

THE ETIOLOGIC ROLE OF IODIZED TABLE SALT IN IODODERMA

A STUDY BASED ON A FURTHER EXPERIENCE OF FOURTEEN YEARS*

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Knowledge of the iodine eruptions in all their clinical varieties is, as usual in medicine, not a recent acquisition. Prince A. Morrow (1) of New York reported the first fatal case in 1886. In a book written by Morrow, entitled "Drug Eruptions" (Wm. Wood & Co., N. Y., 1887), he states that the bullous type of iododerma was first described by O'Reilly of New York as early as 1854. Morrow's book was reprinted as part of a volume entitled "Selected Monographs in Dermatology", by the New Sydenham Society, in 1893, at which time its bibliography on iodine eruptions already consisted of 88 references.

The connection between the long-continued use of iodized salt and the production thereby of iodine acne and severe and even fatal iododermas, is of comparatively recent observation. Shelmire (2) in 1928 reported seven cases of severe, inveterate acne in women, all of whom had used iodized salt exclusively for a period of from six weeks to one year. To none had iodides been administered medicinally. Roentgenotherapy and routine treatment for acne proved useless. All recovered on cessation of the use of iodized salt. Of added interest is the fact that Shelmire, in discussing the author's paper on iodized salt read before the American Dermatological Association (3), stated that two of the seven patients had a recurrence of their acne form iododerma on again taking iodized salt.

THE FREQUENT USE OF IODIZED SALT

The use of iodized salt in this country dates from 1924, when it received the endorsement of the Committee of the Pediatric Society of the Michigan State Medical Society as a prophylactic measure in the prevention of goiter. It was first manufactured by the Salt Producers' Association on May 1, 1924, and marketed throughout Michigan. In the treatment and prevention of simple goiter, iodized salt has received the enthusiastic endorsement of many eminent authorities. Hartsock (4) quoted the following from an address made by Dr. Charles H. Mayo before the Wayne County Medical Association on January 26, 1924: "Iodine is almost an absolute preventive of goiter. That has been proved beyond question. Given in table salt it is a preventive for goiter." Slemmons (5), the city health commissioner at Grand Rapids, Michigan, stated: "Iodine is not a medicine. It is simply a replacement of one of the needed elements in food. We urgently ask that the people of our city use iodized salt both for the table and in cooking."

* Received for publication March 4, 1947.

The Council of Pharmacy and Chemistry (6) of the American Medical Association decided that iodized salt was suitable for use by the public on its own initiative. "Hygeia" during 1925 and 1926 carried many full-page advertisements of the Morton Salt Co. advocating the indiscriminate use of its iodized salt, which contained 0.02 per cent of iodine in each 2-pound package.

These eminent endorsements started such a flood of iodized salt that Kimball (7) in 1928 stated that 91 per cent of the homes in Michigan were using iodized salt exclusively. In a letter to Roy D. McClure, chief surgeon of the Henry Ford Hospital, under date of September 1, 1931, the largest salt distributor in Michigan stated that in 1930 he had shipped 58,643 cases of iodized salt and only 7,057 cases of plain salt. Letters from other leading distributors paralleled these figures. This enormous consumption of iodized salt was possibly limited to those States in which goiter was endemic; yet in New York City, which is not in the goiter belt, I personally ascertained some years ago that one large chain grocery store company with approximately 100 retail branches, sold 2,000 packages of iodized salt a month. Many of the grocery stores sold iodized salt even when it was not requested. Despite this enormous output, Plummer (8) stated that there was rapid increase in the incidence of exophthalmic goiter and adenomatous goiter with hyperthyroidism in 1924. This increase reached its height in 1926 and 1927, and did not diminish until 1931.

The popularity of iodized salt with the general public, used not as a preventative of goiter, but as a supposed general tonic, over the space of months and even years, goes on undoubtedly at the present time in the States of New York and New Jersey. This is definitely proven by the fact that of several thousand patients with cutaneous disease questioned by the author, fifty per cent of them stated that they had used iodized salt for long periods. How many drug eruptions in some of these patients were blamed on other drugs than iodine is purely speculative, but nevertheless interesting in view of the fact that outside, of the dermatologic fold, few if any patients are questioned on that subject.

