CONFERENCE REPORT

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Radioiodine and thyroid carcinoma: KI prophylaxis in children

Giorgio Giovannelli
Department of Pediatrics, University of Parma, Italy

Abstract. The Chernobyl disaster was followed by a large increase in the incidence of thyroid carcinoma in children. It has been proved that KI prophylaxis may prevent such a heavy consequence. Italy has no more nuclear power plants in activity but is surrounded by the several ones of the neighbouring countries; moreover, relevant amounts of nuclear material are still present in the territory. Therefore a nuclear risk is present in Italy as well as in other close countries and a KI prophylaxis should be organized for our children, at least for those living within 200 miles from a possible source of radioiodine pollution. Guidelines concerning KI prophylaxis exist and are internationally shared in their general outlines.Guidelines we recommend for italian children are summarized in part II ("theory"). However, to be timely and effective, KI prophylaxis must be organized long before the nuclear alarm, and the coordination of its several steps needs to be checked through a mock trial. We suggest a model of organization and describe the practical aspects of carrying out a KI prophylaxis for 82.000 subjects aged 0-18 years living in the Province of Parma (Progetto Sperimentale Parma, PSP). The main goal of PSP is to offer a controlled and reliable model of KI prophylaxis,which could be applied in any other area (previous local adjustement), whenever the central or regional Authorities will consider it necessary or desirable.

Key words: Radioactivity, radioiodine, thyroid carcinoma in children, KI prophylaxis

(I)
A FEW NOTES ABOUT RADIOACTIVITY AND RADIOIODINE

Radiations have been playing an important role in Medicine for more than one century.

While old physicians and pediatricians were curious about these new diagnostic tools and familiarized themselves with X-rays (even too much, sometimes), modern physicians do not show as much interest for nuclear medicine, although we are living in the "atomic era" and problems related with artificial radioactivity are increasingly growing on our planet.

Therefore, it may be unusual but is certainly up to date to dedicate a session of a pediatric congress to the radioisotopes of Iodine and in particular to I-131 (the first to find a medical application, precisely in a boy with a big goiter).

After the accident of Chernobyl and the following medical experience, no pediatrician should take no interest in the effects of nuclear energy on individuals and populations. No doubts that the Chernobyl disaster was unique under many aspects and it is highly improbable that such an event may occur again; however, several hundreds of atomic power plants are in activity all over the world.

Moreover, technical incidents may no longer represent the only possible source of environmental nuclear pollution, considering the global-scale propagation of modern terrorism, highly motivated, generously financed and unpredictable as to its strategies.

I think it may be appropriate to remind shortly some basic knowledge about radioactivity in general, its related current terms and quantities, as well as some short notices on the radioisotopes of Iodine.

Radioactivity is a natural phenomenon and man lives together with it from the origins of life.

Every day our body is passed through by natural radiations of three different origins:

- *Cosmic rays*, coming from stars and, to a minor degree, from the sun.
- *Cosmogenic radionuclides*, arising from the interaction of cosmic rays with the athmosphere and the earth's crust (e. g. C-14, which has a half-life of 5. 730 years).
- *Natural (or primordial) radionuclides*; these date back to the solar system formation and are still active. Among these the Uranium series, headed by Uranium-238, with a half-life of 4, 5 billion years, the Thorium series, headed by Thorium-232, with an even longer half-life (14 billion years) and also the K-40, widespread distributed in nature and such an important costituent of the human body.

As a whole, these 3 different types of natural radiations represent the so-called " natural background radiation", which is continuously incurred by everyone from conception to death, more or less depending on the geographic area one is living in (Figure 1).

In Italy "background radiation" appears to represent 2/3 of the average annual effective dose, estimated in 4, 2mS. (Figure 2).

Even the fossil sources of energy contribute to irradiate the population, although at a minor degree compared to nuclear ones (Figure 3).

mSv is the thousandth part of the Sievert and the Sievert (Sv) is the unit of the so called " effective dose". Among the dosimetric quantities in radiological protection, the "effective dose" has the primary interest for the biologist and the physician.

These quantities are arranged in sequence as in Figure 4, i. e. : following an internal and/or external irradiation, organs absorb a definite quantity of energy pro mass unit. This quantity is called "absorbed dose" and is expressed in Gray (once, in rad).

