

Scalp Tourniquets For Chemotherapy-Induced Alopecia

By Mary B. Maxwell

Imaginative clinicians have tried a variety of interventions in an attempt to prevent chemotherapy-induced hair loss in cancer patients. Rubber bands, soft rubber tubing, and various inflatable cuffs have been placed around the head, and cold hair dryers, ice packs, and room airconditioners have been directed at the scalp.

Use of a scalp tourniquet has been the most persistent suggestion since 1966, when two letters to the editor appeared in the *British Medical Journal* declared that the use of an inflatable cuff around the head for five minutes at the time cyclo-

phosphamide (Cytosan) was injected, seemed promising in preventing hair loss^(1,2). The few brief evaluations of scalp tourniquet effectiveness in the literature since then, however, have been highly impressionistic and contradictory^(3,4,5,6). Either no controlled studies had been undertaken, or they had not been reported because of the negative results.

Two main issues were involved in planning a study of scalp tourniquet use: the viability of the rationale for the scalp tourniquet use and the feasibility of testing it, given the contingencies of modern treatment procedures.

The rationale for using a scalp

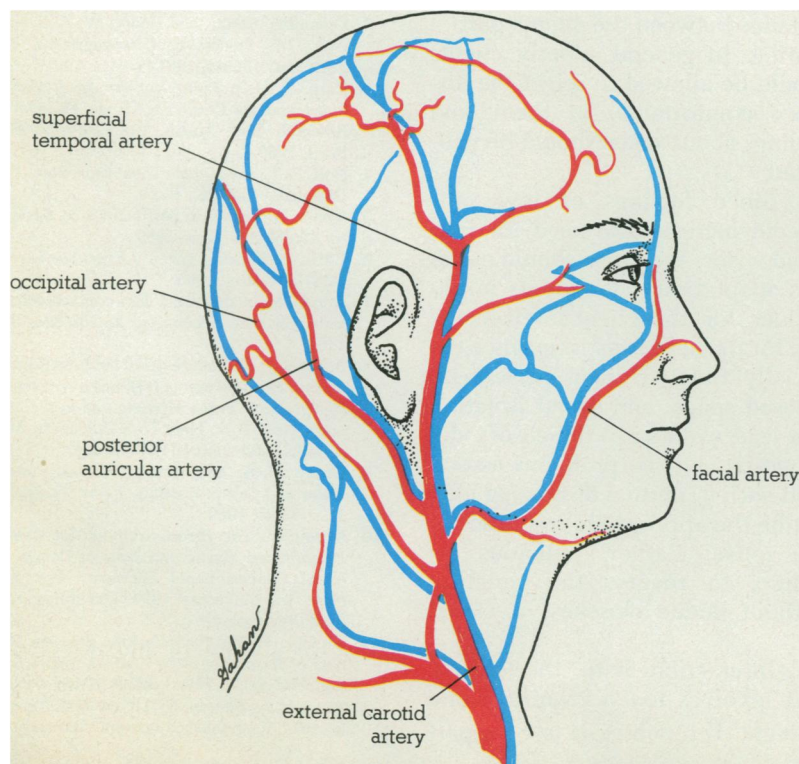
tourniquet is that drug contact with hair follicles can be minimized because the scalp is supplied by superficial blood vessels, which can be temporarily occluded by pressure, and because the drugs are rapidly cleared from the blood after injection, presumably because of tissue fixation⁽⁷⁾. Theoretically, then, it was necessary to look at the nature of normal hair growth, the effects of cancer chemotherapy on scalp hair, the scalp blood supply, and the pharmacokinetics of the drugs to evaluate the hypothesis that a scalp tourniquet could prevent hair loss.

How Hair Grows

Each hair grows at a steady rate, independently from all the others⁽⁸⁾. Each follicle has a bulbous base of mitotically active matrix cells from which all the cells of the hair shaft differentiate and grow. Cells move up in rows to the upper bulb and elongate vertically, being forced upward to emerge finally at the skin. Matrix cells have no diurnal rhythm and not even starvation suppresses their rapid, constant division.

