A Clinical Evaluation of Thermography and Heptyl Aldehyde in Breast Cancer Detection

WILLIAM R. VOGLER and RALPH WALDO POWELL

(National Cancer Institute, U.S.P.H.S.; and Robert Winship Memorial Clinic, Emory University, Atlanta 22, Ga.)

Recent reports by Lawson et al. (6-8) on skin temperature elevations over malignant lesions of the breast and a drop in these temperatures following the administration of heptyl aldehyde suggest the possibility of devising a screening procedure for the diagnosis of breast cancer. Using a thermocouple, Lawson recorded the temperatures in 26 patients subsequently found to have breast cancer. He reported a temperature rise of from 1.3 to 3.5°F., averaging 2.27°F., in either the area over the tumor or the ipsilateral areola. He also noted decreased temperatures over cystic lumps.

In 1932 Strong (9) reported a delay in the onset of mammary cancer in Strain D mice fed varying amounts of oil of gaultheria. It was thought that enzymatic activity was inhibited by oil of gaultheria. Supposedly, this decreased activity was responsible for the delay in the onset of mammary cancer in mice. The active ingredient was heptyl aldehyde, found in the low boiling fraction of the oil. The drug proved to be unstable and locally irritating at the site of injection. The addition of sodium bisulfite not only stabilized the drug but made it less irritating and at the same time did not alter the effect of the drug on mammary cancer. Baumann (2) in 1938 found no inhibition of tumor growth in several animal species with different types of cancers. In all cases the drug was given orally. In 1940 Boyland (3) found the drug to be only moderately effective orally, and Strong (10) stated that the best results were obtained when it was injected parenterally. He found also an optimal dose which was less effective when decreased or increased. With this optimal dose he obtained liquefaction in 58.6 per cent of tumors in mice. Herbut et al. (5) in 1951 reported their experiences using heptyl aldehyde-sodium bisulfite with natural thyroxin in treating Walker rat carcinoma 256. The drugs, when injected subcutaneously and separately, produced complete tumor regression in 25 per cent and improvement in 36 per cent of their animals. Lawson (7) noted a rarity of breast cancer in Eskimo women whose diet consists of large quantities of rancid fat which contains oil of gaultheria.

Abels et al. (1) in 1944 reported no success in clinical trials of heptyl aldehyde-sodium bisulfite in patients with advanced breast cancer. Using pure heptyl aldehyde Lawson (6) reported a favorable response in one patient. He noted that, within 5 minutes of an intramuscular injection in the gluteal region, two patients experienced a pain response in malignant tumor sites. Extending his study to patients with localized breast cancer, he found that 80 per cent showed some reaction to the drug 4-8 minutes following injection. This was usually characterized by pain or a "tight sticking feeling in the tumor itself." In every case of breast cancer he noted a "distinct drop in skin temperature over the tumor within ten minutes after injection." In benign and inflammatory conditions of the breast he noted no thermal changes after administration of heptyl aldehyde.

Obviously, the development of a safe, reliable test for the early detection of cancer is of singular importance. In view of the above-mentioned reports, we undertook the following clinical study.

MATERIALS AND METHODS

We attempted to answer the following questions.

1. Are skin temperatures significantly higher over malignant breast lesions than over benign lesions?
2. Can heptyl aldehyde be administered safely, and does it have any beneficial or harmful effects?
3. Will heptyl aldehyde lower skin temperatures over malignant lesions?

With the use of a thermocouple manufactured by U.M.A., skin temperatures were measured on patients who had been referred to the Robert Winship Memorial Clinic with breast masses. The patient was placed on an examining table, the breasts exposed to room temperature for 15-30 minutes, and, once stabilized, the temperatures in each quadrant, areola, and over the lesion were

Received for publication September 4, 1958.

1 U.M.A., Inc., 56 Cooper Square, New York, N.Y.
taken by one of us. This was repeated on the opposite breast. The presence of clinical signs of malignancy was recorded and the examiner's impression noted. After the final diagnosis was established either by histological examination of solid tumors or by aspiration of a cyst, often with cytological examination, the data were analyzed. Those not having a confirmed diagnosis were excluded from the study. The patients were then divided into two groups, those with cancer and those with benign tumors (fibroadenomas, intraductal papillomas, localized mastitis, and cysts). First, the average temperatures of all quadrants of each breast were compared. Then in the breast with the lesion the lower temperature in any quadrant except the lesion quadrant was subtracted from the temperature over the mass. The mean temperature elevation was determined for each group and a "t" test done, according to the formula:

\[ t = \frac{\text{difference between means}}{\text{standard deviation}} \sqrt{\frac{N_1 N_2}{N_1 + N_2}} \]

where \( N_1 \) = number in the cancer group and 
\( N_2 \) = number in the benign group.