Source	Average effective dose (mSv/yr)	
	in the world	in Italy
"Background radiation"	2,4	3,1

Figure 1. Average annual irradiation from natural sources (in adults)

Category	Source		Average annual effective dose (mSv/yr)
•"Background radiation"			3,1
• Anthropic activities, as:	Medical activity, radiology	1,00	1,1
	Television and computer (4 hrs/day)	0,01	
	Fallout from nuclear (military) tests	0,01	
	Other exposures of technological origin	0,01	
	Flights	0,002	
	From nuclear power plants	0,001	
		total	4,2

Figure 2. Irradiation from natural and artificial sources in Italy

Energy source	Collective dose
Nuclear	**200** man-Sv/GWa
Coal	**20** man-Sv /GWa
Peat	**2** man-Sv /GWa
Geothermal	**2** man-Sv /GWa

* 1 GWa = 8,76 billion kWh

Figure 3. Estimated irradiation dose to the population from nuclear and fossil energy sources (related to the entire production cycle)

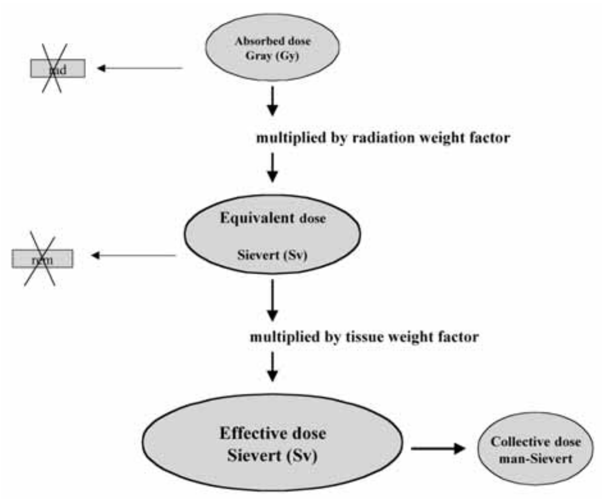

Figure 4. Main dosimetric quantities and related units

However, depending on the type of radiation (and other factors), the biological effect produced by the same absorbed dose may be different. Hence, the need to multiply the absorbed dose by a corrective coefficient (the so called "weight factor of the radiation"). E. g. : fixing 1 the weight factor of photons and electrons of all energies (X, gamma, and beta radiations), the weight factor of neutrons and alfa particles may range from 10 to 20 depending on their energy.

In this way a new quantity is obtained, the "equivalent dose" to the organs, which is expressed in Sievert (once, in rem).

It is clear how the absorbed dose is of prevalent interest for the physicist and the equivalent dose for the physician and biologist. However, those latter cannot be satisfied yet, because the different organs and tissues of our body show a different sensitivity to radiations (let's think of the gonads in comparison with the skin). Hence, the "equivalent dose" must be multiplied by a corrective coefficient specific for each organ/tissue in order to finally obtain the "effective dose".

The effective dose is expressed in Sievert (Sv) and is the sum of the irradiations received by the different organs; e. g. , referring to 1 Sv effective dose, we intend a uniform total body irradiation with an equivalent dose of 1 Sv to each organ.

Conventionally, "individual dose limits"exist, recommended by the ICRP (International Commission for Radiological Protection) and are adopted also by our Country. These are:

1 mSv/year for the general population.

20 mSv/year for professional exposure (100 mSv in 5 years, with a maximum of 50 mSv/year).

These individual dose limits (also labelled as "acceptable" or "tolerable") are very useful for safeguarding people, particularly workers, and to evaluate the effectiveness of applied protective measures, but they do not necessarily represent an indicator of biological damage. It would be a mistake to believe that under 1 mSv/year any damage to the population could be excluded as well as that overcoming this limit certainly a damage would occur.

It may be useful to recollect that these recommended individual dose limits do not include natural background radiation and radiation due to medical interventions for diagnostic or therapeutic purposes.

The biological effects of ionizing radiations may be divided into somatic and genetic (Figure 5).

These can be divided further into deterministic and stochastic (Figure 6), an important difference for the physician to know.

In fact, while deterministic effects (only somatic, acutely appearing) are certain and the more serious the higher the dose of irradiation (*), stochastic effects (both somatic and genetic) are uncertain and their probability to occur is directly proportional to the irradiation dose.

- Somatic effects:
  These concern the somatic line cells.
  These present before this cell-line disappears with the death of the individual.
- Genetic effects:
  Genetic mutations (dominant or recessive)
  Chromosome aberrations.

Figure 5. Biological effects of radiations

(*)In fact we know the "50% lethal dose", i. e. the one causing within 30 days the death of half of the exposed subjects; it corresponds to 5 Gy gamma-rays acute total-body irradiation (equivalent to 5 Sv).

1) <u>Deterministic</u>

- **These are only somatic**
- **These present acutely and are related to a threshold dose. For ex.:**
  - hemolymphopoietic system: threshold dose >1 Sv Appearance after 3 weeks
  - gastrointestinal system: threshold dose >5 Sv Appearance after 3-5 days
  - central nervous system: threshold dose >20 Sv Appearance after 0,5-3 hrs
- **seriousness is related to the absorbed dose**

2) <u>Stochastic</u>

- **These can be both somatic and genetic**
- **Somatic effects have a late onset and are unrelated to a threshold dose. For ex.:**
  - Leukemias
  - Solid tumors (thyroid, skin, skeleton)
  - Degenerative diseases
  - Lens cataract
- **the probability of presentation is related to the absorbed dose**

Figure 6. Harmful effects of radiations

As to small irradiation doses, like those naturally concerning man always and everywhere, we cannot say anything certain about their effects; we do not know a possible threshold under which to exclude possible effects and vice versa. Hence, the "linearity without threshold" hypothesis has been conventionally accepted; on the basis of this hypothesis it is assumed that even the smallest dose or irradiation is associated with a probability other than zero to produce a stochastic damage and that this probability is proportional to the "effective dose".

