

RADIOTHERAPY OF CANCER OF THE CERVIX AT THE RADIUM INSTITUTE, PARIS, FRANCE

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CLINICAL experience with radiation therapy in cases of cancer of the cervix has shown that by the use of this method in inoperable cases it is frequently possible to obtain palliative results and occasionally permanent regression of the disease. In early operable cases the results of radiotherapy have in a number of clinics been comparable to those obtained by surgery.¹ Some clinicians² have adopted this therapy in preference to operative treatment, especially as the primary mortality with its use is negligible in comparison with that following surgery. While it is generally conceded that radiotherapy is of value in the treatment of cancer of the cervix, the method of its application still remains a moot question. In this paper it is the intention of the writer to present the view held on this subject at the Radium Institute at Paris, France.

When a case of suspected carcinoma of the cervix is seen at the Radium Institute for the first time, a thorough clinical examination is made. The extent of the involvement, patency and size of the uterine canal are determined. A bacteriological examination of the vaginal flora is made. A biopsy is performed and a plan of treatment is outlined.

Histology. If the histological report is epidermoid carcinoma the case is treated only with radiotherapy. Surgery is not resorted to even in early operable cases, except if the growth proves to be an adenocarcinoma. In the latter a radical hysterectomy is done three or four weeks after a thorough course of radiotherapy has been given. Nearly all recurrences of early cervical cancers, irradiated at the Radium Institute, were adenocarcinomata. Hence, these growths are regarded as radioresistant, an observation which has also been made by Lahm,³ Adler⁴ and others. Among the epidermoid carcinomata, those with a predominance of prickly cells and a tendency towards glandular differentiation

are considered to be less radiosensitive than those with complete stratification and development of hornified cells. However, this variation in structure does not influence the plan of treatment in epidermoid carcinomata.

If the growth is of the papillary cauliflower variety spreading along the surface without apparent invasion of the deeper structures, the tumor is regarded as more favorable for radiotherapy than when an infiltrative ingrowing tendency is noted. Infiltrations of the anterior or posterior vaginal septa are looked upon as especially grave; rectovaginal and vesicovaginal fistulae usually follow energetic radiotherapy of this complication.

Infection of the deeper structures is considered a contraindication to radiotherapy. This occurs especially frequently in the infiltrative variety of cancer. For instance, radiation is not given in the presence of parametritis or pelvic cellulitis. Neglect of this precaution has at times been followed by a localized chronic peritonitis which slowly saps the strength of the patient, or by the rapid spreading of the infection and death from bacteremia. Obese, anemic women suffering from chronic, debilitating diseases, such as diabetes, nephritis, etc., appear to have been especially subject to this complication. The only exception to this rule is made in cases of early papillary cauliflower growths, as the infection here is usually localized to the surface of the neoplasm, and the shedding of the radiation slough carries away with it the entire area of infection. Latent infection in the peritoneal tissues is regarded as dangerous. Exacerbation of the infection has followed internal or external irradiation by roentgen rays or radium, or the preliminary intrauterine instrumentation alone. A sterile pyometra has thus become secondarily infected after dilatation, and latent salpingitis lighted up by irradiation. Bumm⁵

and others⁶ have reported similar experiences. To clear up infection, daily vaginal and occasionally intrauterine irrigation of sterile water, or normal salt solution are employed; also swabbing with glycerine or 10 per cent glucose solution, as suggested by Nogier. For staphylococcus infection surgical cleanliness and vaccines are employed. For spirillum infections, bismuth paste locally and salvarsan intravenously are given.

After the extent, the clinical and his-

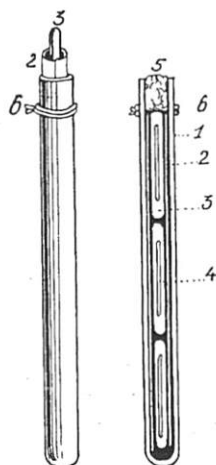


FIG. 1. Uterine applicator. 1. Rubber catheter. 2. Aluminum foil. 3. Platinum filter. 4. Radium or radon tube. 5. Cotton plug. 6. Ligature tying catheter.

tological variety of the growth have been determined and after the infection has been taken care of, a plan of radiotherapeutic procedure is outlined.

