Fibrocystic Breast Dysplasia

An Abridged Laboratorical and Clinical Summary

William R. Ghent and Bernard A. Eskin

Presented at World Congress of Surgery 1989
Published in Proceedings of World Congress of Surgery 1989; 33: 622.

FIBROCYSTIC BREAST DYSPLASIA
AN ABRIDGED LABORATORICAL AND CLINICAL SUMMARY

INTRODUCTION:

The purpose of this summary is to present our theory that Fibrocystic Breast Disease is the result of a trace element deficiency.

The incidence of fibrocystic disease is epidemic in North America. The American Academy of Pathology reports that fibrocystic changes involve 50-80% of adult females on this continent. A similar involvement of Russian, Australian and European women seems to be the case.

The frequency of this syndrome appears to rule out "hormonal dysfunction" as the etiology, and also negates the position that premenstrual soreness and tenderness is a normal physiologic cross to bear.

The high incidence of this problem suggests that the condition could be secondary to a common environmental toxin, or a common deficiency. The toxin theory is negated by the disparate regions of the world in which the syndrome occurs. The deficiency theory, supported by laboratorical and clinical studies, is presented.

BASIC SCIENCE STUDIES:

Dr. Bernard A. Eskin of the Medical College of Pennsylvania (MCP), has produced an animal model for fibrocystic disease in the Sprague Dawley rat. This requires total iodine deprivation. The characteristic pathologic triad of cystic spaces, epithelial/apocrine hyperplasia and fibrotic replacement of the fatty matrix is reproduced in this laboratory setting and compares positively with the human. This model is the only one of all that have been used that shows fibrosis to a major degree (Figure 1). This is in marked contrast to the normal female rat breast, (Figure 2).

The reintroduction of Na or K Iodide into the diet of the rat model reduces the cystic spaces, and the fibrosis to a minor degree, but leaves the epithelial hyperplasia intact, (Figure 3).

The changes of iodide deficiency in the thyroid are reversed and a normal microscopic picture is obtained.

A protein bound iodide, Iodine Caseinate, akin to the binding found in thyroxine, controls the hyperplasia but leaves the cysts and the fibrosis intact, (Figure 4).

A third form of iodine submitted to the replacement test was Aqueous Molecular Iodine (AMI). This is the basic element from which all of the 130 compounds complexed with the iodine molecule arise. AMI when administered as replacement therapy in the rat returns all elements of the triad of fibrocystic disease to normal, (Figure 5). The thyroid is unchanged in microscopic appearance and continues to present the picture of iodine deficiency as compared to the iodides which alter the thyroid pathophysiology.

Thus, by experiment, a hierarchal form of response to iodine or complexed iodides was established from our investigations.

CLINICAL STUDIES:

The clinical application of Eskin's work has paralleled the results of the laboratory. We have tested Lugol's solution (NAI), Iodine Caseinate, and AMI. The Lugol's and Iodine Caseinate series was reported in 1985. We found symptomatic and objective improvement with these substances but not to the degree expected by the patient or ourselves. These two compounds are thyrotropic, while on-going investigation has proven that AMI bypasses thyroid metabolism.

CLINICAL SERIES:

Our present series emcompasses 1365 women volunteers observed through 4813 women years. In the process of the evolution of the observation of this syndrome a clinical protocol of evaluation and documentation using a standard form has been developed, (Appendix 1 and 2). This includes a numerical subjective evaluation of "0" which indicates a worsening of symptoms. "1" which indicates no change. "2" which indicates a lessening of symptoms with residual mild premenstrual discomfort,

through "3" which indicates pain free breasts. In #3 category women who are premenstrual should not be able to predict their periods by breast discomfort.

Objective evaluation has been aided by a numerical scoring system in which each quadrant of the breast is given a numerical equivalent, 1 = U.O.Q., 2 = U.I.Q., 3 = L.I.Q., and 4 = L.O.Q., (Figure 5). The parameters that are assessed are - (1) micronodularity, (2) tenderness, (3) fibrosis, (4) macro-cysts, (5) turgidity (hyperactivity). Re-evaluation included a 6th category, decrease in breast size from (1) no change, to (8) more than three brassiere cups in size. The numerical scoring system is a simple addition of the numbered quadrants of the breast involved with any or all of the parameters. Thus a breast involved with all five modalities of fibrocystic disease would present a score of 50. A breast with no involvement would present a score of "0".

