TAB N

MEMORANDUM

TO: **Members of the Advisory Committee on Human Radiation Experiments**

FROM: **Advisory Committee Staff**

DATE: **August 31, 1994**

RE: **The Thyroid Studies: A Follow-up Report on the Use of Radioactive Materials in Human Subject Research that Involved Residents of State-Operated Facilities within the Commonwealth of Massachusetts from 1943 through 1973**

Submitted by the Working Group on Human Subject Research to Philip Campbell, Commissioner, Department of Mental Retardation, Commonwealth of Massachusetts (June 1994)

In December 1993 a Task Force was appointed by Philip Campbell, the Commissioner of the Department of Mental Retardation of the Commonwealth of Massachusetts, to examine reports of human radiation experiments involving residents of state-operated institutions.

The main report of the Task Force was included as Tab E in your briefing book for the meeting of July 5-6, 1994. In that report, the Task Force stated that its examination of a series of thyroid studies would be issued as a supplementary report.

Enclosed in this tab is the supplementary report on the thyroid studies. It places the studies within the context of medical knowledge of their times (pp. 1-12), examines the risk from the doses administered to subjects (pp. 13-26), and discusses how consent was obtained, with copies of the letters sent to parents/guardians of subjects requesting consent (pp. 27-31). It concludes with a section on "Findings and Recommendations" (pp. 32).

THE THYROID STUDIES

A
Follow-up Report
on the Use of
Radioactive Materials
in
Human Subject Research
that Involved
Residents of
State-Operated Facilities
within the
Commonwealth of Massachusetts
from
1943 through 1973

Submitted by
THE WORKING GROUP ON HUMAN SUBJECT RESEARCH
to
Philip Campbell, Commissioner
Commonwealth of Massachusetts
Executive Office of Health & Human Services
Department of Mental Retardation
June 1994

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Heartfelt gratitude goes out to you all ...

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Introduction

Please Note: This report is a follow-up study to the Task Force on Human Subject Research's original study entitled " *A Report on the Use of Radioactive Materials in Human Subject Research that Involved Residents of State-Operated Facilities within the Commonwealth of Massachusetts from 1943 through 1973.*" This introduction will only briefly touch on the steps taken in that investigation. For an in-depth look at this process and those findings please see the original report. Copies are on file at the State Archives in Massachusetts, the Library of Congress in Washington DC, the Boston Public Library, the Newton Free Library and the Howe Library at Fernald School.

In the spring of 1993, President Bill Clinton directed federal agencies to implement a post-Cold War declassification process that would allow citizens to gain access to archival records that had previously been denied to them. The Department of Energy (DOE) initiated a massive release of documents for public inspection beginning in the summer of 1993. Subsequently, private citizens, advocacy groups, and the press began to review these declassified records and make public many previously unknown, or little-known, experiments and research studies that had used radioactive materials throughout the United States.

In November 1993, the *Albuquerque Tribune* of New Mexico printed a series of articles by Eileen Welsome that detailed research dating back to the 1940s which involved the injection of plutonium into human subjects. The reporting of these events was a catalyst for the establishment, by President Clinton, of the President's Advisory Committee on Human Radiation Studies and its Human Radiation Interagency Working Group.

In December 1993, the *Boston Globe* published an article written by Scott Allen in which he identified the Walter E. Fernald School as one of the institutions in Massachusetts where radioactive material was administered to residents by researchers from the Massachusetts Institute of Technology (MIT). It was reported that young male residents of Fernald, who were members of a "Science Club", were used as subjects in nutritional studies using radioactive materials in the 1940s and 1950s.

Out of concern for the nature of the facts revealed in the *Globe* article, the identified institutions stated publicly that their current staff was unaware of these studies. The institutions also pledge their commitment to work cooperatively and openly to respond to the need for full and accurate public reporting.

Following the initial meetings to plan a course of action for an objective and immediate review, Philip Campbell, Commissioner of the Department of Mental Retardation (DMR), created the ***Task Force on Human Subject Research*** to design and conduct this comprehensive study. Their charge was to secure all available facts on such studies within the facilities operated by the Commonwealth of Massachusetts.

In April 1994 a final report was published that outlined all of the findings of the study. The report included an appendix that reproduced some of the archival records so as to allow the public an opportunity to view relevant correspondence and file records relating to the studies. In this tangible manner, the Task Force sought to fulfill its mission of a full and accurate disclosure of all of the facts found.

While doing the research on the nutritional Calcium and Iron studies (which involved the unearthing of literally thousands of pages of archival records) for the original report, information was discovered concerning a set of Thyroid studies that were not originally known to exist. These Thyroid studies became a point of focus and potential concern due to the use of ^{131}I (iodine-131; a radioactive isotope) used as a tracer in these biomedical studies. This report focuses exclusively on the Thyroid studies. The The chart below outlines the studies by name, number and years of research and publication. The asterisk by the subject numbers and identities signifies that each chapter holds details on identification issues.

Thyroid Studies

Year of Research	*Year of Publication*	*Study*
1952	1954	Thyroid Function in Persons with Myotonia Dystrophica 6 Subjects: identities found* *(Study No.1)*
1952	1957	Thyroid Function in Persons with Down Syndrome: Fernald 28 subjects: identities found* *(Study No.2)*
1961	1965	Thyroid Function in Persons with Down Syndrome: Wrentham 104-167 subjects: 42 identified* *(Study No.3)*
1961	1962	Nuclear Fallout Study: Wrentham 70 Subjects: ?identities overlap* *(Study No.4)*

* Please see these chapters for clarifying information on the identification of subjects process and relevant issues

Study #1: Thyroid Function in Persons with Down Syndrome
Fernald (1957)

The following definitions are offered to address the issues in all of the studies in this report.

The Thyroid Gland :
Many of the activities of our body are controlled and regulated through a set of chemicals (*hormones*) carried by the blood and lymph systems. The term hormone was coined in 1902 in connection with the discovery of *secretin* - a substance secreted by the duodenum to stimulate pancreatic secretions. The formal study of these hormones (endocrinology) did not begin until the 1920s. These hormones (defined as a chemical substance produced by an organ or tissue which has a specific effect on tissues that are relatively remote from the tissue of origin) are secreted by the endocrine glands; these include the pituitary, adrenal glands, pancreas, duodenum, testes or ovaries, placenta, parathyroids and the *thyroid gland.*

The thyroid gland is a highly vascular organ with two lobes joined by an isthmus (bridge of tissue). It is normally found in the front of the neck with two lobes (halves) that lie on either side of the "windpipe", just below the "Adam's apple".

Iodine is found in foods such as seafood, salt, bread and milk. The thyroid gland takes this iodine out of the blood stream and uses it to make the full level of hormones needed to guide such bodily functions as the rate of metabolism; body temperature regulation; protein, fat and carbohydrate catabolism in all of the cells in the body; skeletal (bone) maturation; heart rate; central nervous system development; muscle tone and strength, and other fine tuning of our bodily functions.

The two most important of the thyroid hormones are thyroxine (T_4) and triiodothyronine (T_3) - (the subscript numbers refer to the number of iodine atoms contained in each hormone molecule). The hormones are stored in the gland until needed. Once released, they ride *carrier protein* molecules throughout the body. The level of hormone is maintained constantly by the pituitary gland. It sends out TSH (thyroid stimulating hormone) to maintain thyroid cell function.

If the thyroid gland puts out too much hormone it causes *hyper*thyroidism. The reverse state, too little hormone, causes *hypo*thyroidism. The thyroid can become infected and inflamed or develop cysts or tumors. Problems with thyroid levels can run in families (often skipping generations before the next manifestation); thyroid dysfunction tends to be found in women more than men; and, there are a set of related inherited tendencies toward other conditions such as premature gray hair, patchy hair loss, white patches on the skin (vitiligo), anemia (pernicious anemia), rheumatoid arthritis, and diabetes mellitus ("sugar diabetes").

