

# THE CONTROL OF ACUTE THROMBOPHLEBITIS WITH ULTRAVIOLET BLOOD IRRADIATION THERAPY\*

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THE sudden appearance of acute thrombophlebitis is one of the most unpredictable and unwelcome complications encountered in medicine. The relative inability of the various methods in vogue today to control this complication satisfactorily is well known and will not be discussed here.

In the last four years we have used the Knott technic of ultraviolet blood irradiation therapy in thirteen consecutive cases of thrombophlebitis with highly satisfactory results. Blood irradiation was found to control the classical symptoms of acute thrombophlebitis rapidly and efficiently in all thirteen cases, which included thrombophlebitis with and without fever, following delivery, operation or acute pyogenic infection.

The Knott technic of ultraviolet blood irradiation therapy has been described elsewhere.<sup>1,2,3</sup> Briefly, it consists of the withdrawal and citration of a predetermined amount of the patient's blood, plus immediate reinjection of that citrated blood through a Knott Hemo-irradiator, a precision machine which automatically exposes the citrated blood to intense ultraviolet rays safely and efficiently, and returns the irradiated blood to the venous circulation of the patient.

We believe that as a result of our observation a new phenomenon, that of a rapid subsidence of the classical symptoms of thrombophlebitis following ultraviolet blood irradiation, has become apparent.

## RESULTS

*Tabular Presentation.* The following table of results, as may be readily seen,

essentially shows the type and location of the acute thrombophlebitis in each patient, the time of disappearance of pain, tenderness, edema, and fever (when present), the number of blood irradiations per patient and the number of hospital days elapsing between the initial blood irradiation and discharge from the hospital. (Table 1.)

*Analysis of Table.* An analysis of the above table shows a definite uniformity of response to ultraviolet blood irradiation therapy. Pain and tenderness disappeared first as a rule; fever if present, disappeared next most rapidly, and edema was last to subside.

Cases 1, 2, 5, 9 and 13 are examples of failures of chemotherapy plus bed rest, local heat, and elevation of the extremity which responded successfully to ultraviolet blood irradiation therapy.

Cases 3, 10 and 11 failed to respond to local heat, bed rest, and elevation of extremity, until blood irradiation was applied.

Case 4 was seen after failure of local heat, bed rest, elevation of the extremity, and of four nerve blocks to alter the course of the disease; an advanced induration of the leg was present also. In all of these nine individuals, as well as in the other four who received ultraviolet blood irradiation therapy alone, pain, tenderness and fever when present disappeared within twenty-four to forty-eight hours. Edema disappeared in twelve individuals within three to fifteen days; in the thirteenth, in whom an advanced induration had appeared during fifty days of failure to respond to four nerve blocks, the patient was able to walk for the

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first time, but edema and induration were still present at the time of hospital discharge, eight days after a single blood irradiation.

#### BRIEF ABSTRACTS OF TYPICAL CASE HISTORIES

CASE 1. No. 46943, age forty, a female, was admitted March 18, 1940, for a nephropexy which was done March 20, 1940. For the first two postoperative weeks the patient's convalescence was relatively uneventful, when on the fourteenth postoperative day she began complaining of pain in the left leg localized over the femoral area. A heat cradle was applied and the leg elevated, and within twenty-four hours the pain disappeared. She was allowed out of bed at this time and within a few hours her leg began to swell, temperature rose to 101.8°F. and her pulse to 120. Despite bed rest, hot compresses and 40 gr. of sulfanilamide the patient's temperature and pulse rate remained elevated for the next five days, then descended slowly with a daily peak temperature ranging between 99° and 100°F. At this time, April 15, 1940, a 500 cc. blood transfusion was given. On the following day the patient's temperature rose to 103.2°F., and her symptoms of pain and swelling which had subsided somewhat became greatly aggravated. Sulfapyridine was given (15 gr. every four hours) for forty-eight hours, but was tolerated badly. The patient's temperature continued for three days to be elevated with a daily peak ranging from 99° to 100.4°F. In addition occasional chills were present. Sulfapyridine was stopped April 17, 1940; blood culture taken on this day was negative, but no improvement was noted in the next forty-eight hours, and on April 19, 1940, ultraviolet blood irradiation therapy was instituted (200 cc. of patient's blood was irradiated according to the Knott technic). Within twenty-four hours the patient's temperature fell to normal; within forty-eight hours her pain had disappeared completely and on April 26, 1940, seven days later, swelling had disappeared. The patient convalesced uneventfully, and was discharged from the hospital April 30, 1940, in apparently excellent condition eleven days after a single blood irradiation.

