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IODINE DEFICIENCY BREAST SYNDROME

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The association of thyroid/iodine and breast disease was first reported by Beatson in 1896 (1). He suggested improvement in metastatic breast cancer treated with high doses of desiccated thyroid. This compound contains a large amount of iodine, both free and protein bound.

Vishnyakova and Muravieva associated iodine deficiency with fibrocystic dysplasia and reported a 78% improvement rate in patients treated with sodium iodide (2).

Laboratorical support for the association of fibrocystic disease and iodine deficiency was furnished by Eskin in 1970 (3). He succeeded in producing a laboratorical model in the Sprague-Dawley rat that closely resembled the microscopic criteria of the human female condition. These mammary changes include epithelial hyperplasia, cyst formation, and interacinar fibrosis. This model was produced by iodine deprivation. Previous models with hormonal manipulation did not reproduce the fibrosis which is the clinical hallmark of the chronicity of this syndrome.

This hypothesis was tested by treating the iodine-deficient rat using sodium iodide, iodine caseinate, or elemental iodine (I_2) as replacement therapy. These studies showed there was a differential improvement in the microscopic architecture with iodine caseinate, reversing the epithelial hyperplasia and the cyst formation with very little change in the fibrotic element. Sodium iodide showed the same changes with the addition of a partial resolution of the fibrous tissue. The final form to be tested, elemental iodine (I_2) in aqueous suspension, efficiently reversed all components of the pathologic state (4).

The clinical application of this theory was begun in 1972, in Kingston, Ontario, in the Great Lakes iodine deficient area of Canada. In total, 1,100 women with Iodine Deficiency Breast Syndrome (I.D.B.S.) have been treated with replacement therapy with one or both of the first two modalities (Lugol's Iodine or Iodine Caseinate - Iodaminol). The series using I_2 will be reported at a later date.

The subject group seen by the senior author with sufficient data available for analysis consisted of 588 patients (5).

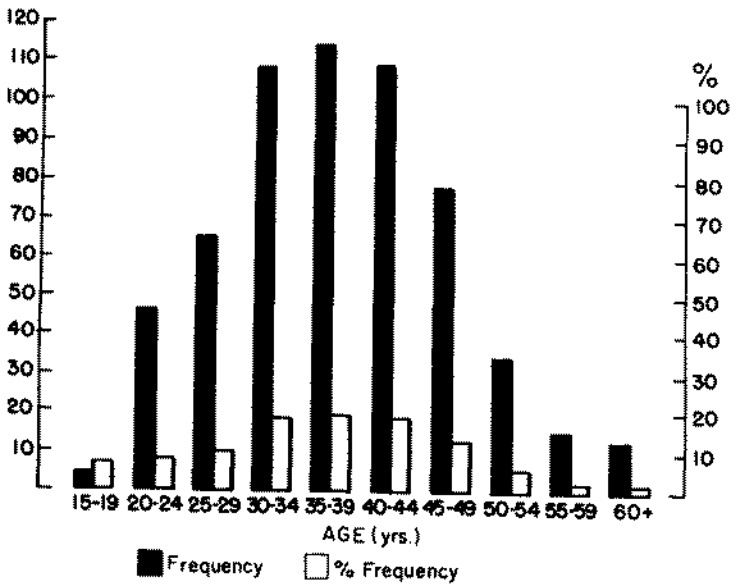

Fig. 1. Bar graph illustrating the age spread of the subject group.

These patients varied in age from 15 to 67 years with a mean of 37.6 years (Fig. 1). Five hundred and five (88.0%) were pre-menopausal and 69 (12.0%) were post-menopausal. The post-menopausal group varied in age from 26 to 55, with a mean age of 44. The post-menopausal group included 33 (47.9%) who were on replacement oestrogen therapy. One hundred and seventy-six (34.9%) of the pre-menopausal group had used birth control pills. One hundred and eighty-one (30.8%) of the patients were nulliparous. The remaining 407 (69.2%) produced a mean of 1.8 children, at a mean age of 22 years for the first pregnancy. One hundred and sixty-nine (41.5%) breast-fed their infants for a total of 5000.0 weeks and a mean of 25.1 weeks.

The past history of this group revealed that 169 (29.5%) had had previous breast problems, including diagnoses of fibrocystic disease, fibroadenomata, cysts, mastitis, and breast abscesses. Cysts were aspirated in 41 patients (7.0%). A variety of treatments including hormones (.3%), diuretics (3.3%), caffeine withdrawal (.9%), and previous surgical biopsy in 139 or 23.0% of the patients was noted.

Of the patients referred for consultation with lumpy painful breasts (95.1%), only 4.9% did not have a pain component. The pain was constant throughout the cycle in 387 (65.8%), while 199 (33%) presented more severe symptoms in a cyclical fashion.

The diagnosis of I.D.B.S. (Fibrocystic disease) was established using thermography, clinical examination, and mammography if indicated by thermographic or clinical suspicion.

RESULTS OF TREATMENT

Lugol's iodine was the only medication available during the early years of this review, and 223 patients received this treatment. In 1974, iodine caseinate became available, and many of the Lugol's patients were switched to this form of replacement therapy. In total, 497 patients have been treated with iodine caseinate.

