a basis for the evaluation of measures involving the use of refrigeration in clinical surgery. Because the tourniquet has usually been employed in conjunction with refrigeration in the treatment of patients, any discussion of the merits and harmful effects of refrigeration preferably should include a consideration of the effects of the tourniquet. In this paper a discussion of the effects of cooling and of the effects of asphyxia produced by the application of a tourniquet will be followed by the presentation of cases in which a form of treatment in harmony with the implications of established physiologic principles has been employed.

THE EFFECT OF REFRIGERATION ON TISSUES

Within physiologic limits the velocity of most biologic processes varies directly with the temperature. At temperatures close to freezing there is almost complete cessation of cellular activity. Another pertinent observation is that conduction in a nerve trunk fails at or below certain critical temperature levels (25° to 30° C. in warm blooded animals),[1] thus accounting for the phenomenon of refrigeration anesthesia.

The changes which occur during and following the prolonged cooling of an extremity are of particular interest. While the tissues are cooled they are anesthetic and their metabolism is greatly diminished. After exposure to cold (3° to 4° C. for 24 to 96 hours) rats' tails show marked degeneration of nerves and muscles in the cooled areas.[2] The dog's forelimb, after immersion in cold water, exhibits edema and paralysis of the involved member, and these signs are followed by degeneration of the cooled peripheral nerves.[3] Similar, but more marked, changes are seen sometimes in shipwrecked sailors on exposure to cold and wet for varying periods. Such individuals may develop long-standing vascular and neurotrophic disturbances, and, in the most severe cases, gangrene of the feet.[4] Thus, the magnitude of tissue changes resulting from exposure to cold may be considerable. Although

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low temperatures may produce some injury by a direct effect upon living cells, there is rather general agreement that cold causes ischemia of the cooled part, and that lack of oxygen is responsible for most of the damage. During cooling there is an accumulation of tissue metabolites, which, after the cooling agent is removed, causes reactive hyperemia and other changes similar to those following the removal of a tourniquet (*q.v.*) although as a rule the changes are not profound enough to produce systemic effects.

Since normal tissues are damaged by cooling, the cells in areas undergoing reparative and inflammatory changes also would be expected to be affected adversely. Inhibition of healing of wounds during refrigeration has been shown to occur in the experimental animal by Large and Heinbecker.[5] Their studies also demonstrated that following the cooling period wound healing was delayed, the degree of delay being roughly proportional to the duration of the cooling period. Degenerative changes were shown to occur in the nerves of cooled extremities,[3] and these are considered responsible, in part at least, for the delay in the healing of wounds long after the actual exposure of the tissues to cold has ended.

Brooks and Duncan,[6] in carefully controlled experiments, observed that the inflammatory reaction to intradermal injections of bacteria and of oil of turpentine was inhibited during the cooling period. Following refrigeration the inflammatory reaction in injected areas was slightly greater than in the controls, with possibly some increase in actual necrosis. Bruneau and Heinbecker[7] found that during the cooling period no inflammatory response developed to *Streptococcus hemolyticus* injected subcutaneously and into joints of dogs' limbs, while after refrigeration the tissues exhibited a decrease in growth restricting action toward the bacterial organisms, the inflammatory reaction being more marked than in the controls. Large and Heinbecker[5] studied the healing of wounds treated by delayed suture after 24- or 48-hour cooling periods, and found that the refrigerated wounds showed a much higher incidence of gross infection, with suppuration, than did the uncooled controls.

THE EFFECT OF A TOURNIQUET

The tissues distal to the area of constriction are ischemic, and if rendered so for a sufficient time, undergo degeneration. Lewis[8] has shown that muscle fibers fail to recover their ability to contract when deprived of their blood supply for 6 to 8 hours; nerves die after 12 to 20 hours, the skin after 24 to 48 hours of ischemia. The tourniquet itself, if narrow and tight, may, by direct pressure on nerves, cause temporary paralysis. During the period of constriction, metabolites causing vasodilation accumulate, so that after the tourniquet is released, a period of reactive hyperemia ensues. If the mass of tissue distal to the tourniquet is large, release of the constriction may result in shock and even in death.

The effect of a tourniquet on the progress of infection varies with the duration of the period of ischemia. The cessation of blood flow presages

an interruption of the inflammatory reaction, which is inimical to the controlling of the infection following removal of the tourniquet. However, if a tourniquet be applied tightly enough to a limb proximal to a gangrenous or infected area, the obliteration of vascular and lymphatic channels at the level of constriction will prevent absorption of toxins and bacteria from the involved region into the general circulation. This beneficial effect will continue as long as the tourniquet is in place, unless the disease process is able to spread above the level of constriction by direct continuity of tissue.