Testing of the thyroid was done in the 1930s through the 1970s via tests such as basal metabolic rate, protein-bound iodine (PBI) and radioactive iodine uptake tests. Today highly sensitive and specific methods allow blood levels of T_4 and T_3 and TSH to be measured much more reliably.

"Your Thyroid: A Home Reference", Wood, Cooper & Ridgway (1982)

A special definition text box will appear in each chapter for disorders, system functions or

associated scientific information as each associated area appears in the chronological order of the studies and research findings.

In 1952, Dr. Clemens Benda (Medical Director at Fernald School) wrote an introduction to the study proposal which outlined the medical understanding of the disorder **Myotonia Dystrophica** at that time:

"Myotonia Dystrophica is a genetic neuro-endocrine disorder in which a specific myotonic reaction of striated muscle is associated with a progressive muscular dystrophy and complex endocrine disorders in which gonadal atrophy, both in males and females, is most characteristic. Extensive clinical and endocrine studies which will be reported elsewhere (noted as "to be published in Medicine'') indicate that in addition to the gonadal atrophy changes in the pituitary of the type of basophilism, anomalies in the adrenal and thyroid pathology are observed. Four autopsies which were available to us, and a survey of the literature, indicate that myotonia dystrophica is usually associated with a resting colloid goiter. The thyroids in our cases weighed 37, 75, 22½, and 30 grams respectively, in contrast to a control material of over 300 cases of other types of neuropathological conditions excepting goiter, in which hardly a single thyroid weighed more than 25 grams. These observations suggest that it might be desirable to study the thyroid function in myotonic patients with the use of radioactive iodide and determinations of protein-bound iodine."

PROTEIN BOUND IODINE (PBI) TEST

A PBI test did not involve the use of radioactive isotopes. It involved the taking of a fasting blood test for laboratory studies. However, it was often used in conjunction with a tracer amount of radioactive isotope which was then signified as a $PB^{131}I$ test. It determined the fraction of the administered dose of radioactive iodine present as a protein-bound iodine 72 hours later. If more than 0.27 percent had been taken up into hormones and released into the blood by the thyroid, hyperthyroidism may be present. These tests are now rarely used as clinical tests of the thyroid. They measured the iodine rather than the actual thyroid hormone level, so any iodine in the blood could elevate the results. This level of insufficient reliability had to be accepted until the more refined and specific measurements of the concentrations of blood levels (serum) thyroxine (T_4) and triiodothyronine (T_3) were developed. They are the tests which are now routinely used.

Benda went on to state: *"there are two forms of muscular dystrophy combined with myotonic reactions, the so-called "myotonia dystrophica" or "dystrophica myotonica" and "Thomsen's Disease" or "myotonia congenita". While the two genetic entities overlap each other, there is considerable argument whether the two conditions represent different model entities or only different manifestations of the same genetic disorder. "*

Note: All persons with myotonia dystrophica in this study did succumb to complications of this disorder at relatively young ages. All were identified and death certificates examined.

In this study[1], six males who had myotonia dystrophica were studied. Three of the subjects were brothers. Each subject was administered a tracer dose of 54 microcuries of ^{131}I in 100 milliliters (approximately 3 ounces) of water with 100 micrograms of ^{127}I as a carrier. An additional 100 milliliters of water was used to wash the glass and drunk by the subjects.

Iodine-131 (^{131}I)

In 1896, the scientist Baumann showed that there was a very high concentration of iodine in the thyroid which Marine and Feiss (1915) and Marine and Rogoff (1916) followed up with further studies that proved the thyroid has a selective affinity for iodine. Based on these tests, many researchers (such as Perkin, Brown and Lang (1934); Watson (1936, 1938); and Elmer (1938) created iodine tolerance tests to measure the level of thyroid function. In 1934, Fermi and his staff prepared a radioactive isotope of iodine (^{128}I , with a half life of only 25 minutes). Hertz, Roberts and Evans (1938) created the first test technique using a radioactive isotope of iodine for studying thyroid function. This included the demonstration that if one administered an increased amount of iodine it would create a lowered uptake of any of the radioactive iodine administered. After that, radioactive iodine was widely employed as the primary tool to study the physiology and function of the thyroid gland. It was not until the 1970s that researchers began to discontinue the use of ^{131}I in children, and over the next decade, in adults as well. Today, in the United States, ^{131}I is used for treatment of thyroid disease, but diagnostic thyroid uptake tests now primarily use ^{123}I (which was not readily available until the 1970s) with ^{131}I less frequently being used for this purpose. However, other countries are still extensively using ^{131}I for diagnostic thyroid uptake tests.

^{127}I is the stable common form of non-radioactive iodine (isotope) that was used as a carrier substance. Carriers were added from time to time to make sure all of the substance being studied was actually delivered. It may be, in fact, that a carrier was used in other studies but was simply not mentioned due to their non-radioactive nature. Earlier it was noted that extra iodine given to a subject could actually inhibit the uptake of the radioactive tracer, however, in this case, the amount was not sufficient to block the thyroid uptake but only acted as a carrier to assure that all of the ^{131}I in the container was actually ingested.

PBI measurements (without the additional use of any radioactive isotopes) were made on 4 of the 6 subjects one week prior to and 3 days after the study administration of the radioiodine tracer. The "in vivo" (in the live subject) measurement of the thyroid uptake was determined on the 1st, 2nd, 3rd, 6th and 8th days after administration by use of a "four channel scintillation counter" (Geiger counter) located at the Thyroid Laboratory of the Beth Israel Hospital in Boston, MA. A small thin rubber container that contained a reference standard

[1]C.E. Benda, D.J. Maletskos, J.C. Hutchinson & E.B. Thomas, "Studies of Thyroid Function in Myotonia Dystrophica", *Am.J.of Med.Sciences*, 228, 668-672 (1954)

source of ^{131}I equal in activity to the dose given internally to the subjects was held against their neck by the thyroid gland to correct for the absorption and scattering of the ^{131}I gamma rays.

The conclusions of this study showed that the ^{131}I uptake and excretion, as well as the PBI values, were normal for all of the subjects. As pathology reports indicated that the thyroid gland was found to be larger than normal in most patients with myotonia dystrophica, the authors concluded that in persons who have this disorder the thyroid gland operates at a lower than normal capacity, but the capacity is sufficient to maintain an output of hormone levels

[redacted]

An article describing this study (see footnote 1) was found while working on the study for the original report. The article contained the initials of the 6 subjects with no further identification.

By reviewing some of Dr. Benda's private records, which had previously been donated to Harvard University's libraries, the subjects in the Calcium studies had been positively identified. Further, they also supplemented records from MIT which allowed positive identification of the subjects in the Iron studies. It was hoped that Benda's records might again serve as a primary source for subject identification. Additional Benda records, secured outside the previous sites, were identified and reviewed.