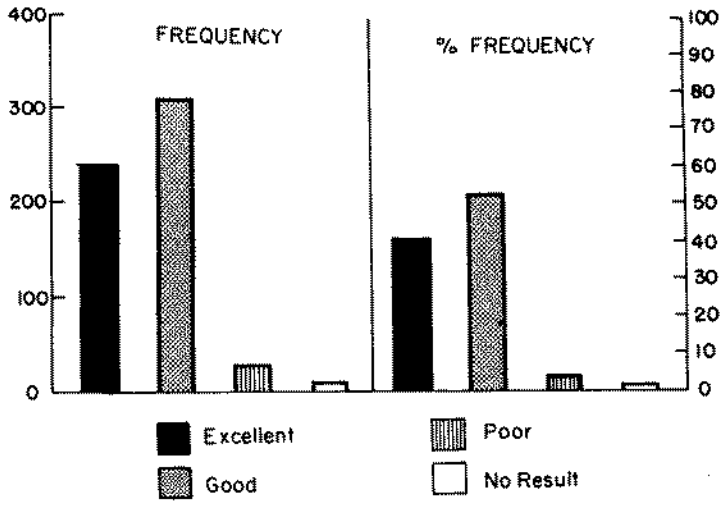

Fig. 2. Bar graph illustrating the results of replacement therapy with iodine.

The results of the treatment were classified as follows:

1)	Excellent	Relief of pain, clinical return to normal with disappearance of all cysts and fibrosis.
2)	Good	Pain only with periods, clinical disappearance of cysts but with continued fibrotic changes.
3)	Poor	Slight improvement in symptoms with a decrease in number of cysts palpable.
4)	Negative	No change from pre-treatment level in symptoms or clinical examination.

Five hundred and forty-six patients were assessed as improved in the Excellent or Good categories, and this comprises 93.4% of the study group. Twenty-eight (4.8%) and 11 patients (1.9%) were classed as a poor or negative result (Fig. 2).

The time for improvement was variable and, to some extent, depended on the duration of the pathological process present. This interval varied from a minimum of 2 days to a maximum of 200 days, with a mean of 48.7 days (Figs. 3 and 4).

COMPLICATIONS

Some complications were noted during the study and involved 53 patients or 9.5% of the sample. Two percent of the ladies developed acne, and 1.7% had slight nausea. These complications disappeared entirely on the maintenance protocol of 10 minims of Lugol's or 10 mg of iodine caseinate biweekly.

Hair loss occurred in five patients. Three patients, upon investigation by a dermatologist, proved to be iron deficient. They were able to resume treatment after this had been corrected, without further problems. Two patients were hypothyroid.

Fig. 3. Pre-treatment mammogram of the left breast of a 54 year old female showing severe dysplasia and fibrosis.

Fig. 4. Post-treatment mammogram of the left breast of the same patient after treatment showing a complete resolution of dysplasia and fibrosis.

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Three patients developed a hyperthyroid state, and two patients became hypothyroid during the follow-up period of 1848 woman years. This is not an increase over the expected incidence of these two conditions in this time frame of surveillance.

Nineteen patients developed a variety of complications on the daily dosage. These included a metallic taste after the ingestion of the iodine, excess flatulence, or diarrhea. Three patients developed iodism, characterized by enlarged, tender cervical lymph nodes, accompanied by coryza. These symptoms subsided in about three weeks after stopping the medication. Two women had increased libido, two had rashes, one developed bleeding gums, and one became depressed.

The development of a malignant lesion during the follow-up period of 1848 years occurred in three women, for an incidence of .00164 cancers per woman-year. This is marginally above the expected incidence of .00160 cancers per woman-year. This is in keeping with Spratt's observation in a follow-up study of patients with fibrocystic disease (6).

The follow-up period in this study must be considered as preliminary. It encompasses a total of 1848 years with a minimum of two months, a maximum of 264 months, and a mean of 37 months. This follow-up is continuing as additional patients are added to the survey, and new modalities of replacement are instituted which show both laboratory and clinical promise of reversing the fibrotic changes.

DISCUSSION

The etiology of fibrocystic dysplasia has remained obscure. The theories have included a prolonged Luteal phase, a reversal of the Oestrone/Oestriol ratio (2), increased median prolactin levels (7), or any upset in these complex interrelationships. All of these etiological theories are supported by good research data and should not be dismissed out of hand. More recent suggestions have implicated caffeine (8) and the increased oestrogen intake in milk drinkers (9).

We would postulate that there is a common denominator underlying all of these concepts, and this is an iodine deficiency state. In this state, it is further postulated that the secreting cells of the breast are sensitized to various stimuli to produce the changes noted. This sensitization can progress to overt malignancy if a carcinogen is added to the rat model and possibly in humans in the goitrous areas of the world.

The rat model of Eskin strongly supports the iodine deficiency theory. The clinical improvement rate of 93.4% is impressive and considerably above other forms of treatment that have been reported in the literature. A further reinforcement is the 89.5% recidivism rate upon cessation of treatment. The laboratory work of Eskin and this clinical review establishes our hypothesis that fibrocystic disease is a manifestation of iodine deficiency in the mammary glands independent of thyroid function.

The nomenclature of Iodine Deficiency Breast Syndrome is a logical replacement for the inexact terminology of the past.

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