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## THE USE OF UREA IN THE TREATMENT OF PERFORATING ULCER

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In the reports of the Subcommittee on Treatment of the Cairo Congress (3) appears the following statement: "The treatment of leprotic ulcers, in the present state of our knowledge, is unsatisfactory, and further investigation in hospitals and institutions is recommended. With regard to perforating ulcer, it is recommended that necrotic bone, where present, should be removed. Rest of the affected limb is a valuable feature of treatment of this condition." In these few words is summarized treatment of one of the most disabling and painful lesions of leprosy, the perforating or "trophic" ulcer associated with bone necrosis. Search of the literature has revealed several contributions which offer some help.

Oberdoerffer and Collier (5) have reviewed briefly the literature on deformities and ulcers, and have advocated a new dressing of mercurochrome, honey, cod-liver oil, zinc oxide, and bismuth subnitrate in a vaseline base, coupled with relief of pressure by canvas pads filled with rice husks; necrotic and septic bone is first removed. They mention the reported successes from periarterial sympathectomy and injection around the ulcers of chaulmoogra preparations or other drugs, and remark that the former has not found wide acceptance, while the beneficial effects of the latter are probably due to nonspecific stimulation.

Radna (7) used weekly injections of creosoted *Hydnocarpus wightiana* oil around the ulcers and in the region of the posterior tibial nerve, with local applications of finely powdered potassium permanganate and passive hyperemia.

The concensus of opinion was well expressed in a symposium published in *Leprosy in India*, in 1933 (11). But little has been added to the principles there expressed, other than the items already mentioned. The definite statement is made that if dead bone is discovered it must be removed, and this means operative treatment. In outline, the principal treatments suggested by various workers may be listed as follows:

## I. GENERAL

1. Rest
  - a. Bed rest in severe cases
  - b. Rest of affected part by use of crutches or local pad supports: grass, husks, felt, rubber sponge (4)
2. Treatment of intercurrent disease, especially
  - a. Helminthiasis
  - b. Septic foci
3. Food; a well balanced diet of high vitamin content
4. Treat reaction if present
  - a. Bed rest
  - b. Laxation
  - c. Intravenous tartar emetic or mercurochrome

## II. LOCAL

1. Cleansing of field
  - a. Removal of necrotic bone
  - b. Debridement of soft tissues
  - c. Drainage of septic areas
2. Stimulation of healing (alternative suggestions)
  - a. Chemical applications: potassium permanganate, copper sulphate, antiseptics, oils, ointments, etc.
  - b. Periulcer injections
  - c. Periarterial sympathectomy

The fundamental principles of local treatment appear to be three: (1) removal of necrotic tissue, including bone; (2) control of secondary infections; and (3) avoidance of pressure. If these can be carried out, healing will take place in most cases in which the patient's general condition is sufficiently good. It may be accelerated by numerous local stimulating applications, of which the latest is Ryrie's shark oil, for its vitamin A content (9).

The first item, removal of necrotic tissue, is the most difficult and the most important. The usual suggestion is surgery, sometimes removal of entire metatarsals. This is an effective procedure in well equipped institutions, although severe deformity may result. But is there no suitable alternative in cases where patients object to surgery, or when for other reasons operation is not desirable? The present study was undertaken in an effort to answer this question.

Previously at the St. Croix leprosarium treatment consisted of simple dressings of various sorts—sodium chloride, boric acid, salicylic acid, mercuric bichloride, or zinc oxide in various solutions and ointments, coupled with general treatment and, in a few cases, bed rest. Complete healing of severe ulcers was a rarity, and some had persisted for years.

At the Carville leprosarium, under McIlhenny's supervision (4), feet are soaked in 1 to 1.5 percent boric acid solution or 8 to 10 percent magnesium sulphate—the choice of solution being determined by the response of the individual patient—to arrest the necrosis and so to decrease the amount of surgery which may be required. Soaks are given for one hour daily, and wet compresses applied during the day and night. About 85 percent of these cases have yielded satisfactory results when cooperation was obtained. I tried this treatment on a few patients, and some small bits of bone were extruded spontaneously. Careful, skilled nursing is required, however, as well as much patience on the part of both staff and patients, which made it impracticable. A chemical method was then sought which would be of equal or greater value.

*Calcium picrate.*—Stewart (10) introduced a new treatment for osteomyelitis, based on his studies of maggot activity. After operation, making the excavation long and narrow, he packed for 24 hours with vaseline gauze, then irrigated with 0.25 percent aqueous picric acid, 8 percent glycerin being added to reduce surface tension. This was followed immediately with a spray of an aqueous suspension of calcium carbonate, 20 gm. in 215 cc., autoclaved. The wound was then packed with dry gauze, and the treatment repeated three times a week, or twice a week in severe cases.

This treatment, without operation, I tried in several of our cases of plantar ulcer, and improvement was observed generally, with extrusion of fragments of necrotic bone. It was later discontinued in favor of urea, except in the case of one patient (Case 4) who never achieved complete healing but seemed better helped by the picrate routine.