Within this batch of records, extensive writings on myotonia dystrophica were found. Within these records, the original drafts of the manuscript for the article were found along with the

Thyroid Function in Persons with Down Syndrome; 2 Articles:
■ Study No.2 - Fernald (1957) & ■ Study No.2 - Wrentham (1961)

Down Syndrome

Down syndrome (formerly referred to as "Down's Syndrome") is a congenital disorder, caused by trisomy (retention of a third copy) of the 21st Chromosome with a birth incidence of 1 in every 1,000 births. *"There are hints in the historical records that an awareness of the condition of Down syndrome existed hundreds, perhaps even thousands of years ago. Images in old paintings and ancient stone carvings suggest that this might be so (Milton & Gonzalo, 1974; Zellweger, 1968). But there can be no doubt that a paper by J. Langdon Down in 1866 stands as a landmark document in the written history of Down syndrome. Down, in attempting to classify the various forms of "feeblemindedness" that he observed, probably influenced by Charles Darwin's thoughts on evolution, concluded that individuals with mental disabilities belonged to various ethnic classifications, including the "Ethiopian and Malay varieties."(..his description of persons he felt belonged to the "Mongolian family"..in light of the era of racial elitism in which he lived)*[1] *Since Down syndrome was first described more than a century ago, many theories have been postulated about its cause..such untenable hypotheses that alcoholism, syphilis, or tuberculosis (were the cause)..by the end of the early 1930s, some investigators suspected that Down syndrome might be due to a chromosomal problem. However, at that time the technology of examining chromosomes was not advanced enough so that this theory could be proven."* In 1956 new laboratory techniques were developed that allowed scientists to visualize and better study chromosomes, (tiny rod-like structures carrying the genes inside the nucleus of each cell) and it was found that the previous theory that there were 48 chromosomes was in error, and that the actual number was 46. In 1959, Lejeune reported that persons with Down syndrome had one extra, small chromosome lending to his observation of 47 chromosomes in this disorder. Instead of the ordinary set of #21 chromosomes, there were three. This led to the term "trisomy 21". Since that time, geneticists have found that this trisomy is most often present, but that there can also be other chromosomal problems such as translocation (attachment to a different group, such as the D or G group) or mosaicism (an error in one of the initial cell divisions so that some cells have 47 chromosomes but others have 46). The National Down Syndrome Congress (a parent advocacy organization) refers to it as "the leading clinical cause of mental retardation." There have been a number of archaic medical terms used for this syndrome such as "mongolism", or the more insulting term "mongolian idiot". The use of such terms as "idiots", "morons", "fools", "feebleminded", and "mentally deficient" was addressed and apologized for in the first report. It is important to bear in mind that Down syndrome has an associated mild to moderate level, i.e.,: rarely a severe level, of mental retardation.

† *-most of above derived from writings by Siegfried M. Pueschel & Jeanette K. Pueschell, 1992; but was supplemented with discussions with Working Group Members and Advisors*

At the time of this study, the accepted medical terminology was "mongolism".

Study No. 2 - Fernald

During this earlier time period, it was Dr. Benda's belief [2] that the thyroid function abnormalities found in a large number of persons with Down syndrome were actually the causal factor in the development of this disorder. To quote from his article, he believed this syndrome was "(the) *result of deceleration of normal growth during the fetal period.*"

Persons who have Down syndrome ultimately have a significantly higher rate of thyroid malfunction. By the 3rd to 4th decade of life, over 25% of persons with Down syndrome will develop hypothyroidism. There is also a unique phenomena found in persons having Down syndrome: a higher finding of an autoimmune antibody relating to the thyroid can be found in the parents of children having this disorder than in the total population. This phenomenon is not fully understood by endocrinologists.

Benda's earlier articles (as footnoted below) had shown " *a possible relationship between abnormalities in development and function of the thyroid gland and the fetal growth process in mongolism is suggested by anatomic evidence of pathologic alterations in the thyroids of mongoloid children and the reported frequency of abnormal thyroid function in their mothers*". Benda shared the belief of a number of his contemporaries that this would be found to be the major causal factor that could lead to the discovery of a "cure" or a definitive "treatment for" mental retardation as stated in his permission letter for this study (see section on Consent).

It is stated further in this article that *"although data are available concerning isolated phases of thyroid function in mongolism, a detailed investigation of the various aspects had not, at the time of our studies, been carried out. This report presents the results of an investigation of the thyroid gland in mongolism, utilizing a variety of recently available techniques."*

The study reported in this article included a total of 28 subject: 21 were persons with Down syndrome (stated as residents of the Fernald School) and 7 parents. Their ages were stated as ranging from 5 to 26 years. The identities of the residents of Fernald and the parents were both discovered in the archival records.[3]

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[2] Benda,C.E. Mongolism and Cretinism, ed. 2. New York, Grune and Stratton, (1949)
Benda,C.E. What is Mongolism?*Internat.Rec.Med.*165:75,(1952)
Benda,C.E., Dayton, NA and Prouty, RA: On the Etiology and Prevention of Mongolism, *Am.J.Psychiat.*99: 822,(1943)
Benda,C.E., Prenatal Factors in Mongolism,*JAMA.*139:979(1949)

[3] [Note: In the Benda papers, we were able to positively identify 22 residents of Fernald whose test results were submitted to the authors for inclusion in this article. Five sets of initials in the report do not match any of the names on the Benda lists. There are ages missing on three of them and the only child below the age of 16 (in this case a girl of 5 years of age) are in that set of five unidentified subjects. Every other record kept by Benda, for all studies, had the inclusion of ages. It may be that these last 5 were persons in the Beth Israel lab files (as were the control subjects whose data was used). However, in the dosimetry and risk evaluations, we will address the 5 year old maximum dosage and risk levels as stated in the article. It does not appear, however, that the 5 year old was one of the residents tested for this article.]

The article[4] also notes that "64 euthyroid (*normal functioning thyroid*) subjects ranging in age from 10 to 65 years served as controls". It was later determined, by conversation with one of the researchers, that this set of control data was from studies done at the Thyroid Lab at the Beth Israel Hospital and did not include other residents from the Fernald School.

The persons with Down syndrome, of all ages, received a standard dose of 70 microcuries of carrier-free radioactive iodine (^{131}I) as a tracer. This was administered orally. The parents, like the control subjects from the other studies at the Beth Israel Hospital, received 100 microcuries.

The measurement of the thyroid uptake of the tracer was done with a four-tube G-M method, modified by a correction factor for scatter and absorption by holding a container of an equivalent dose of ^{131}I against the neck of the subjects. Measurements were taken at three separate intervals over a five day period.

On page 553 of the article, it is stated that "*thyroxine metabolism was studied in 2 mongoloids (sic) by following the rate of disappearance from the plasma of intravenously infused ^{131}I labelled thyroxine and by measuring the appearance of radioactivity in the thyroid after the infusion.*" This shows that two subjects were administered 55 microcuries of ^{131}I thryoxine in addition to the ^{131}I iodide thyroid tracer. Since the two tracers differ in their biological behavior, a simple addition of radioactivity is not a scientifically proper calculation. However, their total radiation dose would be increased. This total dose is discussed in the section of this report that oulines the outside experts' opinions.

Following the findings, a second set of 23 control subjects was compared. Record review has determined that they were subjects from the Beth Israel Thyroid Lab and not residents of the Fernald School.

The conclusion of the study was that the ^{131}I uptake and excretion levels were within normal range for the subjects with Down syndrome, as was the turnover rate of labelled thyroxine. Nor was any significant abnormality found in the 7 parents. The subjects with Down syndrome did demonstrate higher turnover rates of iodine, which suggested that a smaller effective portion of the thyroid gland was working at an intense rate in order to maintain normal levels of thyroid hormones.

The researchers were from Harvard Medical School and the Beth Israel Hospital in cooperation with Fernald staff. The research was supported by the National Institute of Arthritis and Metabolic Diseases and the Atomic Energy Commission.