Kimball (9) in an article in the Journal of the American Medical Association published January 12, 1946, again stresses the complete safety of iodized salt and its great success as a prophylactic in goiter. He states in the last paragraph: "My recommendation would be that the American Medical Association, the American Public Health Association and the Federal Food and Drug Administration cooperate to give the entire country a natural salt containing 0.01 per cent potassium iodide or its equivalent. The term "iodized" should be eliminated at once and emphasis be placed on the use of a whole salt or natural salt to prevent food deficiencies. The need is for only one kind of salt and this standardized so that it contains the important food elements which are found in the natural, unrefined salt. The prevention of endemic goiter will then be as nearly completed as any public health measure can ever be." Kimball completely ignores the occurrence of iododerma, sometimes resulting in death, in patients who have used iodized salt for long periods.

DANGERS FROM INGESTION OF IODINE

Death from iodine saturation or sensitivity is not as rare as commonly supposed. Let us review briefly the reported cases.

1. Morrow (1) reports a male patient with a severe bullous, tuberous eruption covering his entire face, arms and hands. The bullae were as large as a pigeon's egg, and the fungating masses completely closed his eyes. The patient was greatly prostrated and seemed dangerously ill. One month previously he had been admitted to the Nervous Hospital suffering from partial paraplegia. A saturated solution of iodide of potassium was ordered and 60 drops were given 3 times a day. This was stopped after he had taken 900 grains, and he was then admitted to Morrow's ward. The patient died five weeks later.

2. Pusey (10) at the Thirty-Fourth Annual Meeting of the American Dermatological Association in 1911 presented the photograph of a baby who died within a week from an iododerma caused by the ingestion of iodine in its mother's milk. Iodine was found in the child's urine. The mother had been taking iodine medication.

3. Tiefenbruner (11) reported the death of a woman aged 49 following the taking of 12 teaspoonful doses of a solution of potassium iodide containing 5 grains (0.324 gm.) to a dose. The lesions were of the fungating tuberous variety.

4. Danel (12) observed a fatal vegetating iododerma in a man aged 51, who had taken 50 cg. of iodine daily for three or four days.

5. Neumann (13) observed a death from medication with potassium iodide for only six days. Iodine was present in the urine. The eruption consisted of large, ulcerated, tuberous lesions. Post mortem examination demonstrated similar lesions in the gastric mucosa.

6. Eller and Fox (14) reported a fatal case of the fungating, tuberous type of iododerma in a man aged 31 after the ingestion of 15 grains (0.972 gm.) of potassium iodide daily for four months. This patient had been taking iodized salt in his food for several years.

7. Hutchinson (15) in 1890 reported the case of a man aged 26, who received potassium iodide for ten weeks. An eruption appeared consisting of large, vegetating, and tuberous lesions. Death occurred in 14 days.

8. Joffe's (16) patient was a man 55 years old with a syphilitic aortitis. After taking sodium iodide for a brief time he developed coryza and a rise in temperature. A few days later his entire face and hands were covered by a bullous eruption, many of the lesions being hemorrhagic. Death occurred in six days of atheromatous changes in the great vessels and endocarditis.

9. Hallopeau (17) observed a patient 50 years of age who received a daily dose of 1 gm. of iodides for a few days, after which he developed vegetating lesions and died in ten days.

10. Wolf (18) had a patient with a generalized papulo-pustular eruption with ensuing ulceration which began after the ingestion of potassium iodide. She died in one week of heart failure.

11. Russel's (19) patient had a generalized bullous eruption with coryza and conjunctivitis after taking potassium iodide for a few days. Death occurred in 10 days.

12. Pollaud (20) reported a patient with an extensive eruption of pemphigoid character which occurred after taking potassium iodide. The patient died.

13. Canult and Barasch (21) reported a case in which papules, pustules and bullae covered the scalp, face, hands, and wrists. On each cheek there was a tumor mass, irregularly shaped and measuring 5 cm. in diameter. Vegetating and ulcerative lesions were present on the chin and neck. The eruption appeared after a few doses of potassium iodide. Iodides were found in the urine. The patient died of edema of the lungs.

14. Wartzki (22) observed a vesiculopustular and bullous eruption in a man 66 years old. It occurred as a result of the ingestion of only three doses of 0.3 gm. each of potassium iodide. The patient had advanced renal and cardiac disease. Death occurred shortly after the appearance of the eruption.