*Urea.*—Robinson (8) reported in 1936 on the use of urea in treatment of chronic purulent wounds, including postoperative osteomyelitis cases. Urea (carbamide) was used because it is a product of the hydrolysis of allantoin, which is the excretion of maggots that he believed responsible for their debriding action.<sup>1</sup> He used a 2 percent solution or a 15 percent ointment or jelly. Others employed stronger solutions, and soon Holder and MacKay (2) were advocating use of urea crystals and saturated solutions. In these strengths urea is both bactericidal and proteolytic, as reported by Foulger and Foshay (1) from experimental work and tests on purulent otitis media.

<sup>1</sup>Urea had previously been used empirically by several workers, starting with Peju and Rajat (6) in 1906.

These reports led me to try urea on plantar ulcers. The results in most cases have been encouraging. Where necrotic bone is present, it has been loosened and extruded, sometimes yielding metatarsal shafts 8 cm. long. Loosened bone may sometimes be removed by gentle manipulation with a hemostat instead of waiting for its spontaneous passage. Following bone extrusion, or in its absence if there is no necrosis, healing of the ulcer has been stimulated.

#### TECHNIQUE

The urea is used in crystal form, packed into the ulcers daily. It is preferable to cover the area with waxed paper to prevent absorption by dressings. In deep sinuses or other places where crystals cannot be conveniently applied, a saturated solution of urea is employed.<sup>2</sup> General supportive treatment was not neglected. No difference was apparent in those of our patients who were receiving intramuscular chaulmoogra preparations and those who were not.

#### RESULTS

In all, 50 ulcers were treated in 27 patients, 35 with urea and 15 without it. When tabulated, the results would seem to be in favor of treatment without that drug—80 percent healed against 60 percent. That, however, does not reflect the actual results. The material is unsuitable for statistical analysis, for the number of cases treated is small, some patients were uncooperative, and several ulcers which had lasted for years were later treated with urea, in some instances with good results.

Brief case reports will illustrate some of the more interesting phases of the results obtained in this study.

CASE 1.—M. F., female, age 41, N2, admitted 1920. No history of previous ulcers. In August, 1937, a small one developed on the plantar surface of the left little toe. Urea was started a few days later. Two pieces of bone were extruded, and healing proceeded smoothly, being complete by October.

*Comment.*—This is the usual story when an ulcer is attacked promptly—rapid and uneventful healing. Unfortunately, many patients did not report their ulcers at so early a stage.

CASE 2.—L. G., male, age 23, L2-N3, admitted 1937. On admission, two deep ulcers were present on the toes of the left foot. Urea was started promptly, and both ulcers, together with a new one which appeared on an-

<sup>2</sup>The "crystal urea"—synthetic carbamide—was obtained in 100 lb. bags from E. I. du Pont de Nemours & Co., Inc., Ammonia Dept., Wilmington, Delaware.

other toe, were healed in about four months. Another ulcer appeared on the plantar surface of the right foot soon afterward; it healed under urea treatment in about three months. In the following month an ulcer was found under the right second toe. This became secondarily infected and so much tissue destruction resulted that the toe was amputated. Urea was used post-operatively, and healing was complete in a month.

*Comment.*—This illustrates the active case in which ulcers appear repeatedly, but prompt treatment and the patient's full cooperation usually result in healing. There is no reason to avoid a toe amputation when there is marked loss of tissue and healing can be aided.

CASE 3.—B. C., female, age 24, N3, admitted 1916. A plantar ulcer which began several years before admission was still present in 1937, with little indication of healing. Several small pieces of bone had been extruded spontaneously at various times. Urea treatment was begun, and after passing a few more small pieces of bone the ulcer, which was two inches long and almost an inch deep, began to heal by granulation. As the foot was very flabby, a plaster figure-eight bandage was applied and the patient instructed to use crutches. Healing proceeded slowly, with some set-backs, but was complete in a little over a year. A roentgenogram at this time showed only the first metatarsal intact, the others being mere spicules, which explained the flabbiness of the foot. When the patient later tried to walk on it, the ulcer recurred. It healed again without difficulty, but she seems fated to use crutches indefinitely.

*Comment.*—This is a typical case of the ulcer which heals fairly readily but recurs as readily because there has been so much destruction of supporting bone. I know of no satisfactory solution to this problem.

CASE 4.—E. C., male, age 36, L1-N3, admitted 1915. Small ulcers were noted on both feet in 1921, which healed spontaneously. In 1930 they had reappeared, and were so severe that the patient was unable to work. By 1937 they occupied about one-half of the balls of both feet. Urea and calcium picrate were both tried; there was definitely better progress on the picrate treatment, though still quite slow. I feel that these ulcers would heal if they were given rest, but that they probably would recur.

*Comment.*—The particular interest of this case is that it was the only one in the series in which, while neither treatment was satisfactory, calcium picrate was more beneficial than urea.