CASE 7. No. 78263, age forty-eight, a female, was admitted to the hospital with a history of nausea, vomiting, and a spreading

infection of the right groin during the previous four to five days. The infection apparently originated from an infected varicose ulcer located along the course of the internal saphenous vein. Physical examination revealed a right-sided saphenous and femoral thrombophlebitis, with marked induration of the right ileo-inguinal lymph glands, a spreading erysipeloid lesion extending from the upper ileo-inguinal region down the inner surface of the thigh halfway to the knee. The lesion was discharging an extremely foul smelling sero-sanguineous fluid from several areas and there was a marked necrosis of adjacent skin areas. Her temperature on admission was 100.8°F., pulse 120. Wassermann and Kahn tests were negative, hemoglobin 11.7, red blood cells 3,950,000, white blood cells 5,000, polymorphonuclears 76 per cent, lymphocytes 24 per cent. The patient was extremely toxic and debilitated. At the end of forty-eight hours her temperature rose to 103.4°F., at which time August 10, 1942, ultraviolet blood irradiation was instituted (290 cc. of patient's blood being irradiated according to the Knott technic). During the first forty-eight hours the patient's toxic symptoms began to subside, the groin lesion broke down in several places, and the foul discharge became more profuse. The patient's temperature remained elevated at 102°F. On the third post-irradiation day the temperature began to drop and the drainage was markedly less. The patient's general condition had improved markedly. On August 15, 1942, the inflammatory process along the course of the saphenous and femoral veins had definitely subsided; pain, tenderness and swelling had disappeared. In the remaining few hospital days a rapid healing of the whole ileo-inguinal skin area occurred and the ileo-inguinal lymph glands, although still palpable, had lost their original induration. The patient convalesced uneventfully, and at the time of discharge on August 21, 1942, eleven days after a single blood irradiation, she was in excellent general condition, and the ileo-inguinal, femoral skin lesion had healed.

CASE 8. No. 70645, age forty-three, a male, was admitted to the hospital October 28, 1941, complaining of severe pain and extensive swelling of the left leg. Physical examination revealed deep, extensive thrombophlebitis of the left leg with marked induration of the edematous tissue which apparently had been present two weeks previous to admission, and

was secondary to a puncture wound of the foot. At the time of admission the patient's temperature, pulse and respiration were normal. Heat was applied and four therapeutic nerve blocks were given on October 30, 1941, November 13, 1941, November 30, 1941 and January 2, 1942. No relief of pain, tenderness or swelling was observed following any one of these blocks, and the patient was unable to bear weight on the thrombophlebitic limb at any time. On January 12, 1942, ultraviolet blood irradiation therapy was given (215 cc. of patient's blood being irradiated according to the Knott technic). Within twelve hours the patient stated that his pain was markedly diminished, and within twenty-four hours said that it had disappeared completely. At the end of forty-eight hours no tenderness could be observed, there was no appreciable reduction in swelling, and the patient was able to balance weight on the swollen limb. He was discharged from the hospital pain free and ambulatory on January 20, 1942, in a relatively improved condition, seven days after a single blood irradiation.

CASE 9. No. 71548, age twenty-four, a female, was admitted to the hospital February 6, 1942, and on February 8, 1942, delivered a normal infant. The first four postpartum days were uneventful, and on the fifth postpartum day an acute bilateral femoral phlebitis developed. A heat cradle and hot compresses were applied, and sulfathiazole gr. 45 initially and gr. 15 every six hours was given. After seventy-two hours of this combined therapy had failed to relieve the patient's symptoms of pain, tenderness and swelling, the sulfathiazole was stopped, and on February 16, 1942, the ninth postpartum day, ultraviolet blood irradiation therapy was administered (225 cc. of patient's blood being irradiated according to the Knott technic). Within twelve hours the patient's temperature fell to normal and the pain and tenderness disappeared. Forty-eight hours later no swelling could be observed. The patient was discharged February 21, 1942, five days after ultraviolet blood irradiation.