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[4] G.S. Kurland, J.S. Fishman, M.W. Hamolsky, & A.S. Freedberg, "Radioisotope Study of Thyroid Function in 21 Mongoloid Subjects, including Observations in 7 Parents", *J.Clin.Endoc.&Metab.*, 17, 552-60 (1957)

Study No. 3 - Wrentham

The second study on thyroid function as it relates to persons with Down syndrome was conducted at the Wrentham School in 1961-2 and published in 1965[5]. The two authors of this article were also involved with the earlier Nuclear Fallout study at Wrentham in 1961 (see next chapter). From conversations with the researchers, it appears that some of the data from that earlier research were used in a pooling of subjects for this second work.

The article noted that the subjects had normal PBI and thyroid uptake studies, but that there was an elevated uptake of T_3 by erythrocytes and a higher than normal circulating thyroid antibody level that bore further investigation. *"The mechanism and significance of these anomalies"* were the basis for this study and discussion.

The subjects included 53 persons with Down syndrome and 51 persons with mental retardation associated with other disorders. Identities were noted only by sex and age groupings for those with Down syndrome. 23 sets of initials were also given for this group. Using these factors, those 23 identities have been established with a good statistical basis for positive identification. An additional 19 identities are also considered sound. The lack of actual archival records deters us from making that claim as "positive" at this time.

The conclusion from the research was that iodine uptake and plasma levels of thyroid hormones were within the normal range for all subjects. The researchers also concluded that red blood cell uptake of the thyroid hormone triiodothyronine (T_4) labelled with ^{131}I could be used as test of thyroid function. This was done using a standard venous blood draw and did not require giving radioactive iodine to the children.

As was the case when the original Calcium and Iron studies were investigated, a major problem was the lack of any standardized and required record keeping or notations of any studies in the actual records of the residents. The researcher's records were kept separately and researchers kept their own personal records in a location away from the research site. The two surviving authors, who were interviewed for this report, did not themselves keep any of the records from these studies. What records may have existed at the Thyroid lab at Beth Israel were either discarded or lost in a flood that occurred in that storage area a number of years ago. Therefore, the task of identifying any potential subjects fell to the time-consuming and frustrating effort of sorting through a pool of over 2,000 records of former and present clients. By defining boundaries in the search that included the age of the resident, date of admission and discharge, sex and disability, we have been able to reduce the number of potential subjects to just under 300 as of the writing of this report.

The researchers were from the Harvard Medical School, Massachusetts General Hospital, and the Boston University School of Medicine. The research was supported by the Division of Radiological Health, Research Branch, of the U.S. Public Health Service.

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[5]K.M. Saxena and C.V. Pryles, "Thyroid Function in Mongolism" *J.Pediatrics* 67, 363-70 (1965)

Study 4: Minimal Dosage of Iodide Required to Suppress Uptake of Iodine-131 by Normal Thyroid
Wrentham (1961)

"Chapman and Saxena from the Unit [The Thyroid Clinic & Laboratory, Mass.General Hospital] *measured the uptake of radioiodine in human subjects when administration was accompanied by varying doses of carrier iodine. The importance of this was that information was needed on the amount of iodine that would be needed to inhibit the retention of radioiodine in the event of fallout from an atomic accident or explosion.* ^{131}I *is the predominant isotope resulting from an accident in a nuclear power plant or explosion of an atomic weapon. They were the first to define the necessary dose in normal human subjects, although there was information on this point from the Mendoza study on iodine-deficient subjects. This problem was the subject of a recent (1989) conference called by the European Community* [note: Chernobyl occurred in 1986]. *The Saxena-Chapman paper had been forgotten, but it was brought to the attention of the attendees."*

-John B. Stanbury, M.D.*

"A Constant Ferment", Ipswich Press, 1991

*on page 90 of this book, the author states that he was a consultant on nuclear accidents to the Atomic Energy Commission (AEC).

A press release was issued by the Task Force on February 8, 1994, to inform the public that a study which fell under what society has come to call "Cold War experiments" (ones that focus on the medical effects a civilian population will suffer from fallout following a nuclear attack or accident) had been discovered in the archival record review.

The body requires iodine as a nutrient, and uptake of the small amounts normally present in the diet is high. The purpose of this study was to determine how much normal iodine was needed to be added to the diet of children to block the uptake of radioactive iodine they might be exposed to from nuclear fallout.

Iodide vs. Iodine

Iodine is a chemical element, in the same group on the periodic table as fluorine, chlorine and bromine (*called halogens by chemists*). It is rarely found alone for it usually combines with another element to form a compound, called iodide. Iodine combines readily with alkali metals, such as sodium or potassium. Most often, we take in iodine in the form of sodium iodide salt. In this study, the ^{131}I was administered orally as both potassium and sodium iodide salt.

This study[5] involved 70 subjects, ranging in age from 1 to 11 who were residents of the Wrentham School. The identities of the subjects have not been fully determined at the time of this writing, as discussed in Study No. 3. Benda, whose personal papers had allowed the positive identification of all subjects of the thyroid studies at the Fernald School had not been involved in this study. None of the researchers involved in this study had kept their records. Using a set of criteria (age, sex, date of admission, status in relation to Down syndrome, etc) we have reduced the pool of potential subjects to 300 persons and a careful record review is underway to try to find identifying information.

The 63 primary subjects were given daily dietary supplements of stable (nonradioactive) sodium iodide, ranging from 100 micrograms to 1,000 micrograms, for a period of 12 weeks. An additional 7 subjects were given a single dose of 1,500 micrograms per square meter of body surface of stable iodide. The Task Force has been informed by outside nutritional biochemistry experts that the stable iodine should have posed no risk in and of itself as it is a normal dietary requirement. Literature cited in the journal article arising from this study stated that even unusually high levels of ordinary iodine would only pose problems if administered for several years. With enriched flour and other foods, the modern diet can easily include about 1,000 micrograms per day of iodide.

Radioactive iodine, ^{131}I, was given as a tracer to measure the rate of uptake of the stable dietary iodine. It appears from Figure 1 of the article[6] that 1 microcurie of ^{131}I was given to 5 2-year-old subjects every 2 weeks for 14 weeks. Thus, each subject received a total of 8 microcuries of ^{131}I.

The researchers were from the Harvard Medical School, Massachusetts General Hospital, and the Boston University School of Medicine. The research was supported by the Division of Radiological Health, Research Branch, of the U.S. Public Health Service.

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[5] K.M. Saxena, E.M. Chapman, and C.V. Pryles, "Minimal Dosage of Iodide Required to Suppress Uptake of Iodine-131 by Normal Thyroid," *Science* 138, 430-31 (1962).

[6] Ibid.

Radiation Experts' Opinions on Dosage and Risk

In the first report by the Task Force, concern was expressed about the ages of the subjects who received these doses of the radioactive iodine tracers and the potential for the subjects to have developed thyroid cancers.

Opinions were sought from a total of 8 persons who currently function as nationally noted experts in the fields of radiation, thyroid studies and epidemiology. One of the experts, Dr. Joseph Lyon, who (while calculating his epidemiological risk factors for the Calcium and Iron studies) brought this potential for concern to the attention of the Task Force and this special detailed follow-up study was called for. In addition, 7 other experts were called together to serve as a *Dosimetry and Risk Assessment Subcommittee* for the Follow-up Working Group. Their reports are contained in the following pages of this chapter.

In summary, there was a consensus that, as Dr. Lyon stated in his report, *"in neither group of children would the radiation dose have been sufficient to increase the risk by as much as a single case".*

Even in the study conducted at Fernald (Study No.2), where the original review of the article and potential dosages had created the basis for the concern and call for this follow up review, the formal dosimetry revealed that it was again a fraction of a single case for increased risk of thryoid cancer being discussed and that, according to Lyon, *".. if a single case (of thyroid cancer) was found (within the group of subjects) it would be impossible to attribute this to the ^{131} iodine exposure".*

These findings are consistent with a large epidemiological study of 35,074 patients in Sweden[8] who were given ^{131}I for diagnostic purposes. The patients did not show an increase from the normal risk of cancer found nationally after periods of 10 to 20 years. The average dose to the thyroid gland in the Swedish studies was 50 rads, about the same as the maximum dose to any subject in the Wrentham study.

