



## Albania 1998 and on

Iodine deficiency in Europe in the 21<sup>st</sup> century





- Albania is a mountainous country with a long Mediterranean coastline
- It is about the size of Wales and has a population of 3 million.
- It is said to be the only third world country in Europe





- I invited Stuart to the conference in 2001.
- We listened to a presentation by Professor Petrit Hoxha the senior Paediatric Endocrinologist.
- He pleaded for someone to do something about Iodine deficiency. Our ears pricked up.
- After we returned home Stuart rang me and prodded me into action.

# Iodine deficiency is the commonest cause of learning difficulty worldwide

- 2.2 billion people are at risk.
- 41 million babies born annually are unprotected from iodine deficiency and its lifelong consequences



Late teenager Pogradec



Adult myxoedematous cretins in the Congo from Delange, F.

- The elimination of Iodine Deficiency Disorders by the year 2000 was a goal adopted by government leaders at the 1990 World Summit for Children.
- In 2002 in a Unicef outcome document headed "A world fit for children" one goal was to achieve sustainable elimination of iodine deficiency by 2005
- For Albania the current target is to eliminate the problem by 2008

A close-up photograph of a young child with a large, protruding nose and significant facial redness, particularly on the cheeks and around the nose. The child has brown hair with bangs and is wearing a grey shirt with a red collar. In the background, other children are visible, including one in a dark blue shirt and another in a grey shirt. A hand is visible on the right side of the frame, resting on the child's shoulder.

A recent evaluation by the World Bank found that micronutrient programs have the greatest cost benefit ratio of all health interventions.

27 3 2003



The  
University  
Of  
Sheffield.



- We set about planning to define the extent and severity of the problem.
- I contacted Michael Zimmerman, an endocrinologist and clinical scientist based at the Laboratory for Human Nutrition, at the Swiss Federal Institute of Technology. He made us an offer we could not refuse.
- Add Maksim Bozo, Lindita Grimci and Valbona Selimaj and we had our team.

Goitre surveys in Albania  
the 1980's found severe  
IDD in the mountains.  
The cretinism rate was  
0.1%

1993 a study reported  
urinary iodines in 8-10yr  
old children ranging from  
2-49 $\mu\text{g}/\text{l}$ , with 63% <20  
< 20 $\mu\text{g}/\text{L}$  = severe iodine deficiency