The anatomical localization of cervical cancer is such that usually two avenues of approach for attacking the disease by irradiation are feasible. The radiation may be applied from without, that is, through the skin, or from within, that is, through the vagina and uterine canal. Where the disease is localized to the cervix, the latter approach is usually easier than the former. Where invasion has taken place into the outer parts of the parametria or pelvic glands this portion of the disease is closer to the body surface and therefore more easily influenced by irradiation from without. When external irradiation is employed it is necessary to traverse a great bulk of normal tissue before reaching the cervix. The

greater portion of the radiation intensity applied on the surface is absorbed in the intervening structures and may affect such radiosensitive organs as the rectum and bladder. When radium is placed in the uterine canal the walls of the uterus act as a screen and increase the distance between the source of radiation and the rectum and bladder. This distance may also be increased by gauze packing in the vagina. After hysterectomy the narrow finger-shaped fornix offers little room for gauze packing. The source of radiation is therefore brought into closer contact with the bladder, rectum, and loops of intestines. Smaller radiation intensities must consequently be given in these cases, which partly accounts for the poor radiotherapeutic results after hysterectomy. In these cases as well as in cases in which anatomical deformities, such as atresia or obstruction of the vagina or of the cervical canal preclude the proper placing of the internal radiating focus, external radiation therapy is principally relied upon.

Only local radiotherapy is relied upon in the treatment of cancer at the Radium Institute. They do not employ roentgen rays in fractional erythema intensities to the thymus, spleen and lymph nodes as suggested by Fränkel,⁷ with the hope of increasing the resistance of the body to cancer. In the majority of cancer patients these organs are undergoing a normal process of age involution at the time when they are first seen. If irradiated with small doses of roentgen rays, this age atrophy is probably accelerated as may be assumed from some experimental work of the writer⁸ on the action of small doses of roentgen rays on the thymus of the rabbit.

No attempts have been made recently to increase the body resistance to cancer by injections of foreign proteins⁹ or of various anticancer vaccines¹⁰ at the Radium Institute. Neither diathermia¹¹ nor the galvanic current¹² has been used to increase the radiosensitiveness of the cancer cells, nor have secondary radiators, e. g., such as those used by Wintz,¹³ been employed to increase the local effectiveness of the rays. Irradiation of metastases in pelvic glands and parametria has not been attempted by inserting radium through bilateral incisions

in the ischiorectal fossae,⁵ or by passing a chain of radium capsules extraperitoneally along the pelvic wall through inguinal and perineal incisions.¹⁴ The experience with interstitial implantation of filtered or unfiltered radium into palpable metastases in the parametria through a laparotomy wound¹⁹ has yielded such poor results that this method of approach has been given up at the Radium Institute.

If the cancer is localized to the cervix, with or without slight invasion of the inner

roentgen therapy had followed treatment with radium, were alive at the end of a like period. Experience with other epidermoid carcinomata, for instance, those of the skin, has also shown that these growths will react to radium after unsuccessful roentgen therapy, while they will not respond to roentgen therapy after radium treatment has proved inefficient.

The principles of roentgen therapy consist in giving small doses of highly filtered roentgen rays for one hour, twice daily,