The present series was assessed at 4-6 months (Group 1, #292), 7-18 months (Group 2, #639), and over 18 months of therapy (Group 3, #434).

DEMOGRAPHICS:

The mean age of the patients in this series was 41.06 years, with an age spread from 11 years to 87 years at the onset of treatment.

Eight hundred and seventy-one (63.8%) were premenopausal. Four hundred and ninety-four (36.1%) were postmenopausal. Two hundred and thirty-six (49.7%) of the post-menopausal women were on Estrogen replacement therapy.

Nine hundred and fourteen (67%) had been exposed to birth control pills. Two hundred and eighty-four (20.8%) of the total series were nulliparous.

Symptoms had been present for a mean of 44.6 months, with a spread from one month to 360 months.

Six hundred and sixty-seven (49.7%) had had a previous diagnosis of fibrocystic disease applied, and 365 (22.3%) had had

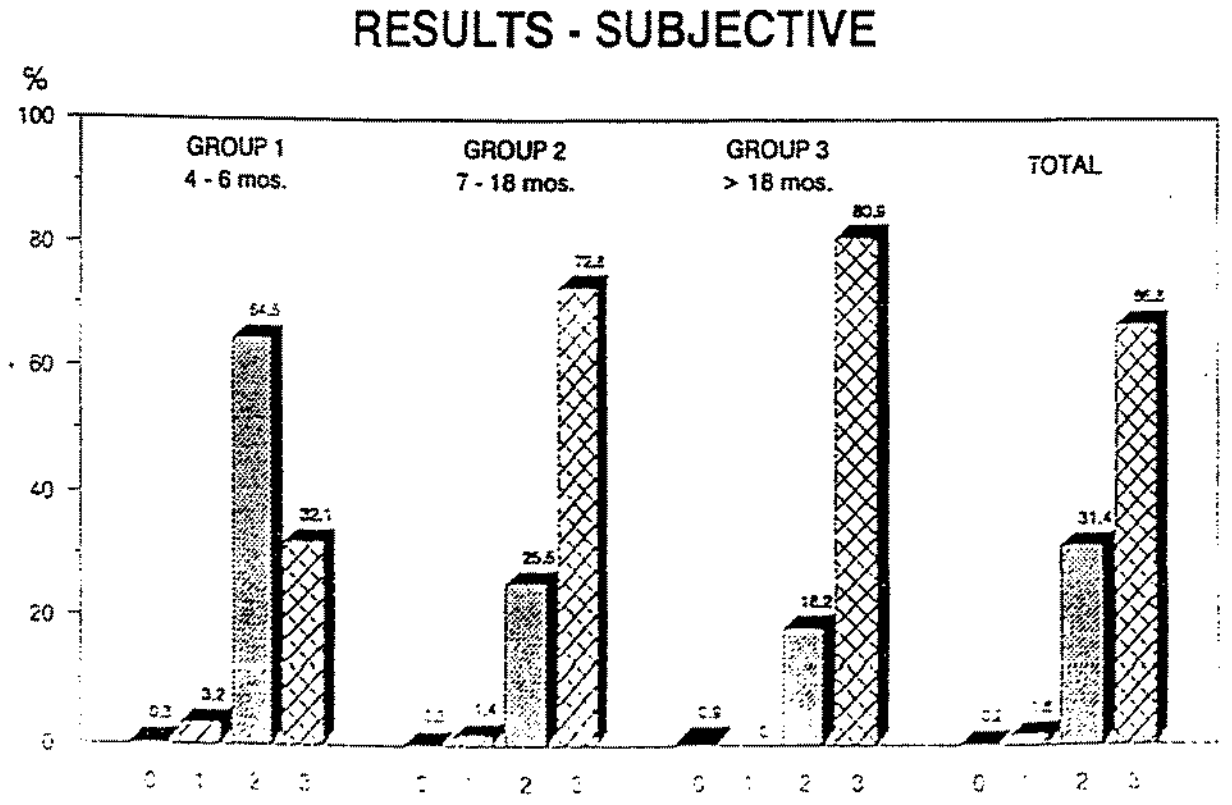
previous surgical biopsies for benign disease. Twenty-four (1.8%) had undergone a unilateral mastectomy for malignant disease. The family history was positive for breast carcinoma in 333 (24.4%).