On returning home the patient began immediately to carry on normal, strenuous household duties, and suffered a recurrence of bilateral thrombophlebitis. She was readmitted to the hospital March 6, 1942, with a recurrence of pain and tenderness of both femoral regions, and a marked edema of both legs; her temperature had remained normal. At this time the patient also complained of dull pain in the right

lumbar region. Blood count and urinalysis taken at this time proved normal. Ultraviolet blood irradiation therapy was repeated the day of admission March 6, 1942 (225 cc.). The following day the patient's pain and tenderness seemed much less severe, although the pain in the right lumbar area persisted. The pain, tenderness and swelling subsided completely but slowly during the fourteen days subsequent to irradiation. Her convalescence during this time was uneventful. At the time of discharge March 20, 1942, her condition was apparently good. No further recurrence of phlebitis has been observed.

CASE 10. No. 76953, age forty-seven, a female, was admitted June 17, 1942, and prepared for vaginal hysterectomy. On the sixth hospital day, June 23, 1942, a supravaginal hysterectomy, bilateral salpingo-oophorectomy and Schroeder amputation of cervix were performed. On the evening of the day of operation the patient's temperature rose to 101.2°F., pulse to 116. This rise in temperature and pulse rate persisted for three days, the temperature then falling slowly to a level ranging between 99° and 100°F., and her pulse remaining at an approximate 100. On the twelfth postoperative day the patient began complaining of some tenderness of the left leg, femoral area, her temperature rose to 101.8°F., and pulse rate to 120. On the following day her temperature rose to 102°F., and pulse to 128. On the next day, with a marked increase in the pain and tenderness along the course of the femoral vessels in the left leg, plus a moderate amount of edema, a diagnosis of acute septic phlebitis was made at this time July 6, 1942, and the leg was elevated and a heat cradle applied. On the following day July 7, 1942, ultraviolet blood irradiation therapy was given (200 cc. of patient's blood being irradiated according to the Knott technic). Forty-eight hours later the patient stated that her pain was greatly diminished and tenderness over the femoral vessels of the left leg was markedly diminished. The patient's temperature, however, rose to a daily peak at a level between 100° and 101°F. for the next five days, although at the end of this period of time all signs of pain and tenderness had disappeared and edema was barely perceptible. It was believed that the large heat cradle which was being used during severe summer weather might possibly prevent normal dissipation of body heat, so this was removed. On the following day the patient's temperature

dropped to 99°F. The patient convalesced uneventfully from this point on with a morning temperature rise during the next few days to 99.6°F. She was discharged July 25, 1942,

eighteen days after a single blood irradiation, in apparently good condition and symptom free.

CASE 12. No. 75417, age eighteen, a female, was admitted June 24, 1942, complaining of