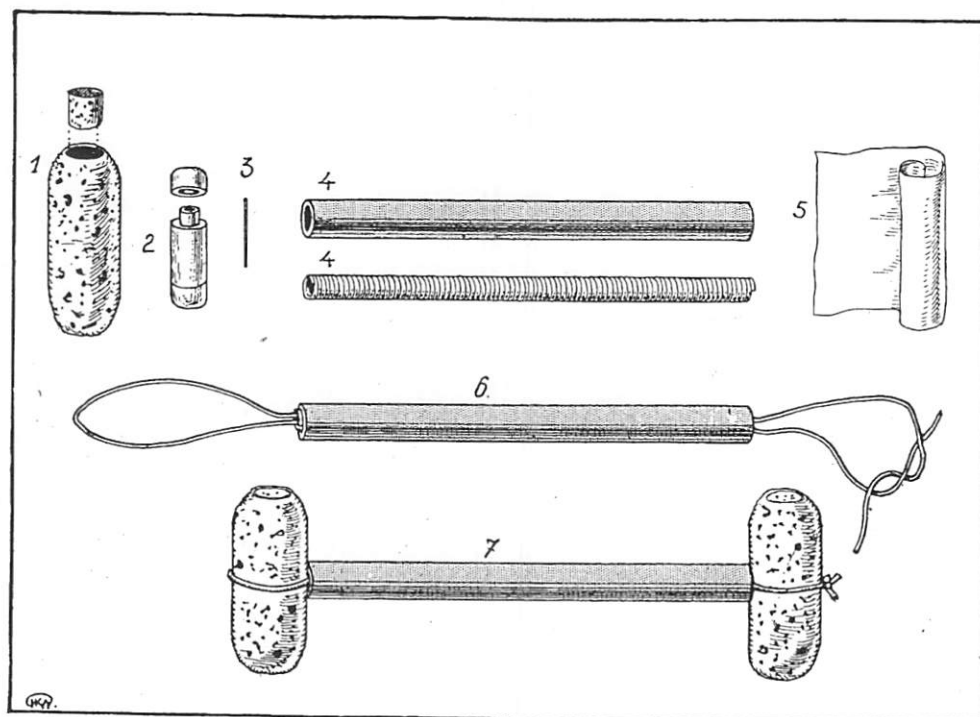


FIG. 2. Vaginal applicators. 1. Cork with plug removed at one end. 2. Platinum capsule for radium. 3. Glass tube containing radon or radium. 4. Steel spring and rubber tube covering. 5. Aluminum foil for secondary filter. 6. The spring of the colpostat ready for attachment of corks. 7. The colpostat ready for use.

portions of the parametria, the uterine and vaginal canals are used as the only localizations for the irradiating substance. External radiotherapy is added only if the disease extends to the outer portions of the parametria or pelvic glands, or if anatomical deformities preclude proper irradiation from within. When radium and roentgen rays are combined, the roentgen treatment precedes the curie therapy. Of 10 cases in which this was done, 3 cases were free from clinical evidence of disease two and three years later, while none of 10 cases in whom

for a period of ten to twenty-five days; i.e., twenty-five to fifty-five hours of actual irradiation are administered during this period. The treatment is interrupted if any symptoms of intestinal irritation, such as diarrhea or cramps occur. The patients usually gain strength, appetite, and weight during the course of the treatment. The radiant energy is administered in the following manner: A 200 kv. transformer machine, 4 ma., 2 mm. zinc, 3 mm. Al and 3 cm. wood filter, 50 cm. focal distance, and usually six or more over-lapping 15×15

cm. fields are used. The fields are abdominal, gluteal, lateral and perineal; each field receives on the average of 2 or 3 H per hour, 12 H producing an erythema and 35 H a second degree dermatitis under these conditions. A total of 100 to 120 H, i.e., 28,000 Solomon R units, or 13,000 Behnken R units are thus given to all fields if internal irradiation is not to be used, or 70 to

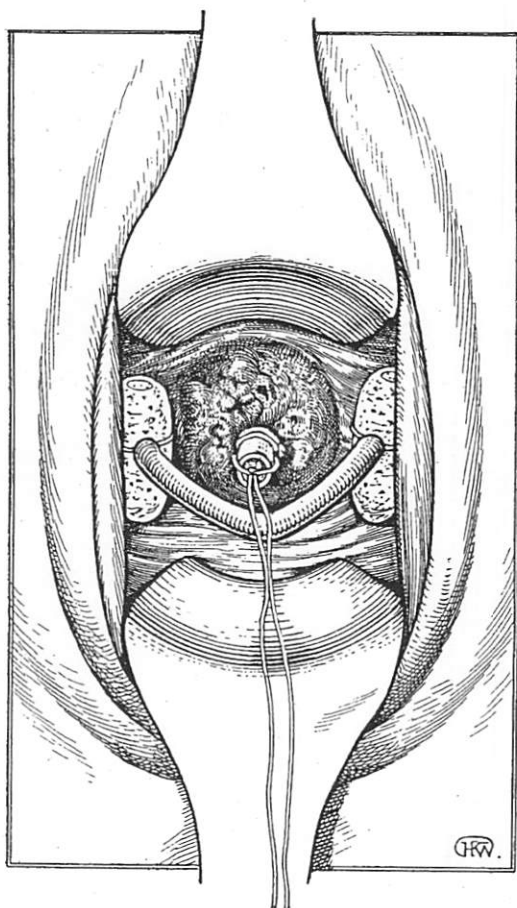


FIG. 3. Cervix viewed from the vagina. End of uterine applicator slightly protruding from the cervix. Corks of the colpostat in each lateral fornix.