At intervals, mitosis stops suddenly, and the hair root undergoes involution and enters a period of dormancy. The old hair is then shed, and a new one begins to grow. Thus, hair growth occurs in three phases: anagen, the phase of active

Circulation To The Scalp



MARY B. MAXWELL, R.N., M.N., (C)A.N.P., is an adult nurse practitioner in oncology at the Portland Veterans Administration Medical Center, Oregon, where she directs a nurse-run chemotherapy clinic. She is an adjunct assistant professor, University of Oregon Health Sciences Center School of Nursing. This paper was given at the Third Annual Congress of the Oncology Nursing Society.

growth, which lasts for approximately three years in the scalp and involves 90 percent of the hair at a time; telogen, the dormant phase, lasting three months and involving 10 percent of hairs; and catagen, or involution, lasting only a day and involving less than one percent of hairs. Hairs on other parts of the body have a much shorter period of anagen, appropriate to their length. For instance, hairs on the arm are in the anagen phase for only three months at a time.

Regardless of its site of action or the mechanism of action, each epilating drug interferes with hair growth by blocking at one step or another the mitotic cycle of the matrix cells in the bulb(9,10). Small doses of the drugs decrease the size of the bulb, causing a constriction in the shaft, which moves up as the hair grows.

Where constriction occurs, hair breaks off easily at that point. The root remains in the scalp, however, since it has already recovered from the trauma of the drug and is still active.

A larger drug dose causes the bulb to atrophy completely, and then the hair is lost, either by falling out spontaneously or following a disturbance, such as combing.

With radiation, acute effects occur in the hair root similar to those from the drugs. Most hair roots affected by radiation enter a state of telogen. Provided that the radiation dose has not been so large as to prevent growth entirely, regrowth of hair is delayed until the next anagen phase begins three months later. At treatment levels used currently for brain irradiation, however, the hair follicles of most patients are irreparably damaged.

Effects of agents that interfere with cell growth can be seen clinically only in growing hairs, that is, those in anagen. Loss of eyebrows and pubic and axillary hair is usually not seen in patients receiving chemotherapy because most of the hair follicles in those regions are in the dormant, or telogen, phase. Patients never experience complete scalp epilation because the 10 percent of hairs in the telogen phase are unaffected by the drugs.

The main sources of the blood supply to the scalp are located in the subcutaneous tissues and sup-



Scalp tourniquet is inflated above the patient's systolic blood pressure to occlude superficial scalp circulation in an attempt to prevent chemotherapy-induced alopecia.

plied by the external carotid artery. In theory, these vessels could be occluded by external pressure. The blood supply to the head is relatively constant. The scalp is considered part of the skin, scalp cells having a similar low metabolic rate. Necrosis due to occlusion, therefore, would not be expected to occur until after many hours of complete ischemia(11). A scalp tourniquet could be left in place for a long time without causing damage.

Chemotherapy Interference

Many different drugs are used currently in chemotherapy. Although they all interfere with DNA synthesis, they do not all have the same characteristics(12). Not all are cleared rapidly from the plasma by tissue-binding. For example, Cytosin, a notorious epilator, is not activated until metabolized by the liver, and it then has a half-life of 6.5 hours. Methotrexate has a half-life of 12 hours. Although doxorubicin HCl (Adriamycin) disappears rapidly from the extracellular space, it evidently can still be found in the bloodstream 27 hours after injection. One of the first anticancer drugs, nitrogen mustard, is extremely rapidly tissue-bound and cleared from the blood, which may account for why it does not usually cause alopecia.

Most pharmacological re-

search has been concerned with the effects of these drugs on tumors; little study has been done on their effects on hair follicles. Patient observations reveal that some drugs are more epilating than others, but whether this is related to half-life, rapidity of tissue-binding, a propensity for localizing in epithelioid tissue, or other factors is not clear. The drugs' cyclic or noncyclic nature does not appear to be a factor. Alopecia has been shown to be dose-related.

Empirically, applying the scalp tourniquet at the time when plasma drug levels are at their peak and leaving the tourniquet in place as long as possible would appear to afford maximum protection to hair follicles.

Drugs given by intravenous bolus injections achieve immediate peak plasma levels and then taper off. In this instance, the scalp tourniquet would seem to be more effective when applied just before injection and left on 20 minutes.