EFFECT OF A TOURNIQUET AND REFRIGERATION USED SIMULTANEOUSLY

The survival time of a tightly constricted limb is prolonged greatly by refrigeration of the part. This was shown experimentally by Allen,[9] and demonstrated, conclusively, to be true by Brooks and Duncan,[10] who found that rats' tails rendered completely ischemic in a pressure apparatus lived many hours longer without the subsequent development of gangrene when exposed to temperatures of 1° to 15° C. than did those at room temperatures. The other effects of these agents used together can be predicted from the known changes following their individual or separate applications.

In summary, then:

a. The benefits of refrigerating an extremity include loss of sensation and diminution of absorption of noxious agents from the cooled area, while the disadvantages lie in a subsequent delay in wound healing, a greater risk of infection, and a varying degree of actual damage to refrigerated tissues left *in situ.*

b. The benefits of the application of a tourniquet to a limb refrigerated *above* the proposed level of amputation include anesthesia and the elimination of absorption of noxious agents, with increased duration of viability of the completely ischemic tissues, while the ill effects, again, include delayed wound healing, greater risk of infection, and actual tissue damage to the refrigerated stump.

c. The benefits of refrigeration with the application of a tourniquet *below* the proposed level of amputation of a limb, as in the other instances, include loss of sensation and elimination of absorption of noxious agents from the part; the further advantage of eliminating interference with wound healing and the spread of infection also is assured.

CLINICAL APPLICATIONS

The management of critically ill patients with gangrenous extremities frequently involves the control of toxemia, of infection, of anemia and of derangements in metabolism. If absorption of toxins from the involved limb can be prevented for a time, the patient's general condition can be improved enough so that operation may be performed with much less risk. This can be accomplished most simply by a tourniquet about the limb above the involved area, but below the level of proposed amputation. Such a plan was

followed not infrequently during the last war, and, more recently, Maxeiner (1941)[11] reported the successful use of "temporary tourniquet amputation" in 12 cases. Adolph[12] advocated a similar method. The results obtained, in general, were satisfactory, but the patients had severe pain until the tourniquet produced anesthesia, and occasionally infection developed above the level of constriction.

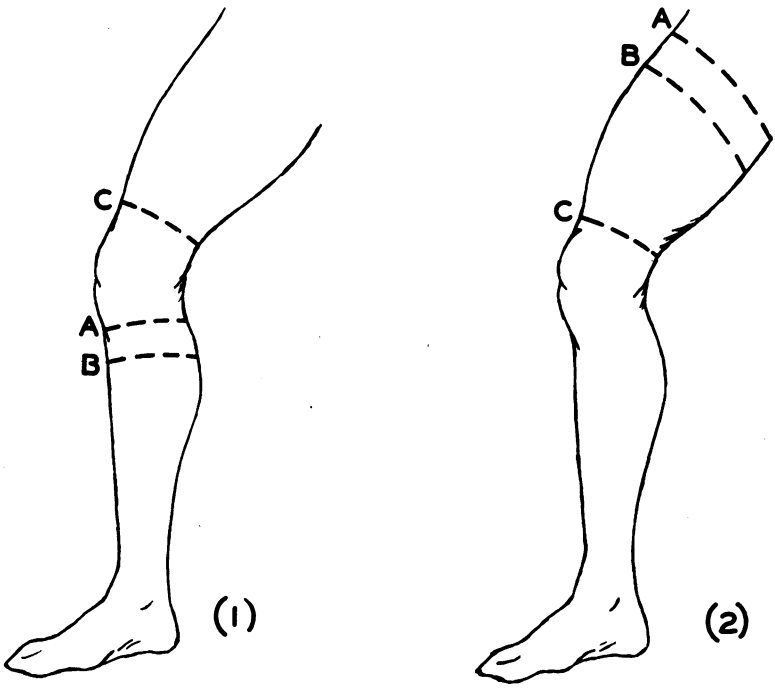

FIG. 1.—Diagrams of methods of use of refrigeration and the tourniquet before operation. A. Level of refrigeration. B. Site of application of tourniquet. C. Level of amputation.

(1) Diagram showing the advocated level of refrigeration, A and the site of amputation. C. Note that the distance AC is considerable.