CASE 5.—A. C., female, age 38, N3, admitted 1917. Left foot: A plantar ulcer appeared soon after admission. There were two periods of healing and recurrence. In 1937 the ulcer was about seven inches long and showed bone at the base; several pieces of bone had been passed at various times. Urea was begun, but not used continuously because of complaints of pain and lack of cooperation. (In most of these patients urea treatment appeared to be not painful, or only slightly so.) Calcium picrate was used for a while, then urea again. More bone was extruded, and the ulcer finally healed in about sixteen months.

Right foot: In August, 1937, a small ulcer was seen on the plantar surface, the result of a burn. Urea was begun, but the foot was so swollen it resembled a mycetoma, with two sinuses exuding pus. There was some improvement, but later swelling and discharge recurred, and operation was required. In September, 1938, the tissues were laid wide open, dead bone removed, and sinuses curetted; the soft tissues were coapted without tension and drains inserted. Urea crystals were packed in at the time of treatment, and crystals and solution used as aftertreatment. Healing was fairly rapid, although some drainage persisted for several months; all sinuses were closed by April, 1939.

*Comment.*—Here in one patient we have both the simple but extensive lesion which heals with conservative treatment, and the deep, secondarily infected lesion which heals only after operation.

CASE 6.—E. M., male, age 37, N3; admitted 1917, paroled 1932, readmitted 1936. During routine examination while on parole he was found to have a rather shallow plantar ulcer on each foot. For six weeks he was treated as an outpatient without success, and was then readmitted. Under calcium picrate treatment bone was extruded from both feet and the left foot healed completely. Urea was started after ten months and healing was complete nine months later. There has been no recurrence.

*Comment.*—This illustrates the possibility of healing in an active patient who is ambulant throughout the period of treatment. Sometimes one questions whether this method, when it succeeds, is not less likely to be followed by recurrence than when the foot has been at rest.

CASE 7.—I. J., female, age 56, N3, admitted 1928. The present ulcer of the plantar surface of the heel began shortly before admission, healed for a few months in 1934, but recurred. Calcium picrate was started in 1937. During the following year three pieces of bone and several bits of ligament were extruded but the ulcer persisted. In 1939 a bone curettement was performed and since then no more bone has been passed, but healing continues to be slow.

*Comment.*—Of the ulcers occurring in patients in whom the disease is relatively inactive, this one has been the most difficult to treat, probably due in large part to the patient's unwillingness to use crutches. A fenestrated felt pad does not appear to be sufficient to relieve pressure.

CASE 8.—H. J., male, age 68, N3, admitted 1937. This patient was treated at a hospital on another island before coming to St. Croix. In 1929 his left leg was amputated for "gangrene of foot; arterial sclerosis, general." In 1931 the distal phalanx of the right great toe was removed because of bone necrosis. A month later a sequestrum was removed from the stump. Leprosy was not diagnosed.

Soon after coming to St. Croix he was admitted to a hospital with a purulent infection of a shortened toe. The diagnosis was obvious, and he was at once transferred to the leper asylum. Under conservative treatment



two pieces of bone were extruded and the toe healed in about three months. In August a plantar ulcer developed at the base of the great toe, healing in three months.

*Comment.*—Circulation is good in the remaining foot, and the patient is active. Could the left leg have been spared in whole or in part if the condition had been recognized as leprosy and treated accordingly?

CASE 9.—J. N., male, age 63, N3, admitted 1910. Ulcers have been present on both feet since 1921. By 1934 the feet were mere stumps, with most of their plantar surfaces ulcerated. Urea treatment was employed, but the patient was not willing to stay off his feet and very little healing has occurred. Some small bits of bone have been passed. He has been regular in receiving treatment and is satisfied with his slow progress.

*Comment.*—In elderly patients with advanced deformities, ulcers may be so resistant that treatment seems of little value, other than to improve the patient's mental condition. I believe that this patient's ulcers could be healed if he were kept at rest; but he feels that it is not worth the cost—and perhaps he is right.

#### DISCUSSION

While no claim is made that urea is a cure-all in perforating ulcers, I feel that it can be a valuable part of the treatment and that by its use surgical intervention may often be avoided. It would be of interest to try it in conjunction with periulcer or perineural injections.

The chief advantage of urea treatment is loosening of necrotic bone and its discharge through the ulceration. It is not known whether the necrotic process present at the beginning of treatment is arrested, or if further necrosis occurs prior to extrusion of bone. Serial x-ray studies, for which facilities were not available, would determine this point. Urea also appears to have a stimulating effect on granulation tissue, which hastens healing of many long standing ulcers.

The patients were all Negroes, and it is possible that other racial groups would differ in their response. I have observed that leprosy as seen in Hawaii is frequently more severe than that found in the Virgin Islands.

#### SUMMARY

The local use of urea, in crystals or saturated aqueous solution, is of value in the treatment of perforating ulcers. It hastens the spontaneous extrusion of necrotic bone and appears to stimulate subsequent healing.

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