Pure heptyl aldehyde was obtained from Eastman Kodak Company, redistilled, placed in ampules, and autoclaved. Each ampule contained 1.2 ml. of heptyl aldehyde (850 mg/ml). The drug was administered intramuscularly in the gluteal region in 1- or 2-ml. doses to several patients with various types of advanced cancer in an effort to note any toxicity or change in skin temperature over metastatic nodules. Because of the reports of Gerai (4) of toxic changes occurring in the livers and kidneys of laboratory animals, renal and hepatic function studies were done before and after treatment with the drug. (These studies included urinalysis, blood urea nitrogen, serum bilirubin, cephalin flocculation, thymol turbidity, bromsulfalein retention, total proteins, and A/G ratio.) At first 1 ml. was administered once or twice weekly. Later as much as 2 ml. was given daily over a period of 6–7 days.

RESULTS

Comparisons of average temperatures for each breast revealed no significant changes in the breast with the lesion in either the benign or malignant group.

The mean elevation of skin temperature over tumors in seventeen patients with subsequently proved carcinoma of the breast was 1.88°F. The mean elevation over 30 benign lesions was 1.61°F. (Table 1). This was found to be of no significance at the 5 per cent level.

The only immediate ill effect noted from the heptyl aldehyde was intense burning and pain at the site of injection. This proved to be the limiting factor in dosage. No changes were noted in blood urea nitrogen levels in any patients. In three patients (Table 2) receiving injections daily or more often over an 8–10-day period, slight rises in bromsulfalein were noted 1–7 days after completion of a course of treatment. In two autopsied patients examination of the liver revealed fatty metamorphosis and focal necrosis more evident in the central lobular areas. Both received the drug in the last month of life. Another patient treated 6 months previously showed minor fatty metamorphosis. One patient showed some tubular necrosis of the kidneys. No effects were noted on the tumor tissue.

No patients revealed any objective evidence of benefit from the drug in the doses given. At no time was pain noted in tumor nodules.

Temperatures taken over primary and metastatic nodules failed to show a drop as long as 1 hour after the administration of the drug in two patients with breast cancer and one with metastatic melanoma in the skin. The test was repeated on one breast-cancer patient the next day, with the same results. One patient with skin nodules in the scalp, metastatic from bronchogenic carcinoma, showed a drop of 1.5°F 10 minutes after injection of 1 ml. of heptyl aldehyde in the gluteal area. He noted no pain in the nodules.

DISCUSSION

In an attempt to devise a screening test for cancer, accuracy, speed, and simplicity are essential. Malignant tissues should have a faster meta-
bolic rate and produce more heat. However, we were unable to demonstrate any significant differences in skin temperatures over benign and malignant lesions, using a practical clinical instrument. Furthermore, we were unable to demonstrate any temperature drop in proved malignant lesions following the injection of heptyl aldehyde. The limiting factor in the therapeutic use of the drug proved to be local irritation. Although the number of cases undergoing therapeutic trial was small, we could demonstrate no improvement and did notice some impairment of bromsulfalein excretion. Although autopsies revealed fatty metamorphosis and central focal necrosis and degenerative changes in the livers, it cannot be stated with certainty that these changes were due to the drug. It is difficult to say why our results differ from Lawson’s. Perhaps some difference in technic or instrument sensitivity is responsible. We feel, since all of our temperature readings were done by one of us in the same room with the same instrument, that our technic was uniform.

SUMMARY

Skin temperatures were measured over benign and malignant breast lesions in a limited number of patients by a thermocouple device. Heptyl aldehyde was given by injection to determine its diagnostic and therapeutic usefulness. Under the conditions of this clinical study, the following conclusions are justifiable:

1. No easily measurable differences existed in the skin temperatures over benign and malignant conditions of the breast.

2. Heptyl aldehyde caused no lowering of temperatures over cancerous nodules, nor did it produce pain in the nodules.

3. In the doses used, heptyl aldehyde was ineffective therapeutically and may be hepatotoxic.

REFERENCES


A Clinical Evaluation of Thermography and Heptyl Aldehyde in Breast Cancer Detection

William R. Vogler and Ralph Waldo Powell


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