15. Hollander and Fetterman (23) reported a patient aged 65 who had been taking yellow mercurous iodide for several months. Iodine was found in the urine. The iododerma started as an ulcerating, granulomatous lesion on the median surface of the left arm. Five months later the patient had some seventy tumorous lesions distributed generally over the body; many were large and rounded, with ulceration and necrosis. Chemical examination of an excised lesion revealed 470 micrograms of iodine per kilogram of tissue. The patient died three days after the incidence of a bronchopneumonia.

These fifteen deaths from iodides present interesting and instructive deductions, namely that in eleven of them, fatal disease began after only sub-medicinal doses of the iodides had been taken for an extremely brief time. In two of them there was a definite history of the use of iodized salt for years, and a sudden outbreak of their fatal eruption within a week or so after the administration of several doses of iodides. Among those who have survived may be found many examples of the malignant type of iododerma, variously termed "iodide sarcoma", "iododerma tuberosum fungoides", "anthracoid iododerma" and "vegetating iododerma." As in the fatal types, they occurred after the administration of small doses of the iodides, months or more after ingestion of the iodides, either in the form of iodized salt or the drug itself. Cases of this type have been reported by Besnier (24), Pospelov (25), Hallopeau (26), Hutchinson (27), Walker (28), Fordyce (29), Rosenthal (30), Hyde (31), and others.

In the author's 2 cases previously reported (3) both had used iodized salt exclusively for months without any ill effects, yet in one of the cases the administration by the patient's family physician of a total dose of from 2.6 gm. to 3.2 gm. of sodium iodide given in the space of about a week, precipitated a tumorous, bullous eruption which became gangrenous in areas, with subsequent ulceration. The patient nearly died. Determinations of iodine in the urine showed 1.467 gm. per liter, and another examination 1.73 gm. per liter. As he recovered, repeated urine examinations were negative. Tests for bromine were negative. In the other case, a generalized outbreak of indurated, dark red papules followed administration of a colloidal iodine preparation in doses of a teaspoonful three times a day for only two days. The patient also gave a history of having used iodized salt plentifully for several months. Two separate tests for iodine early in the treatment revealed 0.052 mg. in 1000 c.c. of urine, and 0.1 mg. in 1.890 c.c. of urine. As he improved, urine tests for iodine became negative. While his general health was unaffected, the eruption confined him to the hospital for two months.

During the past year, the author has observed 3 cases of generalized iododerma. A brief description follows.

Case 1. A woman aged 21 had used iodized salt for years. After taking a cough mixture containing an undetermined amount of potassium iodide for four days only, she developed an extensive bullous eruption almost entirely covering her hands, arms, and legs. She had never had any prior skin trouble. She recovered in about six weeks. Several months later she inadvertently used iodized salt again for a short time, with a recurrence of her eruption, but to a lesser extent.

Case 2. A woman aged 24 had been using iodized salt exclusively for years. She stated that her cutaneous eruption had been present for five months. On her first visit, a large

number of dark-red, indolent nodules and papules, covering most of the face, arms and body, could be discerned. She was well in six weeks, after the discontinuance of her iodized salt and the administration of enteric coated tablets of sodium chloride in 1 gm. doses, 8 to 16 gm. being taken daily with plenty of fluids.

Case 3. A woman aged 45 presented an extensive bullous eruption around her elbows and knees. This had been present for four months, and had first been noted on her abdomen. She had thyroid disease for which she had used iodized salt for years. The patient disappeared from observation after a week so no follow-up work could be done, but the eruption had all the definite earmarks of iododerma.

IODIZED SALT IN RELATION TO ACNE

The importance of the role played by iodized salt in the etiology of acne in many patients is increasingly recognized by dermatologists. Shelmire's (2) work has already been mentioned. In the discussion of the author's (3) paper on iodized salt as an etiologic factor in iododerma, Jamieson (32) stated:

"In the goiter belt, as we are, and encountering so many patients who use iodized salt as a routine measure, we are finding increasingly often that many patients have their symptoms unrelieved by ordinary measures. This is particularly true in cases of acne, as Dr. Bechet mentioned. I think we should be grateful to him for bringing out the fact that iodized salt is detrimental to many patients. Patients from the age of 35 years up have very persistent acne, of acne rosacea type, with hard, quite red, papular lesions. This is found so frequently that I make it a rule to have these patients discontinue the use of iodized salt before attempting medication, and often the condition clears up without medication. This was emphasized in an English woman, seen about a year ago, who had never suffered from acne. Within a month after she came to this country, acne of a severe type developed. With no history of a previous acne, I thought it might be iodism and had her discontinue iodized salt. Following this and the use of saline solution intravenously, she made a prompt recovery. I think the paper of Dr. Bechet should call the attention of dermatologists, particularly in the goiter belt in Michigan and Canada, to the fact that various cutaneous lesions may be more promptly cured by stopping the use of iodized salt as a routine measure."

Mitchell (33) in discussing the same paper stated: "I have seen a number of these cases, the most definite one being that of a man aged 35 who had had acne during the adolescent period. He had been married for two years and was much disappointed because he had been under the impression that marriage was good for acne, but he was now married and the acne was worse than ever. His wife was a great believer in iodized salt. He had never heard of it, but went home and found they had been using it for two years. Its use was stopped; his acne cleared up, and he has had no trouble for several months."

It has been my experience that iodized salt acts in two ways as an etiologic factor in acne. Firstly, in the typical iodide acne, the lesions consist of dusky red to brownish-red papules occurring on the face, arms, shoulders and back. Although the lesions are numerous and discrete, there is a complete absence of comedones, pustules and seborrhea oleosa. This is the true type of "acne form"

iododerma. That iodized salt is the sole etiologic factor is proved by the fact that the lesions disappear when it is eliminated, and ordinary salt administered by mouth or intravenously, and recur if iodized salt is again taken.

The author presented a patient before the New York Dermatological Society on February 23, 1938 (34), with the diagnosis of acneiform iododerma, and the following history. "J. M., a woman aged 29, stated that ten years previously she received a course of roentgen therapy for acne vulgaris. After the completion of the course she remained well for three years. She then began for the first time to use iodized salt exclusively, and some months later noticed a few discrete, indolent papules on her face. A few of these became cystic. The lesions greatly increased in number in the following few weeks, and when first seen both cheeks were covered with a large number of indurated, dusky-red nodules and papules. There were no comedones, oily seborrhea or pustules."

Secondly, in *ordinary acne vulgaris*, with pustules, cysts, comedones and oily skin, iodized salt is a contributing factor in many patients. One can almost invariably get a history of its use for months to years previously in patients whose response to roentgenotherapy is greatly delayed. That this is true has been amply proved by personal observation and the analysis of a total of 240 cases of acne treated by me in the past two years. Of this number there were 92 who, besides presenting the typical clinical picture of ordinary acne (comedones, oily skin, pustules, and cysts), also gave a history of the ingestion of iodized salt for years previously. All showed lack of improvement with roentgenotherapy (eight to ten treatments). All began to improve rapidly only after the oral ingestion of 8 to 15 gm. of sodium chloride daily in the form of enteric coated tablets of 1 gm. each, as recommended by Wise and Sulzberger (35). This is contraindicated in patients with nephritis, marked hypertension, and a tendency to edema of the legs.

Of the 240 cases of acne, 18 presented acneiform iododerma without comedones, seborrhea, or pustules, and the results of roentgenotherapy were most unsatisfactory until sodium chloride was administered both by mouth and intravenously.

COMMENT

Public health officials, and many eminent medical authorities, have enthusiastically endorsed iodized salt as a preventive of goiter. In the goiter belt of Michigan and Canada this may be necessary and proper. But in my opinion, it is not only improper but actually dangerous to state that iodine is not a medicine but simply a replacement of one of the needed elements in food; that it is harmless and can be used indiscriminately by the general public in perfect safety; that iodized salt containing 0.01 per cent potassium iodide or its equivalent should be the only salt given the entire country; that the word "iodized" be eliminated entirely from the package; with no mention made of the considerable number of patients who, after using iodized salt for years, have developed severe, often incapacitating, and sometimes fatal iododermas following the administration of submedicinal doses of the iodides.