(2) Diagram showing the method of refrigeration anesthesia as employed by Allen, and others. Note that the large mass of refrigerated tissue AC is not excised.

Allen, in certain experiments,[13] found that a tourniquet could be applied painlessly, if the limb were refrigerated first. He suggested the use of refrigeration together with a tourniquet in the preparation of poor-risk patients with gangrenous feet for amputation, and introduced the clinical use of refrigeration anesthesia for such operations.[14] The type of procedure advocated by him, and his coworkers,[15] is indicated in Figure 1. The disadvantage of this method appears to lie in the fact that much of the cooled, and, therefore, damaged tissue is not excised. It is felt preferable that all refrigerated tissue should be removed at operation. This can be done by applying the tourniquet and the cold distal to the level of amputation as indicated in Figure 1.

ILLUSTRATIVE CASES

Case 1.—H. H., a 54-year-old white female, known to have diabetes mellitus, was admitted to the Barnes Hospital, April 10, 1943, with a three-month history of spreading infection of the right foot. Examination showed a toxic, drowsy, but rational female, who seemed critically ill. The temperature was 39.6° C. The right 5th toe was absent, and there was a large, foul, necrotic, sloughing ulcer on the lateral aspect of this foot, from which thick pus could be expressed. Induration and swelling were present up to the ankle. There were no palpable arterial pulsations in either foot, but both popliteal pulses could be felt. Laboratory findings included Hb, 42 per cent; W. B. C. 17,000;

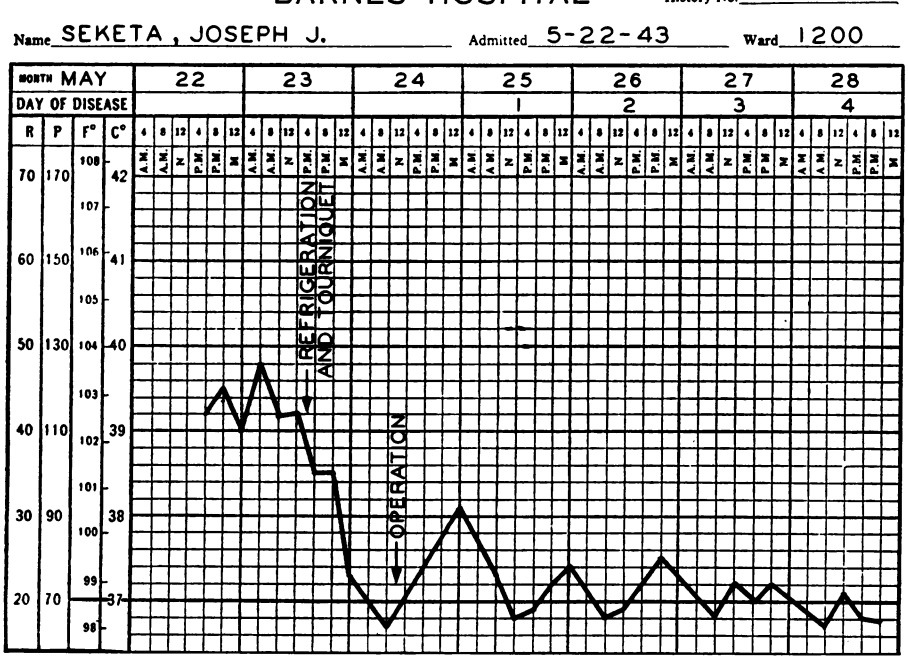

CHART 1.—Case 2: Temperature chart. Note the failure of response to intravenous sodium sulfadiazine and general supportive measures during the first 24 hours of hospitalization, and the marked improvement following refrigeration and the application of a tourniquet.

urine, one plus sugar, numerous W. B. C.; blood sugar 324 mg. per cent; blood N. P. N. 13 mg. per cent. Insulin, whole blood, fluids and sulfadiazine were given. In the evening of the day of admission, ice bags were placed about the right leg and foot almost up to knee level and two hours later a tourniquet was applied to the leg just below the knee. The patient gradually became more comfortable, and within six hours the temperature had fallen to normal. Twelve hours after refrigeration had been instituted, a right midthigh amputation was performed, under spinal anesthesia, without release of the tourniquet. The wound was closed with drainage, and the drain was removed after 24 hours. The postoperative course was uneventful, the wound healed *per primam*. The patient was discharged from the hospital, May 8, 1943, 28 days after admission, in good condition.