If the drug is given by infusion, hair follicle protection is more difficult to achieve. It is not possible to leave the scalp tourniquet in place for more than 20 minutes, as it will become too uncomfortable for the patient. Although the patient experiences no dizziness, syncope, or headache, the head feels tightly "squeezed," and the scalp soon becomes numb. Since peak plasma levels are more slowly reached with infusion, it seems reasonable to apply the tourniquet when the plasma levels are highest, for example, during the last 10 minutes of infusion and for 10 minutes after it is stopped.

Scalp tourniquets should probably not be used with the leukemias or lymphomas where the chemotherapeutic objective is the destruction of every single malignant cell. However, brain metastasis would not be a problem with solid tumors, as the blood supply to the brain itself is not occluded, only that to the scalp.

An experimental study was designed to test the hypothesis that application of a scalp tourniquet would reduce the amount of hair loss if the tourniquet was used during the period of highest plasma concentration with selected chemotherapeutic drugs(13).

The sample was drawn from patients at the Veterans Administration Medical Center, Portland, Oregon, who were about to be treated with chemotherapy for advanced bronchogenic carcinoma. The study was planned originally to include randomization to five possible different chemotherapeutic treatments, a national study with four arms and one local study. The participation of 40 to 50 patients was anticipated. Just after the study began, however, the national study was changed. Only the local portion of the design, called COCA, could be implemented.

The COCA regimen consisted of four notorious epilators, Cytoxan (40 mg./kg.), vincristine (Oncovin, 2 mg.), methotrexate (0.6 mg./kg.), and actinomycin-D (2 mg.), given consecutively at two-week intervals for an eight-week cycle. Cytoxan was given by infusion and the others by I.V. bolus.

The independent variable was an inflatable scalp tourniquet attached to an aneroid manometer. In the experimental group, the tourniquet was to be inflated to 10 mm. Hg above the patients' systolic blood pressure at the time chemotherapy was given. Patients were

taught how to use the tourniquet and how to control the pressure themselves. The control group would have only the chemotherapy.

To document the dependent variable, the extent of scalp hair loss, each patient in the study was to be photographed before chemotherapy began and then every two weeks for three months. Maximum hair loss was expected to have occurred by that time.

Five large black and white photographs of different angles of the patient's head were taken each time. At the end of the study, an independent panel of judges decided on the extent of hair loss for each patient by comparing the photographs taken before, during, and after therapy. The judges rated each patient's hair status on a continuum from 100 percent to 0, arriving at independent decisions for each set of photographs. The decisions were then averaged.

During the 12 months of the study, only 9 patients, 5 experimental and 4 control subjects, met the criteria for admission. Seven patients died before the end of their three-month study period. The last photographs before their deaths

were used for the final evaluation. The patients in experimental and control groups had essentially similar characteristics.