One thousand and two (73.4%) presented with painful breasts; the remainder had lumps or tenderness as a complaint. The pain was premenstrual in 562 (56.0%), while the pain was without pattern in 195 (19.4%), and involved the total cycle in 245 (24.5%).

In 134 (9.8%) pain was severe enough to interfere with their daily activities and/or sexual encounters. Two hundred and sixty-eight (19.6%) complained that the soreness of their breasts was sufficient to wake them at night. The majority of these patients had had previous medical advice re. caffeine withdrawal, sleeper bras, mammograms, and a number had been treated with masculinizing hormones (Danazol).

The total group presented two women in whom their breast pain had reached a level that divorce was pending by their husbands; fortuitously this has been averted with Aqueous Molecular Iodine treatment.

RESULTS: The following subjective and objective evaluations are presented:



PRE TREATMENT OBJECTIVE SCORE

	Group 1	Group 2	Group 3	Total Series
Mean	30.120	31.290	31.164	30.99
Range	1 - 80	3 - 80	4 - 100	1 - 100

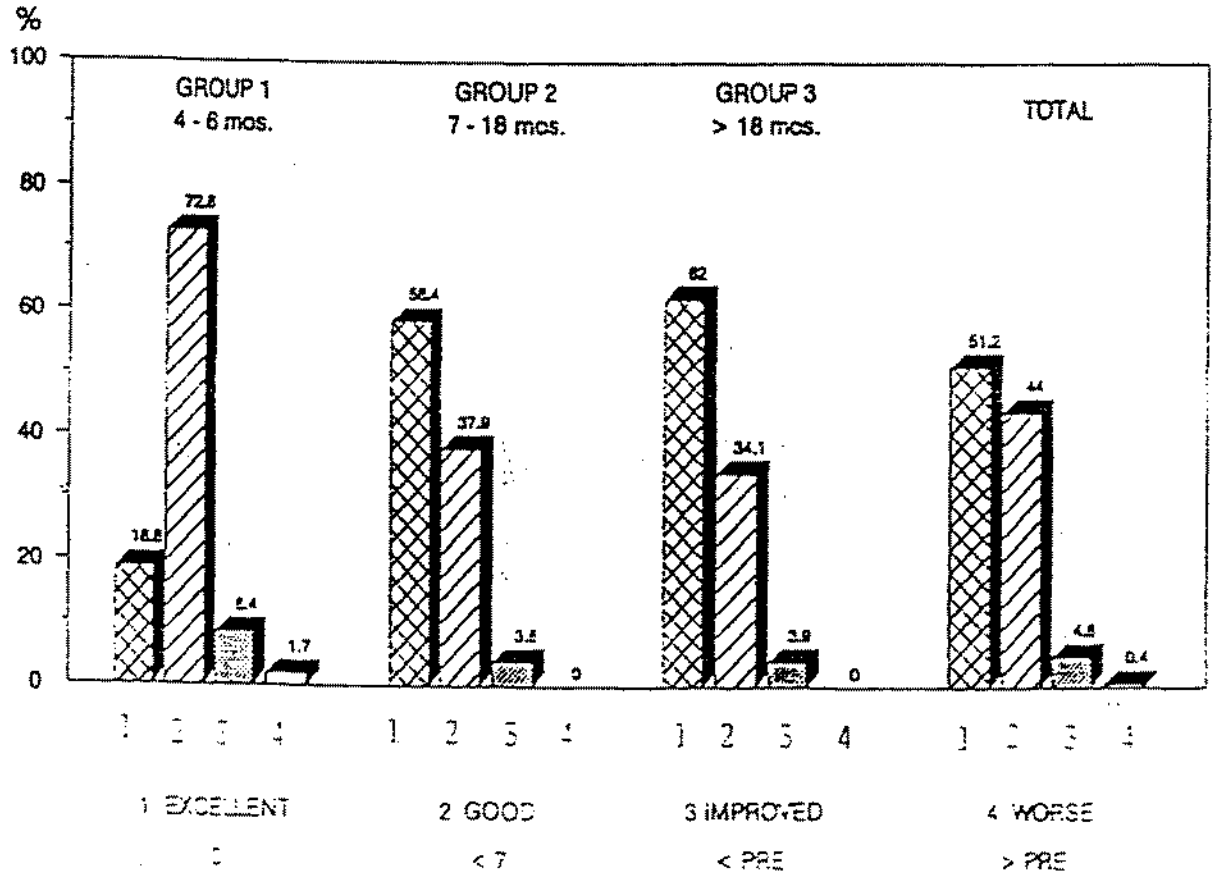
POST TREATMENT OBJECTIVE SCORE

Mean	3.151	1.754	1.505	1.974
Range	0 - 46	0 - 62	0 - 40	0 - 62

SCORING:	0	6	< pre	> pre

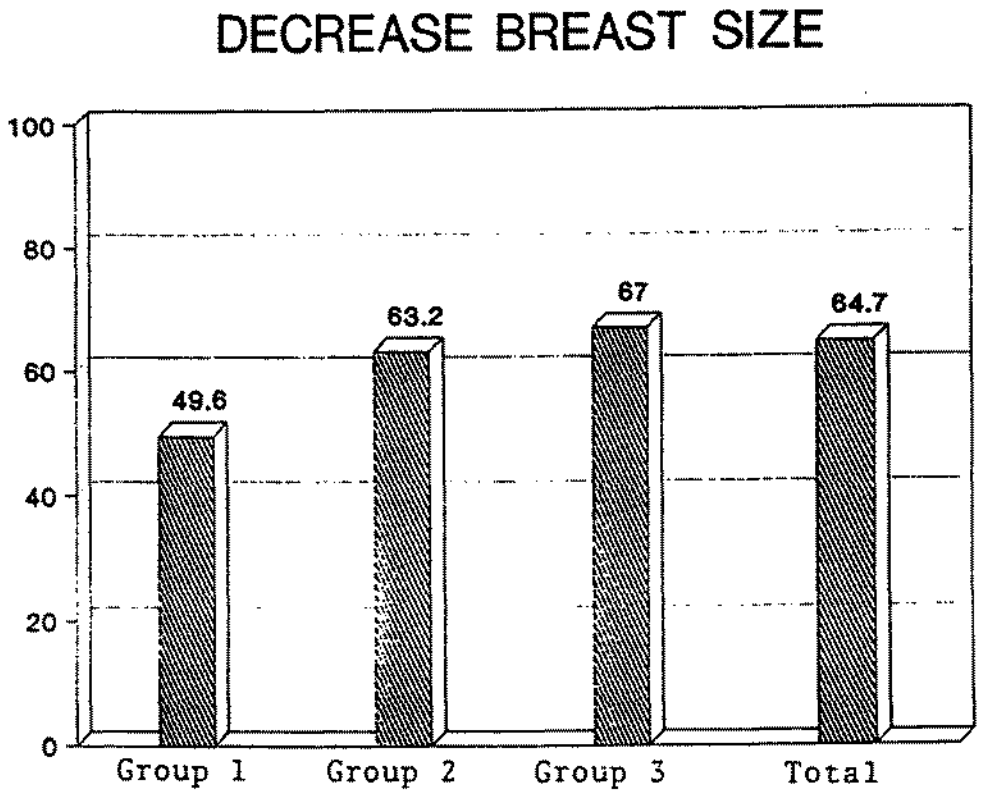
(P=0.00)

RESULTS - OBJECTIVE



BREAST MASS:

An objective measurement of the pathologic change that occurred during treatment is afforded by a decrease in breast size. One hundred and thirty-five (49.6%) in Group 1, 412 (63.2%) in Group 2, 413 (67%) in Group 3, and in total 906 (64.7%) reported a decrease in breast size that varied from one-half a brassiere cup to five brassiere cups. The last patient had planned a surgical reduction which was avoided.