The following pages hold the text of the opinions offered by the 8 outside experts who were gathered to do an independent and comprehensive dosage and epidemiological review. Special attention is called to the report by Dr. Lyon and the Summary & Discussion pages of the Dosimetry and Risk Assessment Subcommittee report.

Additionally, a graph is shown below which demonstrates the level of full body dosage received from the studies vs. an annual background dose for a resident of Denver. This allows a comparable reference to that used in the graphs for the Calcium and Iron studies in the original Task Force report.

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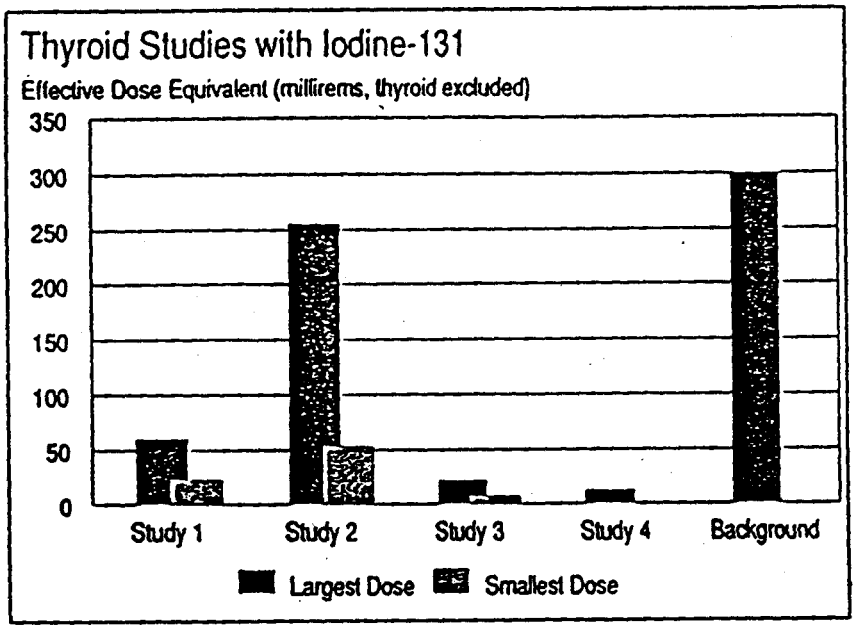
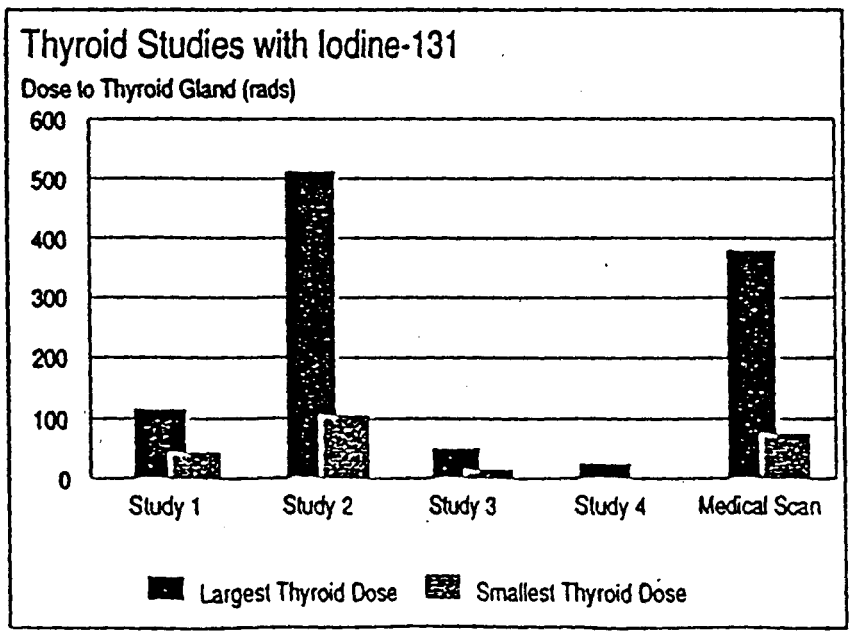
[8] L.E. Horn, K.E. Wiklund, G.E. Lundel, N.A. Bergman, G. Bjelkengren, U.C. Ericsson, E.S. Cederquist, M.E. Lidberg, H.V. Wicklund, and J.D. Boice, Jr., "Cancer Risk in Population Examined with Doses of I-131," *J. Nat.Cancer Inst.* 81, 302-306 (1989).

However, with the administration of ^{131}I, there is a unique characteristic that impacted this charting. The isotope is taken up almost exclusively by the thryoid. Therefore, a second chart was needed that shows the dosage to the thyroid gland in isolation However, the standard for this dose should not be an annual background dosage for accurate comparison of dose and risk. Therefore, the standard it is measured against is a medical scan done in the 1960s using ^{131}I for an average patient entering the thyroid lab for a diagnostic evaluation in that era.





Report on Thyroid Cancer

Joseph L. Lyon, M.D., M.P.H.

I have reviewed the data prepared by Drs Litster and Shore concerning the possible increases in thyroid cancer that might have followed the radioactive iodine studies at Wrentham and Fernald Schools. I think that their estimates of radiation doses are

since it would be expected to produce half (0.55) extra case of thyroid cancer. If one case were seen it would be impossible to determine if the case was the result of the radiation received from ^{131}iodine.

The children exposed to radioactive ^{131}iodine at the Fernald School also had Down's syndrome, and those with Down's syndrome rarely survive past their middle fifties. We would expect only 0.084 cases of thyroid cancer if they all lived to age 74. The radiation received from the radioactive ^{131}iodine would increase the number of thyroid cancers seen if this group lived to age 74 from 0.084 to 0.284. Again the number expected is small, and even if a single case was found it would be impossible to attribute this to the ^{131}iodine exposure.

Dosimetry Interpretation and Risk Assessment Associated with the I-131 Thyroid Studies of Individuals at the Wrentham and Fernald Schools (1954 - 1965)

Members of State School Thyroid Studies

*S. J. Adelstein, M.D., Ph.D.**
Leonard Bushnell, M.D.
*Frank P. Castronovo, Jr., Ph.D.**
Margaret Dale, J.D.
*J. Anthony Parker, M.D.**
Richard Phara, M.D.
*Edward W. Webster, Ph.D.**

**Members of the Dosimetry and Risk Assessment Subcommittee*

Report date June 13, 1994

SUMMARY AND DISCUSSION

The radiation dose (expressed in rems) after receiving radioactive iodine (I-131) is dependent on 3 factors:

o the amount of radioactivity administered (microcuries);

o the fraction of the radioactivity which is taken up by the thyroid gland;

o the age of the person receiving the radioactivity.

The age factor is very important since the weight (size) of the thyroid gland in grams is much smaller in young children than in adults, and, therefore, the amount of radioactivity in one gram of thyroid tissue (which determines the radiation dose) is much higher in young children. For example, in a 1-year old child the thyroid weight is about 2 grams compared with 20 grams in the average adult, leading to a radiation dose about 10 times greater in the child compared with an adult concentrating the same amount of I-131 in their thyroid. But in a 10-year old child the radiation dose would only be about two times greater than in the adult because their thyroid glands are closer in size to those in adults. In this report the thyroid gland radiation dose and also the dose to the remainder of the body have been calculated for each person who received I-131 in the 4 studies reviewed, taking account of their age, the size of the thyroid gland, the gland uptake of I-131, and the amount of I-131 administered.