TABLE OF RESULTS OF ULTRAVIOLET BLOOD IRRADIATION THERAPY IN THROMBOPHLEBITIS

| No. | Age and Sex | Veins Involved | Type Etiological   | Symptoms Present at Time of Initial Blood Irradiation |      |            |                                    | Results   | No. of Uvbit*       | No. of Days in Hospital after Initial Uvbit |
|-----|-------------|----------------|--|---|------|------------|------------------------------------|---|---------------------|---|
|     |             |                |  | Edema   | Pain | Tenderness | Fever °F.                          |   |                     |   |
| 1   | 40 F        | LF             | Postoperative (nephropexy)   | +   | +    | +          | 99-104.4                           | Disappearance of pain, tenderness, and fever in 24 hrs., of swelling in 7 days.   | 1                   | 11  |
| 2   | 30 F        | LF             | Postoperative (appendiceal abscess)  | +   | +    | +          | 98-100.8                           | Disappearance of pain, tenderness, fever and swelling in 48 hrs.  | 2                   | 11  |
| 3   | 33 F        | LF             | Postoperative  | +   | +    | +          | None                               | Disappearance of swelling, pain, and tenderness in 48-72 hours.   | 1                   | 14  |
| 4   | 42 F        | LF             | Postoperative (hysterectomy)   | +   | +    | +          | 99-101.6                           | Definite reduction of pain, tenderness, and swelling in 48 hrs., temperature falling to normal. All disappeared in 7 days.  | 1                   | 7   |
| 5   | 32 F        | LF             | Postpartum   | +   | +    | +          | 103.8                              | All symptoms began to subside in 48 hours.  | 1                   | 22  |
| 6   | 18 F        | LF             | Post-Caesarean   | None  | +    | None       | 102.0<br>staph-albus<br>septicemia | Leg pain disappeared in 24 hrs., temperature normal after 2nd irradiation.  | 2                   | 11  |
| 7   | 48 F        | RF<br>RS       | Postinfections (infected varicose ulcer, erysipeloid skin lesion, lymphadenitis) | +   | +    | +          | 103.4                              | Pain, tenderness, edema disappeared in 5 days; skin infection also subsided in 5 days.  | 1                   | 11  |
| 8   | 43 M        | LF             | Postinfectious, wound of foot  | +   | +    | +          | None                               | In 48 hrs. pain and tenderness subsided, but not edema; able to walk for first time, since onset of pathology.  | 1                   | 8   |
| 9   | 24 F        | LF<br>RF       | Postpartum   | +   | +    | +          | 101-102                            | Pain, tenderness, swelling and fever disappeared in 12 hrs. Patient readmitted with feverless recurrence which subsided completely in 14 days; no further recurrence. | 1<br>1 (recurrence) | 5<br>14                                     |
| 10  | 47 F        | LF             | Postoperative (hysterectomy)   | +   | +    | +          | 102                                | Pain, tenderness, and swelling gone in 5 days; temperature fell to normal on 6th post-irradiation day, after removal of heat cradle.                                  | 1                   | 18  |
| 11  | 65 M        | LF             | Postinfectious (severe dental caries)  | +   | +    | +          | None                               | All signs of phlebitis disappeared in 15 days; teeth extracted, renal colic present, in remaining 13 days.  | 1                   | 28  |
| 12  | 18 F        | RS             | Postpartum   | +   | +    | +          | 99.6                               | Pain, tenderness gone in 10 days; fever and swelling in 72 hours.   | 1                   | 7   |
| 13  | 32 F        | RF<br>LF       | Postpartum (also pulmonary embolism)   | +   | +    | +          | 103.8                              | Leg and chest pain, tenderness and fever disappeared in 48 hours; swelling in 4 days  | 1                   | 7   |

Key LF—left femoral.  
RF—right femoral.  
RS—right saphenous.  
LS—left saphenous.

\* Uvbit—ultraviolet blood irradiation therapy.

severe pain and swelling of the right leg, giving a history of an uneventful delivery and puerperium one month previous to admission. Physical examination revealed extreme tenderness along the course of the internal saphenous vein popliteal space, Scarpa's triangle and the right parametrium. Bed rest, elevation of leg and sedation were all given this patient, as well as stilbestrol. Twenty-four hours later the patient's symptoms remained unrelieved, and ultraviolet blood irradiation therapy was instituted (200 cc. of patient's blood was irradiated according to the Knott technic) at 11 A.M., June 29, 1942. At 9 P.M. the same night, the patient stated that her pain had subsided completely, and it was obvious that the swelling, while still present somewhat, had diminished markedly. Her temperature which never exceeded 99.6°F. fell slowly to normal during the next seventy-two hours, and she convalesced uneventfully pain and swelling being completely relieved and temperature normal at time of discharge on July 6, 1942, seven days after a single blood irradiation.

It is interesting to note that case reports Nos. 8, 1 and 9 portray typical failures of nerve block and sulfa drug therapy to retard the progress of acute thrombophlebitis. In Case No. 10, the failure of classical conservative treatment by means of heat and elevation of the extremity is demonstrated. In Case No. 7, we find that ultraviolet blood irradiation therapy alone has been used, with a definitely decreased hospitalization time. This latter, in our opinion, represents ideal treatment for acute thrombophlebitis in that the progress of the diseased process is usually checked by one blood irradiation, although a second one may be occasionally necessary.