Actual breast mass is composed of the normal secreting elements, fibrous tissue stroma, fatty matrix, and the abnormal cystic and fibrous tissue components of the fibrocystic syndrome. During the period of investigation six patients did not repond to Aqueous Molecular Iodine therapy. Previously they had been unresponsive to Danazol, Tamoxifen and Progesterone therapies. Combinations of hormonal and A.M.I. therapies were used, again without relief of symptoms, or improvement in the clinical

evaluation. Subsequent subcuatneous mastectromies have cured the pain and, on pathologic examination, the reason for non-response was apparent; the architecture of the breast was completely disruptured by an almost malignant overgrowth of fibrous tissue.

We must conclude that although fibrocystic disease is a benign condition it has the capacity to destroy the human female breast.

SIDE EFFECTS:

Side effects have been noted in 152 (~~11.13%~~ 10.6%) of patients in this series. These have been mild and easily reversed with a lower dose or temporary cessation of the medication. Only two patients were unable to ingest A.M.I. in its present form.

The side effects include:

Acne	15	1.0%
Nausea	8	0.5%
Diarrhoea	2	0.1%
Hair Thinning	13	0.9%
Hyperthyroid	2	0.1%
Hypothyroid	4	0.3%
Rashes	3	0.2%
Iodism	2	0.1%
Headaches	3	0.2%
Increased pain	78	5.7%
Miscellaneous	22	1.6%

The 5.7% of our series that exhibited increased breast pain did so within the first six months of treatment. The pain lasted from three to six weeks and then subsided. In each instance the increase in pain seemed to correspond to a sudden softening of the fibrous tissue plaques.

Thyroid involvement is not above the expected incidence in our area in the time frame concerned. Six of the patients with acne were found to have elevated testosterone levels, and ten patients of the group with hair thinning were found to have depressed iron stores, low oestradiol levels or lowered T3

levels. The hair thinning was corrected when these abnormalities were treated.

It is of some interest that two patients in this series, sisters with hereditary M.E.N.II, had undergone total thyroidectomy prior to the development of their fibrocystic syndrome. They both have responded to Aqueous Molecular Iodine therapy. This suggests that the action of Aqueous Molecular Iodine is not mediated through the thyroid. This reinforces the basic research findings that the direct action of the iodine molecule is in the breast itself at the terminal and intralobular duct cell level.

During the period of this study 25 women became pregnant. Iodine therapy was stopped when the patient thought she might be pregnant; no problems have been encountered. This is in keeping with long term studies using iodine instead of chlorine to purify water that have been reported from Lowell Prison in Florida, and from various U.S. military establishments around the world.

In addition, Aqueous Molecular Iodine has been approved by the Health Protection Branch for water purification of rural wells and has been used in the town of Gander, Newfoundland. The daily ingestion of iodine with this method of water purification is approximately 50-75% of the dose used in our series.

A diagnosis of carcinoma occurred in four women in our series. This is an incidence of 0.00082 cancers per woman year, which is below the projected incidence of 0.00164 cancers per woman year in Ontario. Three patients had an undiagnosed carcinoma when referred for treatment.

Thirty-three patients on initial examination were judged to have mammary hypertrophy in addition to fibrocystic disease. Three patients had sufficient reduction in size to decide against a surgical approach, whereas 30 patients have had reduction mammoplasties.

One patient developed a colonic carcinoma during the study period. This is not above the projected incidence in the

population in the time frame under study.

DOUBLE BLIND TRIAL;

A double blind prospective study was completed at the Virginia Mason Clinic in Seattle in 1987. Fifty-six volunteers were enrolled in the study. Twenty-three received Aqueous Molecular Iodine and 33 received a placebo. The placebo was concocted with a brownish vegetable dye and flavoured with quinine.

The patients were evaluated at a mean of 191 days. Subjectively 65.2% of patients were improved in the treatment group. A placebo effect was noted in 33% of the non drug group.

The objective evaluation in the treated group showed a reduction of 65.2% in their numerical score, as compared to an increase of .3% in the untreated group.

In addition, a highly significant correlation between subjective and objective improvements in the drug group was noted.

One patient in the group whose thyroid indices were low-normal at the start of the study became hypothyroid and required Thryoxine therapy. No other changes in the pre and post-treatment thyroid indices were noted.