Deaths do occur in these cases from sensitivity to iodine due to the long-continued use of iodized salt, and that small doses of the iodides furnish the "trigger" mechanism was proved by Eller and Fox's patient. This was mentioned by Dr. Sigmund Pollitzer (36), in discussing my paper: "It was a clear case of bulbous iododerma due to a few therapeutic doses of potassium iodide in a man who had been using iodized salt for several years and evidently had become sensitized. There was considerable criticism of the paper at that time, and it was said that iodized salt could not do that; that iodides were too soluble and diffusible to be retained in the system. But as a matter of fact, the patient excreted iodides in the urine for the three months of his stay in a hospital, during which special care was taken to exclude iodine from his diet, and at necropsy a few square centimeters of his skin yielded a considerable amount of iodized salt." The author believes that this case showing retention of considerable iodine in his urine the day before death and in his skin at necropsy, with no ingestion of any iodine whatsoever for several months prior to death, would tend to prove that iodine from iodized salt can become stored in the tissues and act as a sensitizing agent.

Our most recent textbooks devote only a few lines to iodized salt as a possible etiologic factor in iodide eruptions, despite the great importance of the subject. The paucity of the literature on this score also evidences a certain lethargy on the part of writers of dermatologic articles. There is a notable exception, however, in the fact that Wise and Sulzberger as editors of the Year Books of Dermatology and Syphilology have repeatedly mentioned the dangers of iodized salt as an etiologic factor in acne and the iododermas. In the Year Book for 1933, on page 11 (35), they state: "Another and probably much more important source is the iodine in iodized salt. This, unfortunately, is now being universally sold without coming within the jurisdiction or under the control of persons adequately educated to understand its sometimes far-reaching deleterious effects. Iodine is a strong drug, and like all active therapeutic agents, can do incalculable harm as well as great good. (We have seen severe iododermas due to the iodine in iodized salt; it should not be sold except under the direction of physicians)." Again, the same authors in The Year Book of Dermatology and Syphilology for 1936 (37), commenting editorially on Hollander and Fetterman's article (23), state: "Even the traces of iodine in iodized salt are a potential grave danger to individuals with iodine hypersensitivity and once begun, iododermas may continue to progress and exacerbate and even, in a few instances, to go on to a fatal termination, despite cessation of exposure and despite all known therapy."

There is no doubt in my mind that iodized salt through induced sensitivity has been responsible for a sufficient number of severe, near-fatal, and fatal iododermas, to warrant this second relation on the subject, gleaned from additional personal experience, and written in the hope that it might impress medical men enough to cause them to investigate the matter personally. This would prevent many iodide eruptions among persons who use iodized salt in the belief that it is a harmless tonic.

It is not my intention to condemn the use of iodized salt either as a prophylac-

tic in goitrous districts, or as a cure for certain types of goiter. But it is timely to call attention once more to the dangers inherent in the promiscuous use of iodized salt by the public at large without knowledge on their part that it can at times cause serious and even fatal illness.

It is the hope of the author that this collection of verified data on the occasional dangers following the prolonged use of iodized salt may cause others to investigate the subject and thereby prevent much suffering, incapacity and even death.

SUMMARY

Since 1924, iodized salt has been recommended indiscriminately to the public; which has been assured of its complete safety. As a result, it is being used by thousands as a tonic, without even the knowledge that it is useful in goiter, and in ignorance of the fact that severe iododermas and even death, have followed the administration of iodine in less than medicinal doses, among its users.

Fifteen deaths are cited from the literature, and three non-fatal cases of iododermas of the bullous type, seen during the past year alone, in patients, using iodized salt, are briefly described for the first time.

The role of iodized salt in the etiology of acne in many patients is well recognized by dermatologists. Its relationship to the acneiform iododermas has been proved by the fact that the lesions disappear on its elimination only, or with the administration of ordinary salt. Recurrences on again taking iodized salt have occurred. Its etiologic relationship in some cases of acne vulgaris is shown by failure of response to roentgenotherapy until its use is discontinued. On questioning such patients, a history of the ingestion of iodized salt is almost invariably elicited.

The author has treated 240 cases of acne during the past two years. Of these, 92 who presented the clinical picture of ordinary acne gave a history of the ingestion of iodized salt for long periods, and showed no improvement with roentgenotherapy. *All improved rapidly after discontinuing iodized salt, and the administration of sodium chloride by mouth or intravenously.* Acneiform iododermas occurred in 18 cases, and the results from x-ray therapy were equally unsatisfactory *until the iodized salt was stopped and sodium chloride given.*

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