Whole blood TSH in 227  
newborn in Tirana  
showed 33% >5 $\text{mU}/\text{l}$



Normal range 0.4 to 4.0  $\text{mIU}/\text{L}$

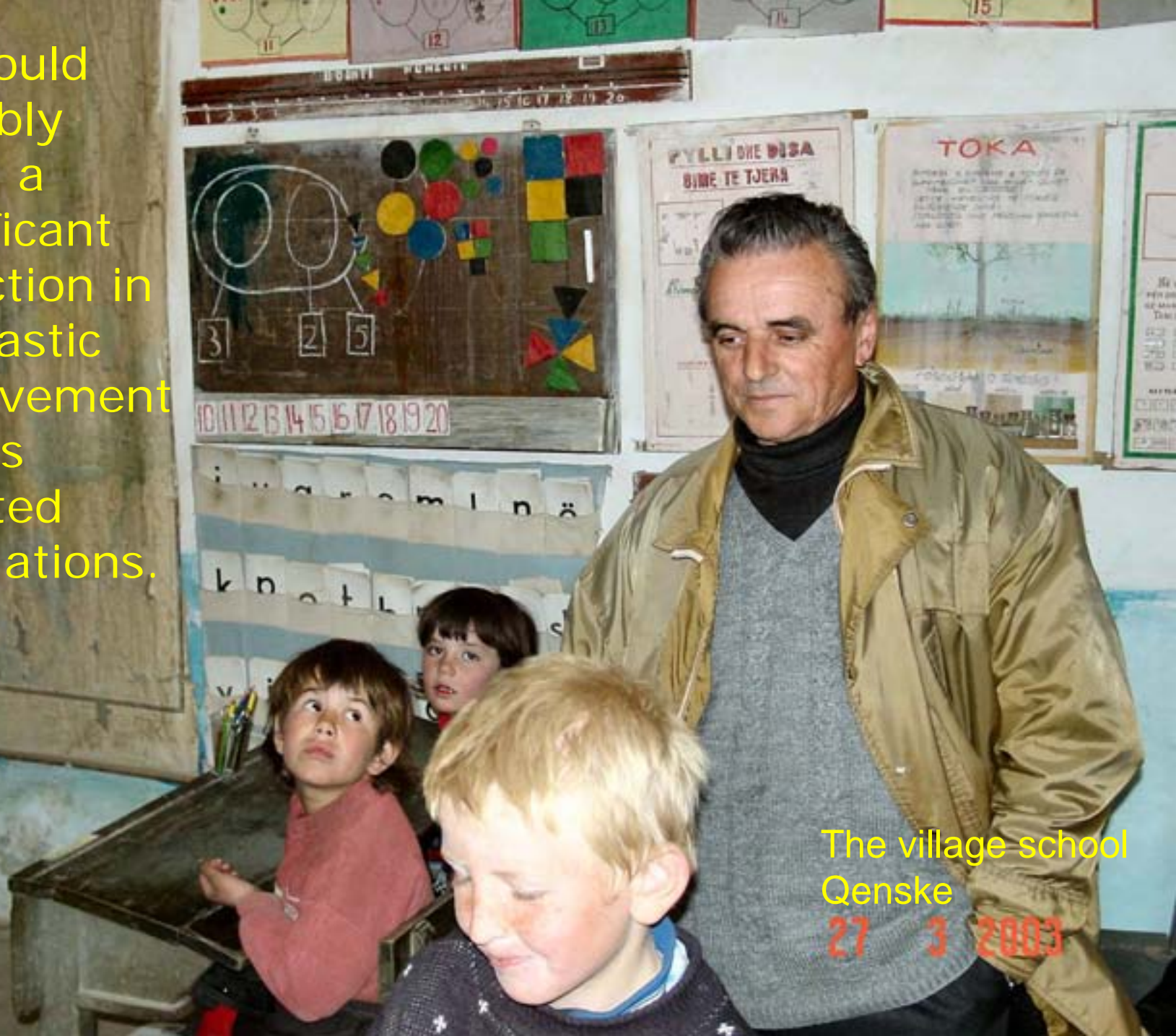
In 2003 we studied 826 5yr to 14 yr old children in mountainous urban and rural Southern Albania.

- Growth.
- Goitre frequency & size.
- Thyroid size by ultrasound
- Urine iodine concentration
- Retail and domestic salt



- The rural children were significantly shorter than the urban children.
- There was severe deficiency in the rural areas, the median urine iodine was  $17\mu\text{g/L}$  and the goitre prevalence 95%, in 20% the goitre was nodular.
- In children in two schools in the town of Korçe the median urine iodine was  $45\mu\text{g/L}$  signifying moderate deficiency. The goitre prevalence was 32%.
- No rural household salt sample was adequately iodised. In urban areas, the salt iodine levels were inadequate in 78% of the households at  $< 15\mu\text{g/g}$ .

We could possibly avoid a significant reduction in scholastic achievement across affected populations.



The village school  
Qenske

27 3 2003



- In 2004/2005 we asked does Iodine supplementation improve cognition in Iodine deficient children?
- We designed a randomised, placebo controlled, double blind study.
- Ethical approval for the study was given by the Swiss federal Institute of technology and the MOH in Albania



Zimmerman, Connolly, Bozo,  
Bridson, Rohner, Grimci  
Am J Clin Nutr 2006; 83: 108-14

- Four other randomized controlled trials measuring the effect of iodised oil on cognition in children have been reported. The results are equivocal.
- Three of the studies found no effect,
- One study found that cognition improved significantly with treatment. Shrestha R.M. in his doctoral dissertation 1994
- However problems of method limit their interpretation.

- In one study, a well controlled trial in moderately iodine deficient but euthyroid Bangladeshi children, treatment with oral iodised oil did not significantly improve cognitive or motor function at 4 months.
- However treatment did not normalise iodine status, and the iodine treated children remained iodine deficient at the time of retesting. Huda SN et al J Nutr 2001:31:72-7

- We studied 310 school children in rural mountainous south eastern albania, 166 boys and 144 girls, aged 10-12 yrs.
- Each child was randomly assigned to receive 400mg Iodine (2 iodised poppyseed oil capsules ) or a placebo capsule of identical appearance containing sunflower oil.
- The dose would provide iodine sufficiency for greater than six months

- A spot morning sample was collected for Urinary iodine assay.
- Whole blood from a finger prick was spotted onto filter paper cards to measure whole blood TSH and serum Total T4 (TT4)
- Thyroid gland volume was measured using a portable echo camera.