Another quantity which is worth mentioning when speaking of radioprotection, considering its epidemiologic and statistical applications, is the "collective dose". It corresponds to the global irradiation dose received by a population and can be calculated by summing the "effective doses"received by the single subjects. It is expressed in man-Sievert.

Thereby we know that the collective dose after the incident in the nuclear power plant of Three Miles Islands in 1978 did not exceed 40 man-Sv, while the disaster of Chernobyl in 1986 caused an estimated collective dose of 600. 000 man-Sv.

Another interesting information comes from the estimation of the collective dose received by the world population during the 2nd half of the last century (Figure 7).

In Figure 8, a summary of some main quantities currently used in radioprotection as defined by the International System (IS) is reported together with the corresponding old definitions and along with a recall concerning Activity and Exposition, because old measurement units (Curie and Roentgen) are still currently found in the literature.

Collective dose (millions man-Sv)	Source
650	Natural sources
165	Medical practice (diagnosis and therapy)
30	Nuclear military tests in atmosphere
2,4	Entire cycle to produce nuclear energy
0,6	Severe nuclear accidents
0,6	Professional exposure

Figure 7. Estimated collective dose from different sources to the world population during the period 1945-1992

<table>
<tr><th>Quantity</th><th>Current unit (IS*)</th><th>Corresponding old unit</th><th>Equivalence between units</th></tr>
<tr><td>Absorbed Dose</td><td>Gray (Gy)</td><td>rad (rad)</td><td>1 Gy =100 rad</td></tr>
<tr><td>Equivalent Dose</td><td rowspan="2">Sievert (Sv)</td><td rowspan="2">rem (rem)</td><td rowspan="2">1 Sv =100 rem</td></tr>
<tr><td>Effective Dose</td></tr>
<tr><td>Collective Dose</td><td>man-Sievert</td><td>man - rem</td><td>man - Sv</td></tr>
<tr><td>Activity</td><td>Bequerel (Bq)</td><td>curie (Ci)</td><td></td></tr>
<tr><td>Exposure</td><td>Coulomb/kg (C/kg)</td><td>roentgen (R)</td><td></td></tr>
</table>

*International System

Figure 8. Main dosimetric quantities and related units

Finally, some brief outlines concerning I-131, which is the focal point of interest of this first session of the meeting.

The disaster of Chernobyl (an accident at the top of the INES scale; see Figure 9) and the following large, rapid increase in the incidence of thyroid carcinoma in children, pointed out the danger of Iodine radioisotopes, which were a relevant component of the fallout (**).

(**) The nuclear power plant n° 4 involved in the accident, had a power of 940 MW, about 1 billion Curie of fuel and in the huge amount of radioactivity discharged, during the long period of graphite fire, the I-131 share was estimated in 7 million Curie

Class	Definition	Outline of the event
0	Deviation	No safety significance
1	Incident	Anomaly (functioning of the plant)
2	Incident	Incident (unusual contamination within the plant and/or over exposition of at least one worker)
3	Incident	Serious incident (inside the plant)
4	Accident	Accident (without significant off-site risk)
5	Accident	Accident (with off-site risk)
6	Accident	Serious accident (to the plant with outside release of radioactivity)
7	Accident	Major accident (serious environmental effects)

Figure 9. The INES scale (International Nuclear Event Scale) as defined by the IAEA and internationally adopted to classify nuclear emergencies (6)

There are 15 radioactive isotopes of Iodine, with different radiation properties and a very wide range of half-life: from one extreme of 1, 35 hr. (I-120) to the other of 17 million yr. (I-129). Among these, no doubt that the best known and the most applied in medicine for diagnostic and therapeutic purposes is I-131; it decays emitting beta and gamma radiations and has an 8 day half-life, i. e. every eight days it reduces by 50% its irradiation power.

Half-life is an importantant characteristic of radioisotopes; it allows us to estimate the duration of the danger due to their irradiation on the one hand and the limit of their utilization for medical purposes on the other.