Case 2.—J. J. S., a 48-year-old white male, was admitted to the Barnes Hospital, May 22, 1943, and stated that he had had pain in the legs and feet during exercise or in cold weather for six years. A month and a half prior to admission, an area of infection developed about the right great toe; this was treated conservatively, but gangrene of

the toe developed and it was amputated with closure of the stump, elsewhere, eight days prior to admission. Three days before entry the foot became painful, swollen and blue. Pain was so severe that frequent injections of morphine failed to give relief.

Examination showed a critically ill, middle-aged male who frequently dropped off to sleep; his memory was hazy and he was obviously quite toxic. The temperature record is shown in Chart 1. The distal portion of the right foot was gangrenous, and the remainder of the foot up to the ankle swollen, puffy and extremely tender. No arterial pulsations could be felt in the foot, but the popliteal pulse was palpable. Laboratory findings included a W. B. C. of 30,000; and a blood culture was positive for *Streptococcus hemolyticus.*

The patient was given fluids, intravenous sodium, sulfadiazine, and gas bacillus antitoxin, without improvement. Therefore, the day after admission, ice bags were packed around the right foot and leg to just below the knee, and when sensation disappeared, a tourniquet was applied to the leg. Improvement in the general condition was dramatic (see Chart 1), and 24 hours later a circular supracondylar amputation was performed under spinal anesthesia. The wound was closed without drainage. Healing *per primam* followed, and the patient was discharged from the hospital, June 8, 1943, 17 days after admission, in good health.

Histologic study of the amputated tissues confirmed the clinical diagnosis of Buerger's disease, with gangrene of the foot.

Case 3.—M. H., a 19-year-old white female, was admitted to the Barnes Hospital May 26, 1943. She had been knocked off a motorcycle three days before, and a compound fracture of the right ankle sustained; this was treated elsewhere. Spreading infection soon appeared, and the patient was referred to Barnes Hospital for further treatment.

Examination showed an acutely ill, toxic young girl complaining of severe pain in the right leg. The temperature was 38° C. There was evidence of an unreduced fracture of the right ankle, on the lateral side of which was a necrotic, foul-smelling wound from which bubbles of gas could be expressed. The entire right foot and leg were swollen, exquisitely tender, and crepitant, and gas could be felt in the subcutaneous tissues of the thigh as well. Roentgenograms confirmed the diagnosis of gas gangrene.

Large doses of polyvalent gas bacillus antitoxin were administered, the leg was packed in ice up to the level of the knee, and a tourniquet applied. The symptoms rapidly subsided, and, four hours later, under general anesthesia (cyclopropane), a guillotine supracondylar amputation was performed, and several incisions were made over the involved portions of the right thigh. The wounds were left open, and they were irrigated frequently through tubes placed therein. Healing was slow but satisfactory. The patient was discharged from the hospital, July 3, 1943, with all wounds healed.

Case 4.—J. M. L., a 50-year-old white female, was admitted to the Barnes Hospital, November 13, 1943, for removal of an acoustic neuroma on the right side. A meningioma was removed through a cerebellar craniotomy on November 16, 1943. During convalescence the patient, who also suffered from rheumatic heart disease with auricular fibrillation, released an embolus which lodged at the bifurcation of the aorta, and although a large embolus was removed from the left femoral and iliac vessels, November 27, 1943, both legs had to be amputated subsequently just above the knee. On December 4, 1943, a right supracondylar amputation was performed. The patient then developed fever of 39.8° C., and this was thought due to infection in the gangrenous left foot. Accordingly, December 6, 1943, ice packs were applied to the left leg up to the knee, and after two hours a tourniquet applied below the knee. The temperature immediately fell to normal, and 18 hours later, a left supracondylar amputation was performed under general anesthesia (ethylene). The wound was closed without drainage. Postoperative progress was slow, but satisfactory. A slight degree of muscle breakdown occurred and drained out through a small sinus track. This had not healed completely

when the patient left the hospital, January 19, 1944, but did so in about two weeks thereafter.

Case 5.—A. C., a 61-year-old colored male, was admitted to St. Louis Homer Phillips Hospital December 4, 1943. He had fallen out of a second story window one hour previously and was unconscious for some time. Examination showed a deep laceration of the forehead and a severe injury to the right eye, which subsequently developed traumatic cataract. As the patient became more alert, he began to complain of pain in the left leg and foot. The latter was cold, insensitive and paralyzed, and the left popliteal and tibial pulsations were absent. There was a small chip-fracture of the lateral condyle of the left femur.