The risk of developing thyroid cancer later in life as a consequence of the radiation dose the thyroid gland received is dependent on 4 factors:

o the amount of radiation dose to the thyroid gland;

o the age of the person receiving the dose;

o the time (years) that has elapsed after the dose;

o the gender of the person.

For the same thyroid dose (rems) children, particularly young children, have a greater risk for developing thyroid cancer than adults. In this report the risk has been calculated employing higher risks per rem for children than for adults, with the risks progressively decreasing for ages 1-5, 5-10, 10-20, and greater than 20. The risk for a person living for 60 years after the radiation dose is assumed to be about twice that for a person living for 30 years. For the same radiation dose females have about twice the risk of males.

The risks for groups of persons in each age group are given in Appendix C for each of the four experiments. They are presented as the number of thyroid cancer cases induced by radiation in a group of 1,000 exposed persons (assumed to be 50% male and 50% female) during the period of 50 years following the administration of I-131. From comparison of column 7 (thyroid cancer incidence) and column 11 (cancer incidence elsewhere in the body), it is evident that the risk of thyroid cancer is about 10 times greater than the risk of all other types of cancer including leukemia. The largest thyroid cancer risk in any of the child groups is a 1% chance (that is, 10 chances in 1,000 persons).

CONCLUSIONS.

Dr. Lyon and the Harvard Medical School team have arrived at similar overall conclusions. Dr. Lyon in his report has deduced the total thyroid cancer risk to be 0.55 extra cases among the 116 exposed children at the Wrentham School aged 1 to 15 years. For the 21 children at the Fernald School aged 1 to 18+ years he deduced 0.20 extra cases. From Appendix C in our report we deduce the thyroid cancer risk in the 116 Wrentham children to be 0.1 extra cases. In the 23 (not 21) Fernald subjects we deduce 0.027 extra cases. We agree with Dr. Lyon that the expected number of extra thyroid cancer cases among the total of 137 subjects in the two schools is likely to be less than one. We also agree that the number of expected cases if there had been no irradiation would most probably also be less than one (that is, about 0.5 cases).

We believe that Dr. Lyon's higher estimates of radiation-induced cases are mainly due to his evident "worst case" assumptions that all the children received "the maximum dose before age 1" and that all the children would live to age 74. Employing these assumptions and the risk value adopted by Dr. Lyon, we have derived 0.30 extra thyroid cancer cases at Wrentham, derived as follows:

0.00000084/rem/year x 44 rems x 69 years x 116 persons = 0.295

Dr. Lyon must have assumed a dose greater than 44 rems. Our calculation of 0.1 extra cases employs ages 1 to 18+ at exposure and a life expectancy of 50 years after exposure. Our highest risk, for children aged 1 to 5 years, was similar to that of Dr. Lyon, viz. 1.0/million/rem/year vs. 0.84/million/rem/year.

Dosimetry Interpretation and Risk Assessment Associated with the I-131 Thyroid Studies of Individuals at the Wrentham and Fernald Schools (1954 - 1965)

Articles Discussed

#1: *Benda, et.al., Thyroid Function in Myotonia Dystrophica, Am J Med Scl, 228, 668, 1954*

#2: *Kurland, et. al., Radioisotope Study of Thyroid Function in 21 Mongoloid Subjects Including Observations in 7 Parents, J Clin Endocrinol, 23, 552, 1957*

#3: *Saxena, et al, Minimal Dosages if Iodide Required to Suppress Uptake of Iodine-131 by the Normal Thyroid, Science, 138, 430, 1962*

#4: *Saxena, et al., Thyroid Function in Mongolism, J Pedi, 67, 363, 1965*

Background

The use of I-131 labeled potassium or sodium iodide (known as I-131 unless otherwise indicated) as an radioactive tracer for thyroid function was quickly accepted by the medical community. This is apparent from the numerous published reports pertaining to thyroid function beginning with the earliest animal studies in 1930's. Concomitant with its use at that time was the challenge to accurately determine the quantity of I-131 within the thyroid gland. This was a direct function of the counting equipment available as well as the suitability of the radioiodine solution. Both of the latter parameters were quite elementary relative to current standards. However, with I-131 the rapidity of thyroidal accumulation could be demonstrated noninvasively with a simple Geiger counter. It became evident that determinations of radioiodine uptake had important diagnostic applications. The published articles listed above pertain to thyroid function determinations in several groups of subjects, primarily children, at the Fernald and Wrentham Schools. In normals, the organ receiving the highest radiation dose after I-131 administration is the thyroid gland. This would be a

direct function of the % uptake value and would much smaller when the thyroid gland is nonfunctioning. All the subjects studied had functioning thyroid glands with a range of % uptake values. The average normal I-131 thyroid uptake @ 24 hours is approximately 25%.

Dosimetry Parameters

The thyroid gland is the primary tissue irradiated after I-131 administration. The relative small size of this organ, especially in children, creates a high concentration condition which directly effects radiation dose. Other organs receive a lesser radiation dose. The primary radiation risk includes the possibility of either cancerous or benign thyroid neoplasms and secondarily, cancer to other organs. Thyroid cancer is easily treatable. The incidence risk is therefore greater than the mortality risk by a factor of 10. The whole body risk can be expressed in terms of effective dose (E) which is the sum of the products of individual organs corrected for their radiosensitivity factors. Since the thyroid gland dominates this value (99 % of total) it can be excluded when calculating the effective dose (see example in Appendix A). A similar situation exists with annual natural background radiation where the lung contribution due to radon is 66.7% of 300 mrem or 200 mrem. The latter value would be expressed as annual natural background radiation minus the contribution from radon inhalation if the lung risk was being determined separately.

Current thyroid uptake studies are performed at Children's Hospital and Massachusetts General Hospital with a radioiodine called I-123. It has a shorter half life than I-131, 13 hours vs. 8.08 days, and provides a reduced thyroid radiation dose. This radionuclide became available during the 1970's. The children's thyroid dose from I-123 is approximately 1 rad.

Patient Studies

Reference #1 above

The myotonia dystrophica patients consisted of 6 males who received 54 microCi's of I-131 each for the purpose of determining thyroid function. The latter values ranged from 15.7% to 42.1% with an average of 29.4%. The ages of the subjects were not provided. However, adults were assumed because the daily urine output was collected in two 1 liter jars and the patients "body build" is mentioned as a source of error when determining % uptake. The thyroid dose averaged 84.6 rads (44.1 - 116.3 rads) with a concomitant effective dose of 4.23 rem (2.26 - 6.06 rem).

The average effective dose minus the thyroid contribution is 0.042 rem.

Reference #2 above

Twenty one subjects with Down syndrome, as well as 7 parents, received 70 and 100 microCi's of I-131 respectively. The age range of the Down syndrome group was between 5 and 27 years old with 4 individual ages not provided. The thyroid dose was highest for the 5 year old (511.8 rads), intermediate for the 13-16 year old group (139.2 rads) and lowest for those greater than 17 years of age (105.4 rads). The effective doses, not corrected for the thyroid, are 25.6, 7.0 and 5.3 rem respectively. When corrected for the thyroid contribution the effective doses are reduced to 1% of these values. The adult parent group averaged 165.2 rad thyroid dose, 8.25 rem effective dose and 0.0825 rem effective dose when corrected for the thyroid contribution. Two children (assumed to be 15 years old) were also injected with 100 microCi's I-131 labeled thyroid hormone (thyroxin). This label behaves differently than the I-131 sodium iodide with the lower large intestine receiving the highest dose (0.518 rad) and the effective dose equaling 0.192 rem.