In medicine Iodine radioisotopes other than I-131, as I-123, I-132, I-125, have been and are sometimes still used, each with different half-life and characteristics of radiations (Figure 10). Along with these, Tc-99m(pertechnectate) owes to be mentioned,

Radioisotope	Half-life	Emission	Estimated Dose (mrad/μCi)
I-123	13,2 hr	gamma	16
I-125	59,4 days	gamma	820
I-131	8,04 days	beta,gamma	1.300
I-132	2,28 hr	beta,gamma	50
^{99m}Tc(pertech.)	6 hr	gamma	0,1

Figure 10. Main Iodine Radioisotopes currently used in medicine and biology

due to its high affinity for the thyroid and the very low irradiation caused to the patient; in fact it often replaces radioiodine for the "in vivo" diagnostics, expecially in children.

As to I-131, the beta radiation is the most feared, because highly ionizing and capable of destroying tissues where it concentrates (particularly in the thyroid) although it has a penetration of a few millimeters. However, such an effective and limited destructive capacity makes I-131 useful for therapy of some thyroid diseases, also in childhood.

A last comment is advisable: after the dramatic consequences of the Chernobyl accident, with particular reference to thyroid carcinoma in children, the WHO lowered the thresholds of the ERLs (Emergency Reference Levels) and the related ILs (Intervention Levels), for a better protection of the thyroid in the population.

At present, the Intervention Levels are:

10 mGy, for subjects <18 yr. and for pregnant and nursing women;

100mGy, for adults <40 yr. ;

5 Gy, for adults >40 yrs. (very low risk for the thyroid; same threshold as for deterministic effects).

Therefore, in children, a prophylaxis with stable iodine should be carried out when the environmental irradiation to the thyroid exceeds 10 mGy.

In terms of calculation and definition of limits for thyroid protection, it is assumed that the internal irradiation caused by ingestion of radioiodine contaminated food would induce the same risk of thyroid carcinoma later in life as an external irradiation.

In conclusion: I hope it was useful to recollect, with these short, rudimentary notes, an otherwise wide and complex matter like that of nuclear medicine. In fact, the whole medical class, not only a few specialists in the field, should start to be somehow interested in certain problems as those related to radioactive fallout.

Prof. Naumann, responsible for the first KI prophylaxis in children on national basis, in Poland at the arrival of the radioactive clouds from Chernobyl (a unic and successfull intervention in Europe), who I invited to Parma in 1987 together with other international experts to discuss what actually had been done in european countries undergoing the radioactive fallout of Chernobyl, ended his presentation with the following words: ”. . . Moreover, I think that another important conclusion is that the medical community, at least in my country but from what I know from other reports also in other countries, was unprepared to deal problems of radioactivity contamination. I think that one important lesson which might be valid for all of us involved in the academic life is that perhaps our programs for the post-graduate medical studies should be partially modified and a certain amount of knowledge on these issues has to be presented to the students and medical staff. ”

I completely agree with him and hope you too feel the need to extend the area of our interest to involve some aspects of modern medicine increasingly related to emergencies. Some of such emergencies were just unconceivable when I and some of you were young physicians, but now the risk of unpredictable emergencies of different origin has grown to a point that in some countries, as in the USA, they are discussed in regular courses of CME for physicians.

(II)

Prevention of injuries related to radioiodine fallout: from theory to practice

1) Introductory remarks

A few years after the nuclear accident of Chernobyl, a very large rise in incidence of thyroid carcinoma in children exposed to the fallout in the surrounding areas, was documented (1).

No rise was observed in Poland, where the population under 18 years had been treated with stable iodine (KI)at pharmacological doses (2; 1).

The prophylaxis with KI in Poland covered 10, 5 million children plus 6 million adults, the latter on a voluntary basis (2).

Adverse effects related to this prophylaxis were negligible. Severe side effects were reported in only eleven subjects (8 children and 3 adults); the major complication was severe bronchospasm which required steroid administration. Mild side effects, mostly skin allergy, were reported in about 260 cases (2). Of course transient hypothyroidism in newborns of mothers treated with KI could not be excluded as well as the possibility of relapse in some cases of previous hyperthyroidism; however, the former is harmless and the latter is very rare in children.

Altogether, Potassium iodide (KI) is considered a safe, cheap and effective drug in protecting children from injuries to the thyroid caused by exposure to radioisotopes of Iodine (3, 4, 5); accordingly, prophylaxis with KI is recommended by the World Health Organization, the Food and Drug Administration, the American Thyroid Association (ATA), the Lawson Wilkins Pediatric Endocrine Society, the Thyroid Foundation of America (3, 4, 5) and by all Institutions and Countries which take care of protecting their population from the risks of a nuclear accident.

This problem is hot, as some recent events in the USA have demonstrated.

On february 28, 2003, in Washington D.C., a Symposium on “Public Health Strategies for Protecting the Thyroid with Potassium Iodide in the Event of Nuclear Incident” was organized by the ATA and the American Association of Clinical Endocrinologists, with the participation of thyroid experts from around the world. This Symposium also brought together public health professionals, physicians, government officials, and allied health care professionals (5).