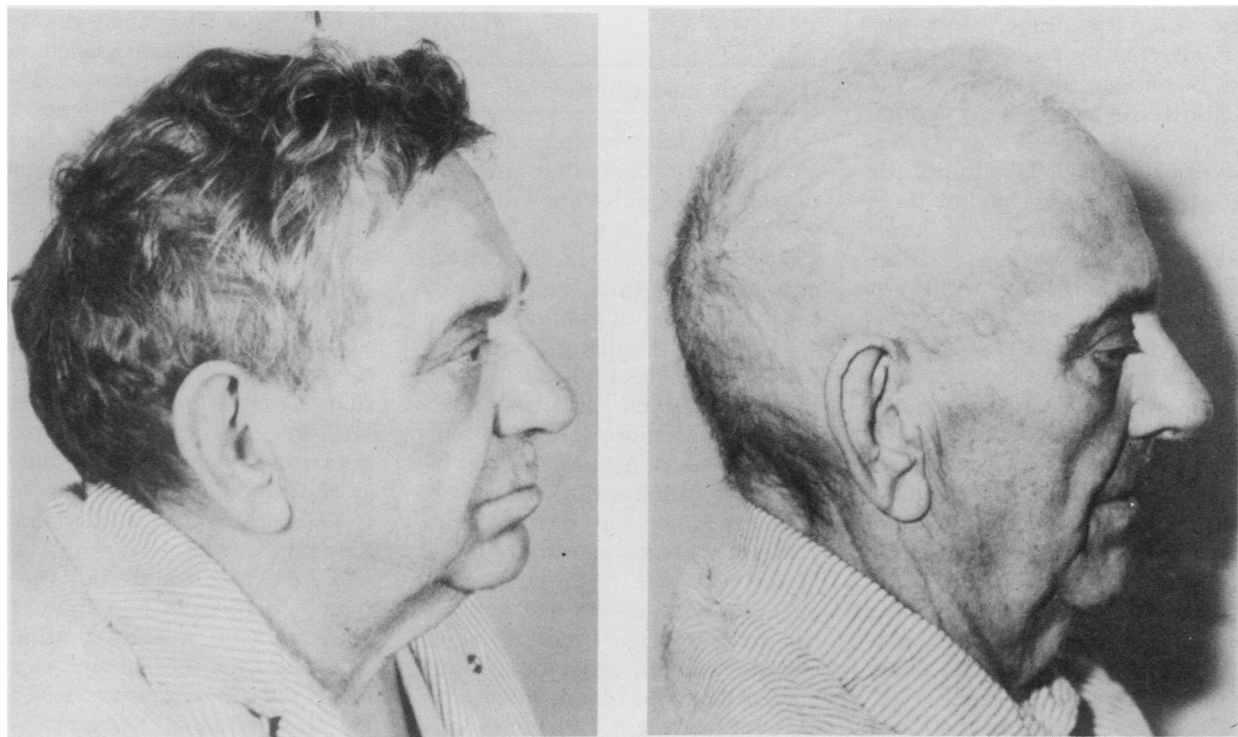
Tables were constructed to illustrate the hair trends of both groups. The Mann-Whitney U test for nonparametric data was used for statistical analysis.

The hypothesis was rejected because the difference between the two groups was not significant. The study revealed that the experimental patients did not lose their hair at a slower rate. No adverse effects from the tourniquet use were apparent.

The two probable reasons for the apparent ineffectiveness of the scalp tourniquet are that the cytotoxic drugs are not all rapidly cleared from the blood and tissue-bound and that the hair follicles could not be well protected from drug effects for a long enough time because of patients' discomfort.

Although patients all received comparable amounts of drugs, hair loss was not equal. One patient had almost no loss; one had almost complete loss, and the others were judged somewhere in between.

The data, then, reveal that factors other than dose-related ones



The photo at left shows the patient before chemotherapy and, photo at right, following chemotherapy. Despite use of the scalp tourniquet, this patient lost his hair.

are involved in whether or not a patient will lose hair. It is clear that a familial tendency to baldness is not involved, as the process of balding is not one of hair loss but, rather, of reduction in hair follicle size from large and coarse to very small and fine(8).

The most likely explanation is that the two patients with little hair loss had most of their hair follicles in the telogen, or resting, phase of the hair growth cycle. One research report did seem to indicate that some people with cancer may have a larger proportion of telogen hairs(10). This hypothesis could easily be confirmed by microscopically examining epilated scalp hairs of patients before beginning chemotherapy treatment and then correlating the percentage of initial telogen hairs with subsequent hair loss.

It appears from this study that scalp tourniquet use may not be effective. The small sample size, however, precludes any firm conclusions, as does the fact that the study involved only one combination of drugs.