#### CLINICAL OBSERVATIONS

The following clinical observations have been made consistently. These findings are easily duplicated, having been produced thirteen times consecutively. In each patient suffering from acute thrombophlebitis, who received ultraviolet blood irradiation therapy, the various classical symptoms subsided in the following manner:

1. *Pain* was the first to disappear; usually the patient stated it had left sometime in the first twelve hours following ultraviolet blood irradiation therapy. In some instances pain disappeared in two or three hours after blood irradiation. The opposite extreme was noted in individuals in whom pain, though much less severe in twelve hours, persisted mildly for forty-eight to seventy-two hours, the longest period required for the disappearance of pain. This striking and rapid relief of pain was usually appreciated most by the patient.

2. *Tenderness* along the course of the affected vein usually disappeared completely two to six hours after the subsidence of pain. This phenomenon is the first objective evidence of blood irradiation controlling the progress of an acute thrombophlebitis.

3. *Fever*, if present, consistently was found to drop to normal in twenty-four to forty-eight hours. The only exception to this was in individuals in whom abscess formation was also present or occurring, in which event the temperature remained elevated between 99° and 101°F. until the abscess was evacuated.

4. *Edema* was the last symptom to disappear and its disappearance time varied from twenty-four hours to ten days.

5. *Coldness* of the extremity, when present, was said to disappear within twenty-four to forty-eight hours following initial ultraviolet blood irradiation therapy.

6. The fact that a new thrombophlebitis (Case No. 9) occurred after a previous one had subsided and two weeks after a blood irradiation, suggests that blood irradiation exerts no prophylactic protective effect, at least for more than two weeks; the fact that the newly occurring thrombophlebitis, in turn, subsided rapidly after ultraviolet blood irradiation therapy and did not recur, speaks for itself.

#### THEORETICAL CONSIDERATIONS

The appearance, following ultraviolet blood irradiation therapy, of several of the known biochemical and physiological effects of ultraviolet, notably the bactericidal,

detoxification and vasodilation effects, as well as the increase in venous oxygen values of individuals with abnormally low venous oxygen content, has been reported by Miley,<sup>4</sup> Knott and Hancock,<sup>5</sup> Rebbeck<sup>6,7</sup> and Barrett.<sup>8</sup>

It seems rather unlikely that any of these four effects of ultraviolet, alone or combined, could completely account for the dramatic result observed in the thirteen cases reported. Therefore, it is not improbable that one or more other physiological or biochemical effects must be considered as partially responsible for this profound and rapid change in the status of the patient with acute thrombophlebitis.

In a recent report, Rebbeck and Miley<sup>9</sup> stated they had made the observation that, in patients with peritonitis with advanced and prolonged paralytic or adynamic ileus, a rapid and consistent restoration of gastrointestinal to normal smooth muscle tone and contractility occurred, often twelve to twenty-four hours after a single blood irradiation. This was observable clinically in this short period of time by the expulsion of flatus, disappearance of abdominal distention, the reappearance of normal intestinal motility and the reappearance of normal abdominal auscultatory signs. Such an effect represents a restoration to normal balance of that part of the autonomic nervous system directly controlling smooth muscle tone and contractility of the abdominal portion of the gastrointestinal tract, a part of the autonomic system hopelessly out of balance before the application of ultraviolet blood irradiation therapy.

Continuing along this line of reasoning it is possible, in the light of the clinical effects observed in acute thrombophlebitis following ultraviolet blood irradiation therapy, to draw an analogy and point out that there also obviously occurs a restoration to normal tone and contractility of the smooth muscle elements of that portion of the peripheral vascular system directly affected by the pathology of acute thrombophlebitis. Again we find in turn a marked restoration to normal balance of those

automatic fibers innervating those blood vessels affected by the thrombophlebitis, fibers which previous to blood irradiation were in an advanced state of imbalance, as shown by their partial or complete atony.