The length of time taken by the U.S. government to recognize that KI needs to be made available for communities at highest risk was the center of much debate. The same criticism had already been expressed by Prof. Ingbar of Boston in his presentation on the Three- Miles Island nuclear incident during the international meeting on “Thyroid and Radioactivity from Nuclear Incidents”, I organized in Parma in March 1987 to assess the measures undertaken in different european Countries (Italy, Poland, Germany, U. K.) to protect the populations as the Chernobyl accident occurred less than one year before (1).

In the USA, the first, concrete intervention in this direction dates December 2001, when the US Nuclear Regulatory Commission wrote to the 34 States that have or are located within 10 miles of a nuclear power plant, offering two free KI pills for every person living within 10 miles of a plant.

After a few months, the newly enacted (2002) bioterrorism bill doubled this distance to 20 miles, beginning in June 2003.

However, the ATA recommends (4) a ten times longer radius of KI distribution (200 miles).

Since no one can predict how far radioactive iodine might spread after being released in a fallout cloud from a nuclear power plant during an accident or attack, the ATA recommends three levels of coverage, according to the distance from the nuclear plant:

- 0-50 miles: distribute KI in advance ("predistribute") to individual households, with extra stockpiles stored at emergency reception centers;
- 50-200 miles: stockpile KI in local public facilities such as schools, hospitals, clinics, post offices, police and fire stations, for distribution upon notification by local health officials;
- >200 miles: make KI available from the Department of Health and Human Services' National Pharmaceutical Stockpile.

These (and others) statements are supported also by the Lawson Wilkins Pediatric Endocrine Society; it is easily understandable considering that Paediatric Endocrinologists – let me say Paediatricians tout court – should be the most interested in preventing the large rise of thyroid carcinoma demonstrated in children a few years after the radioactive iodine fallout of Chernobyl.

The more precocious KI prophylaxis is, the more protective it will be.

When not administered 6-12 hours in advance, the drug should be administered within the first few hours after the exposure to radioiodine. In any case it must always be administered, even later. To achieve a prompt administration, the KI stockpile in the country and the net of its distribution to children must be organized long before an impredictable contamination.

KI prophylaxis neither prevent, nor replaces all other possible safety measures, as sheltering, restriction of some foods (see milk), evacuation etc. However, all these measures are unable to protect children from thyroid carcinoma without a previous, adequate KI administration.

It has been recently reported that for the possible risk of contamination from a nuclear submarine parking in the harbour of Portsmouth, thousands of stable iodine pills were distributed to the schools of Hampshire, in the U.K ; an example of rational organization of such a prophylaxis.

In the U.K. attention to these problems was focused since 1989, when a Working Group on Stable Iodine Prophylaxis was convened by the Department of Health (DH) to provide advice on all aspects of the use of stable iodine as a protective measure following an accidental release of radioiodine, also reviewing and taking into consideration the guidance published by the WHO in the same year.

Since the WHO updated its guidelines in the light of additional information gained from the incidence of thyroid cancer in children after the accident at the Chernobyl nuclear power plant, in April 1999 the National Radiological Protection Board (NRPB), following the request by the DH, convened a 2nd UK Working Group (WG), to review the latest WHO guidelines in the context of emergency planning for nuclear accidents in the UK.

This 2nd WG completed its report in 2001 (3). This highlighted that the prime focus of emergency planning against release of radioiodine should be the protection of children, pregnant and nursing women. The report goes further into many details as to the organization of the prevention with stable iodine (***). These were useful for the planning of our project for KI prophylaxis in the province of Parma.

2) The situation in Italy

Italy has no more nuclear power plants in activity.

Four of these (Trino Vercellese, Garigliano, Latina, Caorso) have been inactivated after the popular referendum for/against "nuclear", held in Italy on No-

(***) In the UK stable iodine is administered as Potassium Iodate, because the licence for manufacturing covers only the iodate form. The 2nd WG states that KI is as stable as Potassium Iodate, that there are no medical grounds to prefer the iodate over the iodide form, and leaves to the DH the decision to extend the licence to manufacture both forms or allow the importation of KI tablets manufactured overseas.
As to the risks of adverse effects from the administration of a single dose of stable iodine (at the age-related recommended dosages), the report states that these are "extremely low" and "should not be considered a significant cause of concern".

vember 8th 1987 (the result was: 90% against). A fifth one (Montalto di Castro) has been blocked at an advanced stage of construction, and converted into a polyfuel power plant.

In Italy, the history of this conversion is well known, at least for its (heavy) economic consequences. May be it is not as much known that after Chernobyl the world production of energy by means of nuclear power plants was not reduced but increased by 40% (6).

Once our nuclear power plants were closed, however, their nuclear fuel did not disappear.

The dismantling of a nuclear power plant entails the production of large quantities of radioactive waste. I do not know the data at present, but I can say that at the end of 1997 the global amount of radioactive material scattered all over in Italy was approximately 750 tons, subdivided as in Figure 11 (6).