CONTRAINDICATIONS TO AMI THERAPY:

1. Pregnancy - Therapy should be stopped when patient suspects pregnancy.
2. Untreated hypo or hyperthyroidism.
3. Active peptic ulcer disease.
4. Sodium Fluoride administered for hereditary deafness or in regions with a high natural fluoride content in the water. Artificial fluoridation is not a contraindication.

DISCUSSION:

Eskin's original hypothesis suggested that fibrocystic breast cysplasia was secondary to a dietary "Iodine" deficiency. Dietary "Iodine" is made up of sodium or potassium iodide. The

latter has been added to our salt since 1929 in the successful prevention of goitre and cretinism.

The work in Eskin's laboratory with iodide and then casein bound iodide showed that a simple dietary deficiency of these compounds was not the complete answer.

Terminology must be clarified at this point. Chemically Iodine is I_2, a purplish solid with an atomic weight of 125.904. This element can be combined with many other ions or proteins to produce 134 compounds containing iodine, many of these may be called "Iodine" in a generic sense. Chemically the only substance that should be called Iodine is I_2.

This element is weakly soluble in water and when it is substituted in the rat model with fibrocystic disease the pathologic changes are reversed completely, (Figure 5).

This laboratorical hierarchal response convinced us that the fibrocystic syndrome was not a dietary deficiency of iodides but a deficiency of Iodine (I_2). Nutritionists in the U.S.A. and Canada are convinced that our daily intake of Iodides is more than adequate, and this fits with our hypothesis of a trace element deficiency of iodine.

Iodine is localized in the breast tissue of both rat and human in the cells of the terminal and intralobular ducts. This area is termed by Alpers, a Seattle pathologist, as microscopically "restless". Many authors localize neoplastic change to this level.

Presuming an iodine metabolic pathway which is similar to that seen in the thyroid, it is our hypothesis that the cells of this restricted breast locale lack the enzymatic ability (peroxidase) to oxidize the iodide to iodine. This would restrict the metabolism of these cells and make them iodine-poor. This state is more susceptible to estrogen stimulation making them hyper-responsive to estrogen (estrogen positivity).

Thus, by both the iodine pathway response and by biochemical binding, the form of iodine is essential to breast normalcy. The

use of AMI permits both basic intracellular changes to occur normally and provides protection to the breast tissues.

Molecular iodine is free of binding encumbrances, and some aqueous molecular iodine ingested is absorbed in this state. This minute amount is sufficient to render the target cells in the terminal and intralobular duct area less sensitive to circulating oestrogens.( )

Once this state is reached the cells react normally and the excess secretions that distend the lobules to form micro and macrocysts cease to be formed. The fluid is absorbed, and finally the fibrous tissue that has been laid down secondary to the irritaiton of the high potassium content of the cyst fluid is eroded by the routine scavenger cells of the patient.

CONCLUSION:

Laboratorical and clinical studies suggest that the fibrocystic syndrome is a manifestation of a trace element deficiency in the form of iodine I_2.

Subjective and objective improvement approached 90% when patients with breast complaints were given this replacement therapy.

PLEASE TYPE OR USE BLACK INK

INVESTIGATOR	PATIENT IDENTIFICATION NO.
DR. WILLIAM GHENT	

DO NOT WRITE IN SCREENED AREAS

PROJECT NO.	STUDY EDP NO.	FE EDP NO.

APPENDIX 1

PRESENT HISTORY

☐ PRE MENSES ☐ MID CYCLE ☐ FULL CYCLE ☐ NO PATTERN

DURATION OF SYMPTOMS

PAST HISTORY

BREAST

OTHER

AGE AT MENARCHE	AGE AT MENOPAUSE	L. M. P.	FAMILY HISTORY M A GM S D
B. C. P.	DURATION	PRESENT	PAST
ESTROGEN REPLACEMENT	DURATION	PRESENT	PAST
PARITY AGE	NUMBER	BREAST FEEDING (*Total Weeks*)	NO. OF CHILDREN BREAST-FED

EXAMINATION

NOTE:

= MICRO NODULARITY

= FIBROUS PLAQUES

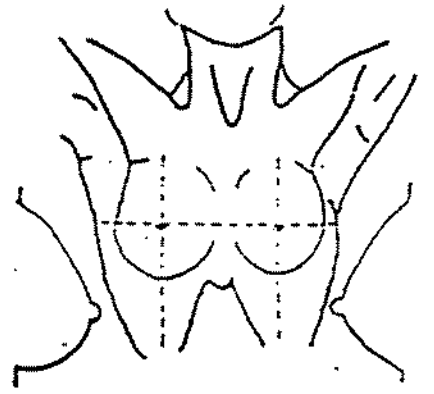
= MACROCYSTS

= HYPERACTIVITY

WEIGHT

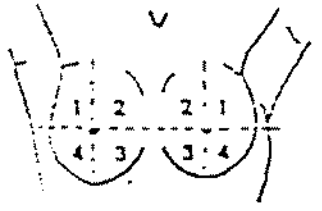
TREATMENT

DOSAGE



RIGHT LEFT

OBJECTIVE ASSESSMENT



	RIGHT	LEFT
1. MICRO NODULARITY		
2. TENDERNESS		
3. FIBROSIS		
4. MACROCYSTS		
5. HYPERACTIVITY		

BREAST PROTOCOL - FOLLOW UP# *1 _ _ _

NAME_____ PATIENT NO.*4 _ _ _ _

DATE OF VISIT *8 _ _ _ _ _ _ NO. OF MONTHS ON IODINE *14 _ _ _ _
L.M.P. *18 _ _ _ _ _ _

DATE STARTED ON IODINE *24 _ _ _ _ _ _

TREATMENT ASSESSMENT IMPROVEMENT IN *30 _ _ WEEKS.

SUBJECTIVE

LOSS OF PAIN	*31 _
LOSS OF FULLNESS	*32 _
BREASTS SOFTER	*33 _
LESS NODULAR	*34 _
DECREASE IN BREAST SIZE	*35 _
OTHER	*36 _

OBJECTIVE

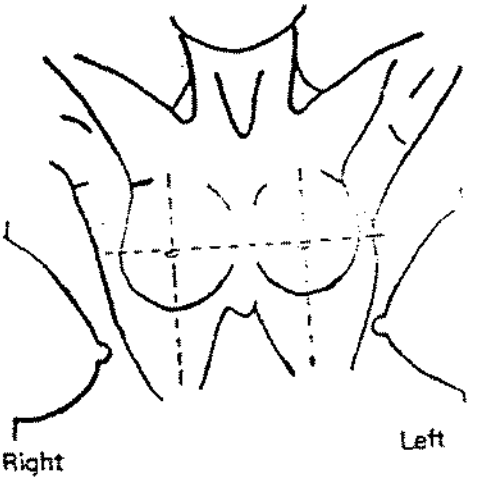
LOSS OF TENDERNESS	*37 _
LOSS OF CYSTS	*38 _
LOSS OF FIBROSIS	*39 _
LOSS OF MACROCYSTS	*40 _
LOSS OF HYPERACTIVITY	*41 _
DECREASE IN BREAST SIZE	*42 _

SIDE EFFECTS

ACNE	*43 _	SKIN RASH	*49 _
NAUSEA	*44 _	IODISM	*50 _
DIARRHEA	*45 _	INCREASED PAIN	*51 _
HAIR LOSS	*46 _	PREGNANCY	*52 _
HYPERTHYROID	*47 _	HEADACHES	*53 _
HYPOTHYROID	*48 _	LOST TO FOLLOW UP	*54 _
		OTHER	*55 _

EXAMINATION

OBJECTIVE ASSESSMENT	Right	Left
1. Micro nodularity	*56 _ _	*58 _ _
2. Tenderness	*60 _ _	*62 _ _
3. Fibrosis	*64 _ _	*66 _ _
4. Macrocysts	*68 _ _	*70 _ _
5. Hyperactivity	*72 _ _	*74 _ _
TOTAL	*76 _ _ _	
SUBJECTIVE GRADING	*79 _	
OBJECTIVE GRADING	*80 _	



PROBLEMS: STOPPED DI* *81 _ _ _ _ _ _
WEAK SOLUTION *87 _
INADEQUATE DOSE *88 _
OTHER *89 _