80 H if radium in the uterus and vagina is to be employed.

For curie therapy the patient is prepared as for an operation—bowels cleaned out, vulva shaved, vagina cleansed, uterine and vaginal applicators prepared and sterilized. Gradual dilatation with Hegar dilators up to size 10 French is performed, and the uterine applicator is inserted as the last dilator is withdrawn. If a pyometra is

discovered at this time or if any infection of the uterus or adnexa is found, irradiation is not started until the infection has cleared up. Should an obstructing cauliflower mass, or ulcerating growth at the external os make the localization of the cervical canal impossible, vaginal irradiation is used first; in eight or ten days, the obstructing growth sloughs off, and the cervical canal can then usually be found; if this cannot be done external irradiation is relied upon.

When the uterine applicator is in place, a small tampon of ichthyol glycerine is placed against the cervix and this is followed by insertion of the vaginal applicators into each lateral fornix. Lastly gauze packing is inserted so as to push the rectum and bladder as far as possible from the radium. The irradiation is continued for five to seven days until the desired dose has been given. The treatment is never repeated unless recurrence takes place. Once a day the applicators are removed, cleansed and the uterine applicator is boiled. A vaginal douche of hot water is given and the applicators reinserted at once.

If fever or chills occur during the irradiation the uterine applicator is removed so as to allow free uterine drainage, while the vaginal irradiation may, or may not, be continued. If the temperature does not become normal within twenty-four hours all irradiation is discontinued until all signs of infection have disappeared.

The uterine applicator consists of a 2 mm. thick, 6 cm. long, para rubber catheter free from metal. It is blind at its uterine end and open at its vaginal end. Its bore is 3 mm., i.e., broad enough to admit the usual radium bearing capsules, which are inserted into it, one behind the other; the vaginal end is securely tied by a silk ligature. There are usually employed three, but at times one or four radium bearing capsules, depending upon the size of the uterine canal as determined at the first clinical examination. The rubber catheter is correspondingly shorter or longer but usually measures 6 to 7 cm. Each radium bearing capsule is 20 to 22 mm. long, has a radiating surface of 0.6×15 mm. and has a wall thickness of 1 mm. of platinum. Each capsule is individually wrapped in alumi-

num foil 0.2 mm. thick to arrest the secondary radiation from the platinum. The upper capsule, nearest the fundus, usually contains 6.66 mg. of radium element; each of the lower tubes contains 13.33 mg. radium element. Rarely when radon is used, the initial quantity is 15 to 20 millicuries per tube; 13.33 mg. element delivers 100 "millicuries destroyed" per hour and 6.66 mg. gives off half of this amount. The uterine applicator usually contains a total of 33.32 mg. of radium element and therefore delivers 30 "millicuries destroyed" in five days, i.e., in round numbers 4000 milligram-hours. The catheter is semi-flexible and adjusts itself to the contour of the uterine canal. It usually has a radiating surface of 6 to 7 cm., a focal distance of over 3 mm. and the rays are filtered through 1 mm. of platinum.

The vaginal applicators consist of similar radium bearing capsules, containing 13.33 or 6.66 mg. radium element. However, they are of 2 mm. platinum wall strength and each capsule is inserted through the center of an ordinary cork 1.5 cm. broad and 2.5 cm. long. This leaves more than 0.5 cm. wall of cork on either side, for focal distance. After the radium capsule with its aluminum wrapping has been inserted into the cork, the open ends are closed by little cork plugs and the cork tied along its long axis by a silk ligature. It is then immersed in boiling paraffin at 120° c. for twenty minutes. This sterilizes the applicator and covers it with an impermeable layer. Two of these corks are usually mounted on a 1 × 10 cm. steel strip covered by rubber tubing and the applicator is then known as a colpostat. The corks of the colpostat are inserted one into each lateral fornix with ends directed towards bladder and rectum and the steel strip bent into a U with the open end towards the cervix. The spring action of the steel strip forces the corks against the vaginal wall and maintains them vertically in the vagina in close proximity to the parametria, while the bladder and the rectum receive the radiation only from the ends of the capsules. As the metal strip passes in front of the os, it also prevents the radium bearing catheter from slipping out of the uterine canal, especially if a small piece

of gauze is placed against the cervix. An additional third or even fourth cork in front and behind the cervix may now be inserted if room permits and circumstances demand it. If the disease appears to be unilateral, the stronger radium capsule is placed closer to the diseased area, while the weaker is inserted into the opposite fornix. About 26.66 mg. of radium element