Moreover, further 500 tons of radioactive waste are produced every year in our country by hospitals, factories and research centers, all employing radioisotopes.

Then, in spite of the inactivation of our nuclear power plants we are not nuclear-free and have to face a large and growing amount of radioactive waste (50-80. 000 cubic meters at present), just like many other countries.

Apart from this, we have to keep in mind that the North of Italy is surrounded by the several nuclear power plants of the neighbouring countries (Figure 12). France alone has 59 installations (covering 80% of its energy requirements) and some of these are probably less than 200 miles from towns or highly populated regions of the North of Italy.

Besides, in spite of the approximately 800 miles of distance, our northern regions were involved by the radioactive fallout of iodine, cesium and other radioisotopes coming from Chernobyl.

MATERIAL	AMOUNT
depleted uranium	80.569 kg
natural uranium	50.906 kg
enriched uranium <20%	335.148 kg
enriched uranium >20%	201.321 kg
thorium	5.640 kg
plutonium	1.765 kg

Figure 11. Nuclear material kept in Italy on 31/12/1997.

Country	n° of NPP
France	59
UK	35
Russia	29
Germany	19
Switzerland	4
USA	104
Japan	53

Figure 12. Nuclear power plants (NPP) working in the following countries.

I still remember the confusion and uncertainty about what to do on that occasion (at all levels, in the country).

Do we want to live once again those moments?

Should we believe that our children do not run the risk of developing a thyroid carcinoma due to radioiodine fallout just because we have closed our nuclear power plants?

Should we fool ourselves moving children to one of those municipal districts (there are several ones in our region) where the Major is proud to exhibit road-signs alleging “denuclearized zone”?

I don’t think so.

As pediatricians we claim that preventing is better than treating, and consistent with this principle we should strive to promote the prevention of risk of thyroid carcinoma in children following environmental contamination by radioiodine.

Here is the reason why 2 years ago, at the 13th meeting of the Italian Society for Pediatric Endocrinology and Diabetology (Trieste, October 2001), I formally asked the Society to take the initiative to organize this prevention, through the effort of its members and the involvement of all the Institutions provided by law.

My request also listed the main points to define and problems to be solved (Figure 13). It received a big round of applause, was endorsed by the assembly and included in the list of the projects to be developed by the Society.

Nothing was been done, so after one year, in the late 2002, I started a personal, unofficial enquire in two Regions (Lombardia and Emilia-Romagna), con-

- To decide standard intervention criteria for KI prophylaxis in the case of a nuclear accident.
- To establish groups of population to protect and the recommended KI doses related to age.
- To arrange KI stockpiles strategically placed all over the country.
- To identify the operators responsible for KI distribution and the correct way to involve these.
- To promote information about the importance and characteristics of KI prophylaxis (to physicians as well as to the population).
- To identify a net of specialized Centers, closely related, for the clinical and scientific follow-up of children involved in a nuclear accident.

Figure 13. Suggestions for adequate KI prophylaxis (13th SIEDP Meeting, Trieste, October 2001)

tacting some Institutions and Organizations involved in the management of emergencies.

I realized that nothing had been organized and even no projects were present for such a prevention, just because in most cases the relationship between fallout of radioiodine and thyroid carcinoma in children was unknown. Moreover, the possibility of a nuclear accident was not taken into consideration due to the inactivation of our nuclear power plants.

People I contacted were really surprised when I stressed that in the case of a nuclear accident with radioiodine fallout a special “pediatric emergency” would arise within the general nuclear emergency, which can be prevented by applying a KI prophylaxis. However, such a prophylaxis, to be effective needed to be organized in the territory long before the emergency alarm starts.

So I decided to organize in the area of Parma an adequate scheme of prophylaxis with potassium iodide (KI) for subjects under 18 years of age (plus pregnant and nursing women), on the basis of updated international experience, and to verify its running through a mock trial.

3) From theory to practice: the PSP (Progetto Sperimentale Parma)

The final aim of PSP is to prevent the risk of thyroid carcinoma in children after inhalation (and or ingestion) of iodine radioisotopes unexpectedly contaminating the environment. However, many other useful goals may be achieved by such a project, as:

- to assess the best way to follow; to estimate the costs to bear; to test the bureaucratic and logistic obstacles to be overcome;
- to identify the official and/or voluntary organizations to ask for synergy and collaboration;
- to establish clearly the chain of tasks and responsibilities which should automatically start up in case of a nuclear accident;
- to define and test the proper modalities to inform long before and gradually the population about the usefullness of KI prevention, in order to avoid irrational concern;
- to explain to people why the administration of stable iodine must be limited to children and how it is not dangerous for them, in order to obtain the greatest collaboration by mothers and relatives in the emergency situation;
- to draft an appropriate, easy understandable information leaflet to be supplied with KI pills packages.