Reference #3 above

Sixty three children were studied as part of an experiment involving the suppression of I-131 thyroid uptake after nonradioactive iodide administration. The children were a variety of ages; 1-3 yo (N=20), 4-6 yo (N=24) and 9-11 yo (N=19). While receiving 300 micrograms of stable iodide each received 1 microCi of I-131 every 2 weeks on 8 different occasions. The % thyroid uptake values varied considerably during this time period from 5 to 24 %. Their average thyroid dose was 44 rem with an effective dose of 2.2 rem and a thyroid corrected effective dose of 0.022 rem. If the 5 and 10 year old children are analyzed in a similar fashion their thyroid dose is 30.3 and 14.0 rem, the effective doses are 1.5 and 0.7 rem and, when thyroid corrected, 0.015 and 0.007 rem.

Reference # 4 above

This investigation used similar methodology as the Science paper (#3 above) where 1 microCi of I-131 was administered to 53 children with Down syndrome and 51 others with mental retardation of another etiology. All subjects were less than 16

years of age with a range of 1 to 15 years old with an uptake range of 10.7 to 50.2 %. Since individual uptake data were not available the dosimetry was determined for 1 and 15 years old for both percentage uptakes: 1 yo thyroid dose range equals 5 to 24.9 rem, effective dose equals 0.25 to 1.25 rem and effective dose minus thyroid contribution equals 0.0025 to 0.0125 rem; the 15 yo values are 0.8 - 4.1 rem thyroid dose, 0.04 - 0.205 rem effective dose and when corrected for the thyroid, 0.0004 - 0.00205 rem.

Risk Estimates

The risk resulting from I-131 radiation exposure is primarily that associated with thyroid cancer incidence and mortality. Thyroid cancer is a relatively rare disease, causing approximately 1000 deaths annually. The overall age adjusted incidence is 3.9 per 100,000 with over 90% survival for radiation induced thyroid cancer. This means that the incidence is much larger than the mortality from thyroid cancer. Not all thyroid cancer is radiation induced. The latent period from radiation exposure to clinical development of thyroid cancer is very long usually presenting itself 5 to 30 years after exposure. Several modifying factors are associated with the risk of radiation induced thyroid cancer. External radiation is 3 times as effective as I-131, children (< 18 year old) are much more radiosensitive than adults, and it is approximately twice as common in females as in males, with the incidence increasing with age. Lastly, risk factors for those of Jewish ancestry appears to be 2-8 times higher than for non-Jewish populations.

The risk estimates for the present investigations are summarized in Appendix B (Estimates) and Appendix C (Summary Table). These risks estimates are for thyroid cancer incidence, thyroid cancer mortality, and all non-thyroid cancer mortality.

APPENDIX A

Worksheet for Calculation of Effective Dose
Radiopharmaceuticals
(Based on ICRP-60, 1991)

Radiopharmaceutical: I-131 Sodium Iodide/100 microCi dose

Study: Example calculation for adult with a 25% thyroid uptake

Organ	Weighting factor	rad/mCi	Dose Equivalent (mRem/100 microCi)
Gonads	0.20	0.129	2.58
Red Bone Marrow	0.12	0.259	3.12
LLI	0.12	0.152	1.82
Lung	0.12	0.266	3.19
Stomach	0.12	1.702	20.40
Bladder Wall	0.05	1.700	8.52
Breast	0.05	0.204	1.02
Liver	0.05	0.129	0.649
Kidneys	0.05	0.215	1.07
Thyroid	0.05	1332.000	6,660.0
Pancreas	0.05	0.196	0.982
Bone Surface	0.01	0.226	0.226
ULI	0.05	0.218	1.09
SI	0.05	1.700	8.52
		Total E =	6713.2 mrem

% thyroid = [6660.0/6713.2] x 10^2 = 99.2%
E - thyroid = 53.2 mrem

APPENDIX B

SUMMARY OF RISK ESTIMATES USED IN THIS REPORT

A. Thyroid cancer (incidence)

Age in years	0-5	5-10	10-20	>20
Absolute risk/10^4PYGy	1	0.5	0.25	0.07
Lifetime risk/million/rad	40	20	10	2.8

Radiation Risk Estimates
I-131 Studies

Total Subject # / Number and School	Ref #	Populations (date of publication)	Age (years)	N	microCi I-131	Thyroid Dose (rem)	Thyroid Risk per 1000		Effective Dose all Cancer (rem)	Effective Dose all cancer minus thyroid risk* (rem)	All cancer minus thyroid risk incidence per 1000
							Incidence	Mortality			
Total equals 23 for Fernald	1	Myotonia Dystrophic (1954)	25 yr adult	6	54	84.6	0.237	0.0237	4.23	0.042	0.03
	2	Down Syndrome** (1957)	5 - 10 yr	1	70	511.8	10.24	1.024	25.6	0.256	0.29
			13 - 17 yr	7	70	139.2	1.39	0.139	25.6	0.070	0.074
			17 - adult	9	70	105.4	0.63 av.	0.063	5.3	0.053	0.025
	2	controls	35 yr adult	7	100	165.2	0.46	0.046	8.25	0.0825	0.038
Total equals 116 for Wrentham	3	residents of Wrentham School (1962)	1 - 3 yr	20	1	44.0	1.76	0.176	2.2	0.022	0.24
			4 - 6 yr	24	1	30.0	1.20	0.12	1.5	0.015	0.017
			9 - 11 yr	19	1	14.0	0.168	0.0168	0.7	0.007	0.008
	4	Down Syndrome (1965)	1 yr to 15 yr	104‡	1	5 - 24.9† to 0.8 - 4.1†	0.2 - 1.0	0.02 - 0.1	0.25 - 1.25	0.0025 - 0.00204	0.003 - 0.015
	4	other mental retardation			1		0.008 - 0.041	0.0008 - 0.004	0.04 - 0.205	0.0004 - 0.00205	0.0004 - 0.002

* assume effective dose minus thyroid contribution is 1% of effective dose
** four individual ages not provided; not included

† range due to variation in thyroid uptake
‡ fifty-three Down Syndrome, 51 other retardation

How Was Consent Sought?

In the report on the Calcium and Iron studies, a significant finding was the lack of disclosure of the key fact that radioactive materials were used as a part of the study. The lack of this key information was seen to be not only evidence for the failure to have gotten informed consent, but also to suggest that it had been a conscious act of hiding the use of radioactive materials.

The letters that were sent out in both of the thyroid studies at Fernald (Studies No. 1 & 2) were found in the archival records and are duplicated in the Appendix of this report, as they were in the earlier report. This was done to meet the need for "full and accurate disclosure of all facts found" as set forth in the first report.

In the nutritional studies that used radioactive Iron tracers, permission letters were sent out in 1946. These letters were not found. The archival records that were found that related to the Iron studies included only correspondence from the researchers at MIT to the Superintendent at Fernald outlining the understanding of the benefits and risks of the radioactive materials that would be used at that time, and correspondence that indicated permission was granted for this study by the existing state and federal agencies that oversaw research at Fernald during that era.

The nutritional studies that used radioactive Calcium tracers sent out their permission letters in 1953. These letters were found. They did not mention radioactive materials would be used as a part of the study. This led to an assumption that this fact was not mentioned in the earlier study's permission letters either.

The letters found for the thyroid studies that involved the use of radioactive iodine at Fernald were written in 1951 (for the thyroid studies in persons with Myotonia Dystrophica) and in 1953 (for the thyroid studies in persons with Down syndrome). The dates of the letters clearly overlap for the time periods that included the Calcium and Thyroid studies.