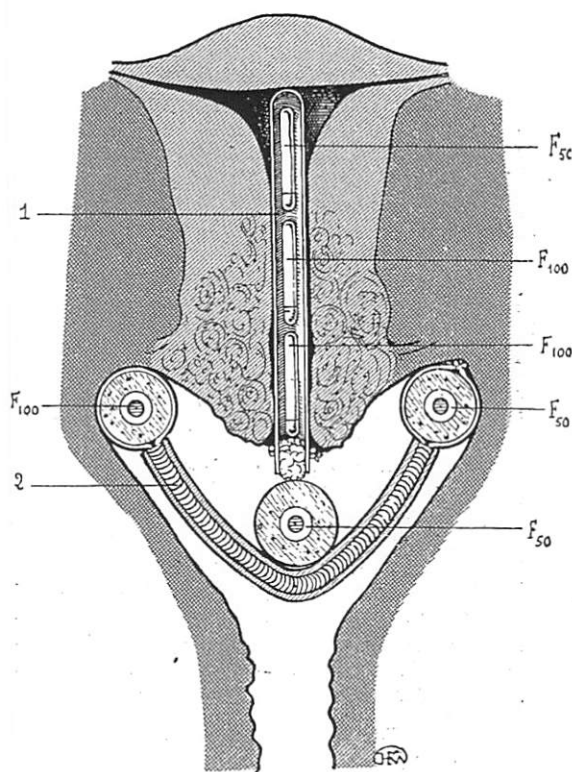


FIG. 4. Cross section of uterus and vagina with radium applicators in position. 1. Uterine applicator consisting of three tubes, the upper focus (F) delivering 50 microcuries, the lower two each 100 "microcuries destroyed" per hour. 2. Cross section of three vaginal "corks" with vaginal radiating foci (F), one delivering 100, the other two each 50 "microcuries destroyed" per hour. Two of the corks are mounted on the colpostat while one is lying free.

is usually employed in the vaginal applicators. If left in place for five days this will deliver 24 "millicuries destroyed", i.e., 3168 mg-hr. In other words, 7200 mg-hr. may thus be given with the uterine and vaginal applicators, while using only about 60 mg. of radium element.

If this method is compared with those in use at other clinics its advantages become apparent. The long radiating surface of the

uterine applicator not only irradiates the entire cavity of the uterus, but delivers a greater depth dose than do the shorter applicators of the same strength used in other clinics.³ The use of the platinum filtration reduces the bulk of the applicator and permits the employment of large radiation doses. Whether the use of such heavy filtration, or its lead equivalent as employed by Heyman is essential may be questioned. Bumm,⁵ Döderlein,¹⁵ Kehrer,³ and Healy¹⁶ who use lighter filters also show good results. The vaginal radium bearing corks are pressed into the fornices by the spring action of the colpostat and the radiating foci are thus brought closer to the parametria than when pessaries are used for holding the radium in position.³ On the other hand, it would seem that exact localization of an applicator against small infiltrations in the vaginal mucosa or cervical crater, can be attained more accurately by such flat and conical applicators as used by Heyman,² while involvement of the vault of the fornix after hysterectomy, may possibly be more easily treated by a bomb as used at the Memorial Hospital.¹⁶ However, it takes 1000 mc. to fill the Memorial "bomb" in contrast to less than 30 mg. of radium needed for vaginal corks as used at the Radium Institute. The continuous slow irradiation may also be of advantage as it probably strikes more cancer cells during the state of mitosis, that is, during a period of their greatest radiosensitivity, than does the same amount of radiation given over a shorter time. The likelihood of infection when a uterine applicator is left in for six days is not as great as might be assumed. There were only 6 among 362 treated and traced patients, with carcinoma of the cervix at the Radium Institute, who died from infection following the treatment. The total dose of 7000-8000 mc-hr. seems to be correct, as lesser amounts or very much larger doses do not yield as good statistics. The results of Clark,¹ who used 4800 mc-hr., divided into two sessions, six weeks apart, are not as good as those of Bumm, Kehrer, Döderlein, Heyman and Healy, all of whom use on the average from 6000-7000 mc-hr. On the other hand, Lahm³ reports bad results from doses

larger than 10,000 mc-hr.; Bumm⁵ noted perforations into the rectum and bladder when larger doses were used. The omission of external roentgen therapy in early operable cases does not seem important, if sufficient radium is used in the vagina and cervix. This is illustrated by the results of Healy who in addition to an excellent radium technique uses roentgen therapy in every case including early operable cases. His results are no better than those of Heyman and Kehrer who limit the use of roentgen therapy to far advanced cases.