Apart from this, PSP offers three more opportunities of general interest.

- its running may be checked through a simulation test involving every step but the last, i. e. the KI pills administration;
- if it works, it can represent a model to be applied in other provinces or areas, after modifications related to the different local situations and requirements;
- it will represent a permanent, useful starting point to develop the possible adjustements needed in the future.

Here, in short, the different steps followed to carry out the PSP and the state of the art.

Step A) Planning

After assessement of the literature concerning this issue, the main need was to gather the basic data referred to the population and the characteristics of our province, and estimate the cost of the project.

Here is, point by point, what was evaluated and/or established in this first step:

- the population aged 0-18 years in the Province of Parma is about 82. 000 units, subdivided as in Figure 14. We further know the distribution of age year by year;
- pills of Potassium iodide (KI) will be used, manufactured in a manner to be easily divided in-

Municipal district	Province
M. 12.163	M. 30.054
F. 11.427	F. 28.093
subtotal 25.390	subtotal 58.147
total 81.737	

Figure 14. Population aged 0-18 yr. in Parma and its Province at the end of 2002

to four segments, each with a content of stable iodine as shown in Figure 15.

- the doses of KI for subjects of different ages have been established and are reported in Figure 16;
- KI, in the recommended doses, will have to be administered only once(orally, with water). Only in the case of ingestion of contaminated food (easily avoidable in our area) a daily prophylaxis with the same doses will be protracted for a while;
- the global amount of KI necessary for our project is 100. 000 pills. These pills of KI are not available at a chemist's; they can be manufactured in Italy on specific and authorized request. Thanks to a local private sponsor, the necessary amount of money for 100. 000 pills of KI is at our disposal; hence, the carrying out of PSP will be free of charge for the local administration (province of Parma)as well as for the regional and national administrations;
- packets of KI pills must contain a leaflet with short, clear, "user friendly" instructions. A draft of such a leaflet (also containing the advice to contact the physician in the presence of symptoms suggestive of an adverse reaction)has been prepared already;
- the lower IL (Intervention Level) to start the prophylaxis was set at 10 mGy (equivalent to 10mSv, taking into account the low LET of the radioisotopes of iodine), just as recommanded by WHO (Figure 17). In the UK this lower IL remains unchanged at 30 mGy (updating of the 2nd WG, year 2. 000), on the basis of cost/benefit considerations related to the already running protective measures.

1 pill contains

KI	stable iodine	activity period
65 mg	50 mg	42 months

Figure 15. KI pill characteristics

Age	Pills	mgKI	mgIodine
0-1 m.	1/4	16	12,5
2m.-3a.	1/2	32,5	25
4-12a.	1	65	50
13-18a.	1 and 1/2	100	75
Adults	2	130	100

Figure 16. Recommended KI doses in subjects of different ages

- Lower: 10 mGy
- Upper: 100 mGy

Figure 17. Lower and upper ILs (according to WHO)

For the province of Parma, as well as for Italy, the advisable lower IL is at 10 mGy, considering the iodine deficiency of the territories; the advisable upper IL is at 100 mGy, as universally accepted after Chernobyl.

Step B) Calling the local Authorities for collaboration

In this second step, I personally contacted all the Institutions and Authorities involved in the management of emergencies in our territory: Municipality, Province, Prefecture, Civil Protection, ASL (local health authority), ARPA (regional agency for environmental protection), University of Parma and Parma main general Hospital, VV.FF. (the fire brigade) and most of the many local voluntary organizations.

I explained to each of them the problem of this particular "pediatric emergency", I stressed the need to organize the KI prophylaxis in children in case (although improbable) of a nuclear accident with radioiodine fallout like that experienced after Chernobyl, and asked for their consent and cooperation in carrying out the PSP in our province, in order to verify the reliability of the project.

It was quite clear to all the contacted Authorities that the PSP was free of charge and did not schedule either drug administration (KI) or any other medical intervention on children.

The difficult point to explain was that KI, to be effective, should be administered as soon as possible (better before)the nuclear accident. As the accident is unforeseeable and the production, distribution and correct administration of KI would require a long time and a lot of people aware of what to do (and not to do), KI prophylaxis must be organized long before.