The letters for the two studies at Fernald that used radioactive iodine clearly and specifically note the use of radioactive materials and the use of a geiger counter to conduct the test.

This leads to the revised speculation that it may be that the decision whether to put that information in the letters to the parents falls more under the broader issues from that time frame that were later noted as portraying the "paternalistic" and authoritative role physicians worked from. They used this type of decision making with all persons in deciding what would or would not be disclosed to them within their medical treatment jurisdiction.

This widespread personal decision making by physicians was the foundation for the movement of the 1960s that led to the development of informed consent as we understand it and define it today. The term "informed consent" was created in 1972 and federal laws of protection passed in that same year (please see the original report for further discussion on "informed consent").

The permission letter from Study No.1 (1951) offered the assurance that the "dose of this iodide is approved and absolutely safe" and "the same study is carried out routinely in any large hospital in this country on patients suffering from thyroid disease". [Note: research for this current report showed that the use of ^{131}I as the tracer material of choice for diagnostic thyroid uptake studies continued until the development of ^{123}I in the 1970s. However, some areas of the United States as well as other countries still use ^{131}I in certain situations today for diagnostic and therapeutic uses].

The permission letters from Study No.2 in 1951 and 1953 stated "the use of this agent is not connected with any harmful effect, and it is used in many routine examinations for thyroid function in first class hospitals of the United States. The examinations are made in connection with the Massachusetts Institute of Technology, and the dosages used are approved by highest authority".

For the parents, the letter graphically states that "the test is not connected with any hardship, and consists entirely of drinking a small glass of water with I^{131} and sitting in a chair for half an hour while the thyroid function is observed through Geiger counters."

Study No. 2's letters included a request for payment of the lab tests which, at that time, were $10.00 per PBI test. The majority of letters returned by the parents giving permission also held explanations why they could not afford to help with the cost of the tests. The cost of the tests for those subjects whose parents could not pay was absorbed by Fernald.

For Studies No. 3 & 4, which were conducted at the Wrentham school, no consent or research records of any kind have been found. All researchers were contacted and areas for potential storage searched to no avail.

MYOTONIA DYSTROPHICA STUDY – STUDY No. 1

June 5, 1951

Mrs. [redacted]
[redacted], Massachusetts

Dear Mrs. [redacted]

We are writing this letter relative to your brother, [redacted]. As you may know, he suffers from a chronic disease entitled myotonia dystrophica.

Up to the present time this disease is very poorly understood. We are very much interested in developing better diagnostic and therapeutic measures to help patients like [redacted], and we are now ready to initiate a study pertaining to the thyroid function in patients with this disease. This study is to be carried out in connection with the Massachusetts Institute of Technology, and consists of blood and other examinations following administration of isotopic iodide. The dose of this iodide is approved and is absolutely safe. The same study is carried out routinely in any large hospital in this country on patients suffering from thyroid disease. In fact, our own study will be conducted partly at the Massachusetts General Hospital. This procedure will not cause any inconvenience or discomfort to [redacted] and may be quite helpful in contributing to our knowledge of this little known disease.

Before proceeding with such a study it will be necessary for us to have your permission to carry it out. We have, therefore, prepared a certificate below. If you are willing to give us permission to conduct the study on [redacted], would you please complete and sign the permission and return the entire letter by mail immediately as we expect to begin by June 15, 1951?

Very truly yours,

Malcolm J. Farrell, M.D.
Superintendent

PLD/S

Date:

This is to state that I give my permission for the participation of [redacted] in the project mentioned above.

Signature

Witnessed by:

Relationship

Date

The Commonwealth of Massachusetts
Department of Mental Health

MALCOLM J. FARRELL, M.D.
SUPERINTENDENT

WALTER E. FERNALD STATE SCHOOL
BOX C, WAVERLEY 78, MASS.

STUDY No. 2
RESIDENT
LETTER
FERNALD

November 19, 1951

Dear Mrs. [redacted]

Our research in mongolism, which has been under way for fifteen years, has provided more and more evidence as to the definite causes and anomalies in this condition. Based on extensive experience over a period of fifteen years on almost one thousand patients, we feel that we are able to extend the research into the field of clinical investigation. We would like to test the endocrine functions of the different glands, especially the pituitary, thyroid and adrenals. Several tests are necessary which are not harmful to the patient but which involve very complicated biochemical and physical examinations which are connected with extensive expenses.

We would like to ask your permission for a blood test on your child, involving the use of a very small amount of radioactive iodide. The use of this agent is not connected with any harmful effect, and it is used in many routine examinations for thyroid function in first class hospitals of the United States. The examinations are made in connection with the Massachusetts Institute of Technology, and the dosages used are approved by highest authority.

We would also like to ask whether you may be willing to pay for the protein-iodide determinations which are made at the Massachusetts General Hospital and for which we are charged $10 per test. If you would support these studies, which may eventually result in a much more effective therapy of mongolism, by contributing any sum of money to a special research fund, we would greatly appreciate such a gift. The fund will be used entirely for research in mongolism, and will help to pay for tests of patients whose parents are not able to pay the expense.

In case you would like to contribute, please make a check payable to the Walter E. Fernald State School Special Research Fund, and please give written permission for making the necessary tests, including the use of radioactive iodide.

Sincerely yours,

Clemens E. Benda

Clemens E. Benda, M.D.
Clinical Director

Approved: Malcolm J. Farrell

Malcolm J. Farrell, M.D.
Superintendent

CEB/dfg

Study No. 2
Parents' Letter
FERNALD

Yes

January 23, 1953

Mrs. [redacted]
[redacted] Massachusetts

Dear Mrs. [redacted]

We informed you in November that we had started investigations on a group of children. The preliminary examinations already show that we are on the way to finding some significant anomalies, and these findings may eventually enable us to treat these children according to their needs.

The Thyroid Laboratory of the Beth Israel Hospital is willing and anxious to do a study of the thyroid function in those mothers who have given birth to a child with the condition under investigation. If you will be good enough to contact us on or before Wednesday, January 28th, we will make arrangements for you to go two mornings to the Thyroid Laboratory at the Beth Israel Hospital. Such an examination should also be of considerable interest to you.

The test is not connected with any hardship, and consists entirely of drinking a small glass of water with I^{131} and sitting in a chair for half an hour while the thyroid function is observed through Geiger counters. We will deeply appreciate your cooperation in this very important matter.

Sincerely yours,

Clemens E. Benda, M.D.
Director of Research and
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Approved: _____
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Findings and Recommendations

These findings are supplemental to the general and overall findings of the original Task Force and its report of April, 1994.

1. Eight experts have calculated that any increased potential for a thyroid cancer is less than a single case for the total population of the subjects of these studies. Further it is their opinion that even if a case were to be found, the relationship to the studies would be impossible to determine. However, just as a preventive examination was reccomended in the Calcium and Iron studies, it is recommended that an assessment examination be provided for all identified or potential subjects in all of the Thyroid studies. This shall include a specific examination of the thyroid.

2. All positively identified subjects should now be contacted per the instructions outlined in the "Contact with Subjects Subcommittee" Report as included in the original report.

3. The lack of archival records for the two studies at the Wrentham School has prevented the positive identification of those subjects. The criteria set forth in the published articles on these studies has allowed the pool of potential subjects to be reduced to 300 names. From within this pool, a set of highly likely subjects has been identified. However, follow-up and contact shall be done with all of the potential subjects.

4. As in the original recommendations, if the subjects (or potential subjects) are not eligible for existing medical assistance, the Commonwealth shall identify a means for this medical assessment to be done.