References

1. Hennessey, J. D. Alopecia and cytotoxic drugs. (Letter) *Br.Med.J.* 2:1138, Nov. 5, 1966.
2. Simister, J. M. Alopecia and cytotoxic drugs. (Letter) *Br.Med.J.* 2:1138, Nov. 5, 1966.
3. Binns, J. H., and Southall, A. C. Intensive cyclophosphamide therapy in advanced malignant disease. *Practitioner* 204:546-548, Apr. 1970.
4. Levantine, A. V., and Almeyda, J. Drug reactions. 23. Drug induced alopecia. *Br.J.Dermatol.* 89:549-553, Nov. 1973.
5. Keaveny, M. E., and Wiley, L. Hodgkin's Disease . . . the curable cancer; Part I. *Nursing* 75 5:48-54, Mar. 1975.
6. Marino, E. B., and LeBlanc, D. H. Cancer chemotherapy. *Nursing* 75 5:22-33, Nov. 1975.
7. O'Brien, Robert, and others. Scalp tourniquet use to lessen alopecia after vincristine. *N.Engl.J.Med.* 238:1469, Dec. 24, 1970.
8. Van Scott, E. J. Keratinization and hair growth. *Ann.Rev.Med.* 19:337-350, 1968.
9. Crounse, R. G., and Van Scott, E. J. Changes in scalp hair roots as measure of toxicity from cancer chemotherapeutic drugs. *J.Invest.Dermatol.* 35:83-90, Aug. 1960.
10. Van Scott, E. J., and others. The growing hair roots of the human scalp and morphologic changes following amethopterin therapy. *J.Invest.Dermatol.* 29:197-204, Sept. 1957.
11. Burton, A. *Physiology and Biophysics of the Circulation*. Chicago, Yearbook Medical Publishers, 1972, p. 8.
12. Cline, M. J., and Haskell, C. M. *Cancer Chemotherapy*. 2d ed. Philadelphia, W. B. Saunders Co., 1975, p. 29.
13. Maxwell, M. B. *The Effect of Scalp Tourniquet Use on Alopecia in Cancer Chemotherapy*. Eugene, Honor Sciences Center, University of Oregon, 1978. (Unpublished master's clinical investigation)

Alopecia And Chemotherapy

By Deborah Welch
Keith Lewis

Part of the stress associated with antineoplastic treatments involves anticipatory fear not only of the treatment itself, but of its related side effects. Nausea and vomiting, diarrhea, mouth sores; increased risk of infection and bleeding, and hair loss are some of the side effects that confront a patient receiving certain types of chemotherapy.

Alopecia can introduce an additional threat to the cancer patient in the form of an altered body image, which serves as a constant reminder to the patient, his family and his friends that he has cancer(1,2). Although the emotional consequences of experiencing alopecia vary with each patient, most patients view alopecia as another stress in dealing with a serious life crisis. Wigs can only partially relieve the emotional stress from hair loss(3).

Many chemotherapeutic drugs are designed to attack cells in their most active phase of replication, specifically DNA synthesis and cell mitosis phases. Unfortunately, these drugs affect the growth and metabolism not only of malignant cells, but also of normal cells involved in the process of active reproduction. These actively replicating cells include those found in the bone marrow, gastrointestinal and germinal epithelium, hair follicles, skin, and embryonic tissue. Chemotherapeutic agents, then,

may be equally toxic to a variety of cells involved in reproduction.

Yet most chemotherapy drugs do not cause alopecia. One reason why hair loss probably seems common in patients receiving chemotherapy is that the drugs which are used most frequently (doxorubicin, cyclophosphamide, vincristine) can cause alopecia. Although the description of how hair is lost with chemotherapy seems straightforward, why certain drugs do and do not cause alopecia still remains unclear.

Scalp hair loss can range from partial to total baldness. If the hair roots are atrophied, complete hair loss usually results either by hair falling out spontaneously in clumps or from combing or washing or both. Doxorubicin (Adriamycin) results in alopecia in more than 80 percent of patients treated with 60-75 mg./m.² and usually causes total hair loss within 21 days(2). Cyclophosphamide (Cytosan) and vincristine (Oncovin) are other major offenders in hair loss. Cyclophosphamide-related alopecia usually is associated with higher intravenous doses of the drug.

If the hair shaft is constricted and the hair root remains in the scalp, the hair will break off easily at the point of constriction. This phenomenon is manifested by a patchy thinning type of hair loss. Methotrexate infusions are often associated with this type of epilation. Some patients who receive 5-fluorouracil also develop thinning of the eyebrow, loss of eyelashes, or both.

Hair loss following methotrexate therapy is associated with the administration of large amounts of the drug and generally occurs with such other forms of clinical toxicity as stomatitis, leukopenia, and

DEBORAH WELCH, R.N., M.S.N., is program coordinator, Cancer Nursing Outreach Program, Fred Hutchinson Cancer Research Center, Seattle, Washington.

KEITH LEWIS, R.Ph., B.S., is an oncology clinical pharmacist, Yale-New Haven Hospital, Connecticut.