The technique described has been in use at the Radium Institute since 1920. In the first and second years, the work was done at various hospitals and lacked system. The results therefore are not as satisfactory as those of the last three or four years, since which time the technique has been standardized and all patients treated under the direct supervision of Prof. Regaud at the Pasteur Institute, Chantin Hospital and Radium Institute.

The improvement in the results becomes evident when one compares the number of cases judged as free from clinical evidence of disease at the end of the first year. These steadily improved with each year: thus in 1919, 14.9 per cent of the cases, i.e., 13 patients, were judged clinically free from evidence of disease; in 1920, 23.8 per cent i.e., 21 cases; in 1921, 40.9 per cent; in 1922, 37.7 per cent; in 1923, 43.9 per cent were classified as free from clinical evidence of disease at the end of one year. That this classification was fairly correct may be seen from the fact that of the 13 cases treated in 1919 eight remained well four to five years later, and of 21 cases of the 1920 series 17 remained well three to four years later.

There were 403 cases of cancer of the cervix treated at the Radium Institute in the years 1919 to 1923. Of these 10 per cent were early operable; 33.5 per cent doubtful and 56.5 per cent inoperable. Of the 403 cases, 41 cases cannot be utilized for statistics as they had been lost sight of while improving, or histological examination had failed to support the clinical diagnosis of cancer, or death had occurred due to intercurrent disease, while the cancer had healed. There were left 362 histologically

proven cases which could be traced. Of these, 211 were inoperable and 151 early operable or of borderline operability. Of the 362 patients traced up to September, 1925, 236 died of cancer; 6 died of infection following the treatment in 1919 and 1920; 28 were living but presented evidence of the disease; 3 had hysterectomies done and the uterus in each showed the presence of cancer on section; 95 patients, i.e., 26.2 per cent of the total were alive and free from clinical evidence of disease; 59 of these were early operable or of doubtful operability, while 36 were inoperable. Of the 95 cases there were treated:

9.1 per cent or 5 operable or borderline cases and 3 inoperable cases in 1919.

19.3 per cent or 10 operable or borderline cases and 7 inoperable cases in 1920.

29.5 per cent or 9 operable or borderline cases and 4 inoperable cases in 1921.

34.4 per cent or 13 operable or borderline cases and 8 inoperable cases in 1922.

43.9 per cent or 22 operable or borderline cases and 14 inoperable cases in 1923.

These results compare favorably with the results of most other clinics and justify the employment of the technique described.

CONCLUSIONS

1. The technique of the treatment of carcinoma of the cervix by radium and roentgen rays should be influenced by anatomical, histological and bacteriologic considerations and the clinical aspect of the case.

2. The technique employed at the Radium Institute of Paris represents an efficient method for this treatment with a small initial quantity of radium.

In conclusion, I wish to thank Prof. Regaud and his associates Drs. Lacassagne, Monod and Coutard for helping me to familiarize myself with the technique described and for permitting me to use their material in publication of this paper, and Miss Turnessen for help in collection of the records.

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CARBON ARC AND FLAME LAMPS IN MEDICINE AND SURGERY

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INTRODUCTION

SINCE the use of carbon arc and flame lamps in medicine and surgery is on the increase, it has seemed interesting to review the physical and historical background of the subject. It is hoped that modern phototherapy will fill a void in the field of therapeutics. In the meantime, these historical chapters may be found of value.

HISTORY OF PHOTOTHERAPY

The virtue of sunlight was known to the ancients. The Old Testament mentions a long line of sun worshippers. Greek and Roman students of the philosophy of medicine made deliberate use of sunlight. The Greeks were in the habit of exposing themselves, unclad, on the roofs of their dwellings for sunbathing as health measures.

We can refer to Hippocrates, the Father of Medicine, who lived about 400 years B.C. on the island of Cos, in the Greek Archipelago. A great Health Temple was erected to Aesculapius, god of the sun, medicine and music. This temple was rediscovered recently, and the remains excavated. We are told that the priests in the temple were also physicians. The natural agencies of air, light, and water were used in the cure of disease, and in the pursuit of both physical and mental culture. Recall that Greece at this period produced the greatest athletes, philosophers and poets of any known civilization. The beauty of the classic Greek form, both male and female, has not been equalled since. The temple, known as the Aesculapion, was built a little inland from the sea on the slopes of a range of mountains,