Whether the effect of irradiated blood is directly on smooth muscle in the instances of paralytic ileus and thrombophlebitis mentioned, whether it is involved with the acetylcholine mechanism directly, whether it is a direct effect on peripheral or post-ganglionic autonomic fibers or a central effect, it is impossible to say. In view of the lack of evidence, especially in acute thrombophlebitis, of central and generalized autonomic nervous system imbalance, and in view of the purely local type of autonomic imbalance, one would consider a localized peripheral action of irradiated blood on that part of the autonomic system in a state of marked and obvious imbalance a distinct possibility. Against this view is the obvious fact that marked generalized peripheral vasodilation occurs with almost monotonous frequency following blood irradiation, that frogs irradiated externally with ultraviolet show vasodilation not only of the cutaneous capillaries but also of the capillaries of the large viscera; both of these effects are possibly due to direct stimulation of the medullary vasomotor centers, of preganglionic parasympathetic fibers, or to a diffuse, generalized post-ganglionic stimulation, and are not necessarily associated with a previously existing breakdown of autonomic nervous system control.

It is interesting to observe that the grossly discernible vasodilation effects noticed following application of ultraviolet blood irradiation therapy occurs in apparently normal humans, as well as in those who are suffering from various disease processes, whereas an increase in tone of normal gastrointestinal smooth muscle is not apparent, at least not to the extent that it produces colicky or cramp-like contractions. Likewise, as just stated, no evidence of an increase in smooth muscle tone, as in acute thrombophlebitis with edema, appears in normal individuals following blood

irradiation, but, on the contrary, only vasodilation. Therefore, it must be assumed that there exists a profound and fundamental regulating effect of irradiated blood upon the autonomic nervous system; this effect could be described as a "normalizing" effect and becomes most apparent in definite imbalance of the autonomic system.

In any event, there exists a close relationship between ultraviolet blood irradiation therapy on one hand and the restoration to normal of an autonomic regulatory mechanism hopelessly out of balance secondary to such pathological processes as found in paralytic ileus and acute thrombophlebitis. That this effect represents a subtle mechanism of an enzymatic or catalytic motive, is theoretically possible and suggests itself. A more simple theoretical explanation would be that individuals who respond to ultraviolet blood irradiation therapy so obviously, may be suffering from ultraviolet deprivation brought about by a breakdown, secondary to various disease processes, of the body's mechanism for absorbing ultraviolet, by an inadequate supply of ultraviolet, or by a combination of both.

Again we wish to emphasize that ultraviolet blood irradiation therapy produces some known and probably many unknown biochemical and physiological effects of ultraviolet energy and is not specific treatment for any disease. However, it is equally true that those disease processes which can be benefitted by the production of the aforementioned effects of ultraviolet energy probably will be controlled efficiently by ultraviolet blood irradiation therapy.

#### SUMMARY

1. In thirteen consecutive instances, individuals with acute thrombophlebitis were given ultraviolet blood irradiation therapy.

2. In all thirteen, a rapid disappearance of pain and tenderness was observed, usually within twenty-four to forty-eight hours following a single blood irradiation.

3. A drop to normal of abnormally high temperatures, when present, was found to occur within forty-eight to seventy-two hours.

4. Edema subsided completely in twelve of the thirteen cases, the disappearance time varying from thirteen to fifteen days. In the thirteenth case, a marked induration was associated with edema and neither had disappeared when the patient left the hospital on the eighth postirradiation day.

5. A complete absence of untoward effects in all patients treated was evident.

6. Of the thirteen cases, five were good examples of the failure of sulfa drugs plus local heat, bedrest, and elevation of the affected extremity to control thrombophlebitis; four received only ultraviolet blood irradiation therapy and bedrest; three had failed to respond to local heat, bedrest, and elevation of the affected extremity; and one represented the absence of any effect, in fifty days, of four therapeutic nerve blocks to influence the disease process; an apparent permanent indurative damage had occurred.

#### CONCLUSION

1. A new phenomenon, the relatively rapid disappearance of the classical signs of thrombophlebitis following ultraviolet blood irradiation therapy, has become apparent.

2. The excellent results observed in the thirteen consecutive cases reported warrants the further clinical application of ultraviolet blood irradiation therapy in individuals suffering from acute thrombophlebitis.

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