It was thought that thrombosis in an arteriosclerotic popliteal artery had occurred following direct injury. There was no evidence of an hematoma in the popliteal space. Conservative therapy was tried, but was unsuccessful. Gangrene of the left foot and lower leg gradually developed. There was severe pain and fever as high as 41° C. Accordingly, December 17, 1943, the left leg and foot were packed in ice and a tourniquet applied below the knee. Improvement was dramatic, the temperature shortly falling to 37.6° C. Twenty-four hours later, under spinal anesthesia, a midthigh amputation was performed. The wound was closed over a small rubber dam drain, around which there exuded a small amount of serous fluid which stopped when the drain was removed 48 hours after operation. The wound healed *per primam.* The patient had some fever after operation, but this disappeared when sulfathiazole, which was being administered prophylactically, was discontinued. His subsequent course, as far as the amputated limb was concerned, was entirely satisfactory, although he was kept in the hospital until February 9, 1944, for treatment of his injured eye. Histologic study of the amputated leg confirmed the clinical diagnosis of thrombosis in a sclerotic popliteal artery, with resultant gangrene.

Case 6.—C. B., a colored female, age 57, was admitted to the St. Louis Homer Phillips Hospital December 10, 1943. She had had a partial amputation of both feet for frostbite nine months previously, and had been living in an unheated basement in the interim. Her present complaint was increasing pain in both stumps for some three weeks, following repeated exposures to cold. Examination showed moist gangrene of both stumps, with swelling and tenderness to midleg level on both sides. Conservative treatment was attempted, but the gangrene extended and infection became more marked. The temperature ranged around 39° C. occasionally reaching 40.6° C. Since both popliteal pulsations were good, it was decided to amputate below the knees. On January 10, 1944, both stumps were refrigerated, and tourniquets applied just above the line of demarcation at the ankles. The temperature fell rapidly to normal, and next day bilateral midleg amputations were performed under spinal anesthesia. The wounds were closed, with drainage. There was some sloughing of the skin margins of the lateral aspects of both wounds, and complete healing had not occurred after one month, but the patient's general condition was at all times satisfactory after operation. It was felt that the delayed healing in this case may have been associated with amputation too close to the refrigerated areas.

COMMENT.—Each of the six cases presented had gangrene of one or both feet associated with infection and toxemia. In one instance (Case 2) there was septicemia. The basis for the gangrenous process, as determined by histologic study, was different in each of the cases—diabetic arteriosclerosis, thrombo-angiitis obliterans, spreading gas bacillus infection, peripheral embolism, popliteal thrombosis and frostbite being found. The patients were operated upon without mortality and without encountering difficulty with the subsequent wound healing. It is felt justifiable, therefore, to

advocate the use of the method to others, in order that through wider experience its real merits may be determined.

The details of the procedure used are not complicated. In all but the last case, ice bags were applied nearly up to the knee (Fig. 1) and the tourniquet placed below the knee two to four hours later, after anesthesia had been obtained. When the patient's general condition warranted it, usually after 24 hours, amputation was performed above the knee, using inhalation or spinal anesthesia. Because it is known that living tissues will conduct cold fairly efficiently,[16] and for other reasons already considered, it is important that the amputation be carried out well above the refrigerated area. None of the patients herein reported suffered from shock during or after the operation, an advantage stressed by the proponents of refrigeration anesthesia.

The small number of cases treated by this method does not warrant any sweeping claims. However, refrigeration was not used in any case unless the patient's condition was so poor, due to severe infection and absorption from the gangrenous part, that the ordinary methods of treatment seemed dangerous. Such cases previously have been treated by guillotine amputation, followed by elective amputation at a higher level at a later date. By the method herein employed the necessity for two operations has been obviated.

SUMMARY AND CONCLUSIONS

Refrigeration of an extremity abolishes pain and lessens the blood and lymph flow. When such refrigeration is followed by, and combined with, the application of a tight tourniquet, absorption of toxic products from an infected gangrenous extremity is, for all practical purposes, eliminated.

Because refrigeration tends to delay wound healing and decreases the power of resistance of tissues to bacterial invasion, the prolonged cooling *of tissues to be preserved* is not advocated. It is recommended that necessary amputations be carried out above the level of cooling.

Because a patient's general condition can be improved so greatly, during the combined use of cold and the tourniquet, by ordinary restorative measures, it is unnecessary to avoid the use of inhalation or spinal anesthesia for amputation.

Six illustrative cases cared for in accordance with the above principles are reported.

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