To reach this goal, the gathered data (step 1) were useful but still insufficient. In fact:

- it is not enough to know the total number of subjects to protect (about 82. 000); one must know their distribution in the different places of the province. Moreover, it is necessary to identify, in each locality, the most suitable meeting points for people to be prophylaxed and the best places where the stockpiles of KI pills (hospitals, schools, chemists, police stations, etc.) can be stored;
- it is not enough to know the total number of KI pills to order; one must define at least some different size of packages, on the basis of the number of children resident in the different areas covered by each stockpile store;
- it must be decided with whom the stockpiles should be leaved for safekeeping, wherever located;
- it must be established as well who will be charged to rapidly distribute and/or correctly administer the KI stored in the territory, when required;
- it must be clearly established, who shall order to start the mechanism of KI prophylaxis, which further has to automatically flow down to the last ring of the chain, i. e. to those charged to bring the pill to the child or the child to the pill (both situations are predictable, also depending on children's ages and local possibilities). This point is to be taken into particular account in our country, where there are so many rules and regulations to allow sometimes different (if not contradictory) interpretations. This may give rise to conflicts of jurisdiction and unforeseeable interferences, capable not only to jeopardize the timeliness of KI administration but even to break off the whole prophylactic chain at different steps. This is the reason why PSP, once completed in its organization, should be followed by one (or more) mock trial, to verify the reliability of every ring of the chain (drug administration excluded).
- last but not least, a further, fundamental point for the success of prophylaxis is an adequate information to people in the covered area, through mass-media, physicians, social operators etc. It should be stressed that PSP is an experimental study in the interest of children, which does not require any kind of medical intervention; that KI does not have harmfull effects; the reason why only children should assume it in case of need; that this study does not mean that the province of Parma has a higher risk of nuclear contamination than the neighbouring provinces but that PSP is the basis to organize a future rational prevention also in every other province of Italy.

I believe that informing the population of the province of Parma may be easier than elsewhere for two reasons.

The first one: thanks to a widespread net of optic fibers is possible to telematically contact even most of the villages scattered on the mountain area of Appennini. Moreover, a Councillorship just for Information Technology and an University Laboratory for Telematic in the Territory (LTT) are active in Parma. They are used to work in tandem when required.

The second one: our population is collaborative in social and sanitary educational activities, being accustomed to them since a long time. Moreover, this population already knows something about thyroid, the importance of an adequate intake of iodine and the general risks of iodine deficiency, thanks to previous campaigns for the prevention of goiter.

I am convinced that PSP offers a rare opportunity to reinforce this campaign, considering that both messages share the goal of safeguarding the thyroid in children.

Finally, it is as well necessary to inform adequately all those having the opportunity to be currently in contact with children: first of all, the pediatrician and the general physician.

Today's meeting "Il Pediatra e la Tiroide", with its first session dedicated to "Radioiodine and Thyroid in the Developmental Age"represents a good opportunity for our Colleagues to update their knowledge and their interest in this field.

Step C) Carrying out PSP

The Prefectorial Commission for NBCR (Nuclear, Biological, Chemical, Radiological) emergencies, i. e. the legal and qualified place to discuss and develop the PSP, shares the project from the beginning and is concretely operating to carry out with the collaboration of many local Institutions and Organizations involved, in particular: the Civil Protection, the Public Health Councellorship of Parma, the Regional Agency for Environmental Protection (ARPA), the Fire Brigade, the Red Cross, the Mountain Communities of Majors, all the other Voluntary Organizations ready to be activated in case of emergency.

Surprisingly, some perplexities have been expressed by the representatives of the territorial Public Health Administration (ASL), such as: "Is it demonstrated that a large rise of thyroid carcinoma in children followed the Chernobyl accident?", or "Is it ethic to limit PSP to the province of Parma instead of extending it to all the other provinces of the Region?".

The Provincial Sanitary Conference (gathering all the Majors of the province) approved the offer of PSP in its meeting of July 1st, charging a restricted technical group (5 persons; I should have been the coordinator) to go into details for its accomplishment. After a long interruption of the Conference activity due to the summer holidays and especially to the death of the President of the Province, the technical group met for the first time a few days ago and shall meet again next week.

The Provincial Councellor for Information Technology, agrees to put at our disposal the telematic net to extend the necessary information to people of the province.

The recently raising concerns about radioactive waste disposal and about the growing , extending danger of fanatic technological terrorism, both largely echoing with media, made clear to many people that the initiative to carry out the PSP is not only useful but also up to date.

Recently, a letter (prot. DPC/PRE/8849893, 10 november 2003) was sent to the Prefecture of Parma and to me by the Direction of the Department for Civil Protection in Rome (direct emanation of the Government Premiership).

In this letter, the Departement of Civil Protection recognizes the relevance of PSP, states its interest for it and asks to be updated on its results.

We are trying to obtain these in the near future, as soon as some conflicts of jurisdiction, some medical misunderstanding (health care and emergency are not the same thing and do not speak the same language), and some bureaucratic difficulties are overcome.

In any case, let's not forget that one of the goals of PSP is to find out the most suitable way through the obstacles of different origins to carry out a timely, effective prophylaxis with KI in children. Hence, the present delay in testing the results of PSP will prevent the same delay anywhere else a PSP-like model will be applied in the future, and should not be considered a waste of time.

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Correspondence: Giorgio Giovannelli
Department of Pediatrics
University of Parma
Via Gramsci 14
43100 Parma, Italy
E-mail giorgiov2@libero. it