Cognitive and motor tests.

Ravens coloured  
progressive matrices

Coding

Symbol Search

Digit span (forwards and  
backwards)

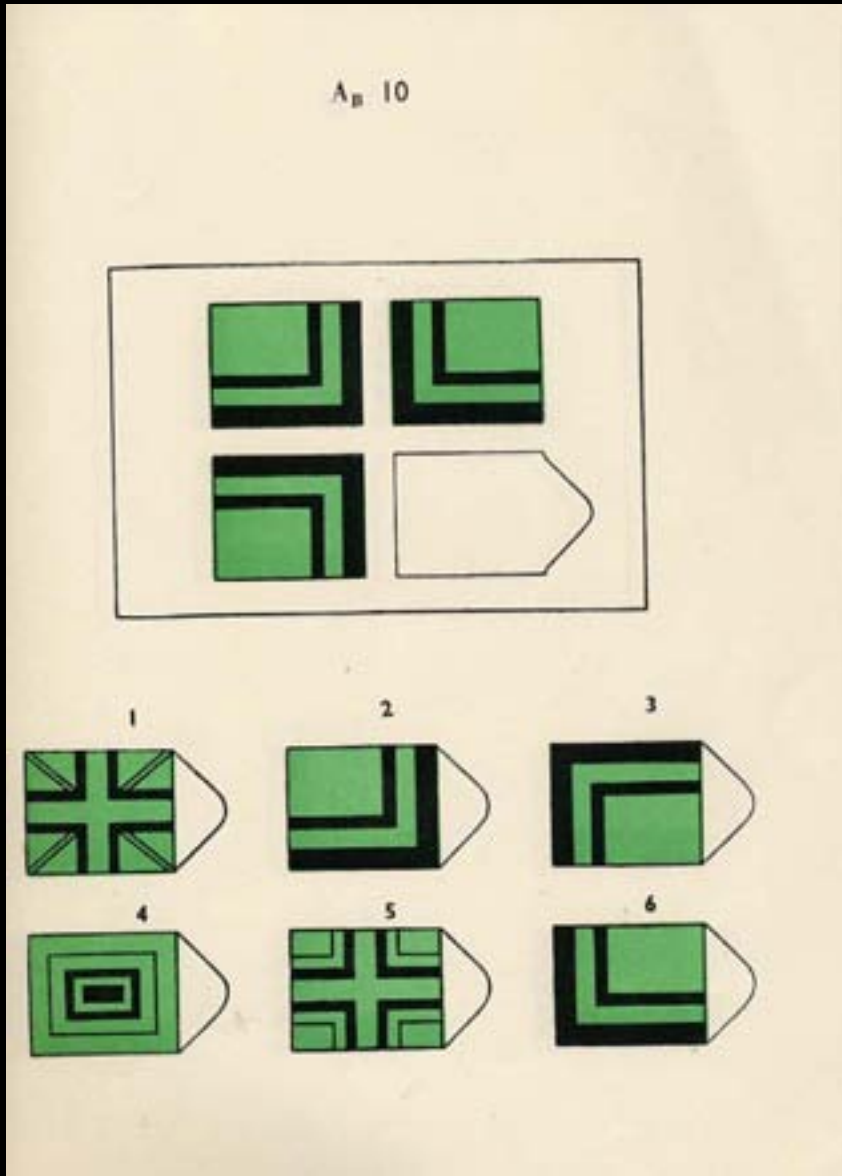
Rapid object naming

Bead threading

Rapid target marking



# Ravens Coloured Progressive Matrices



- This measures the ability to reason and solve problems.
- There are 3 sets of 12 visual problems. The child is shown a pattern with a missing section and selects 1 of 6 alternatives to complete the pattern.
- The problems become progressively more difficult.
- The test continues until the child is satisfied with the choices made.

# Coding

- The child copies symbols each of which is paired with a digit from 1-9.
- After a demonstration and a brief period of practice, the child is given a sheet with 93 numbers and asked to put appropriate symbol against each number as quickly as possible.

CODING B ✓  
(8-15)

1	2	3	4	5	6	7	8	9
÷	)	+	⊥	∩	∨	(	-	⊥

SAMPLE																								
2	1	4	6	3	5	2	1	3	4	2	1	3	1	2	3	1	4	2	6	3	1	2	5	1
3	1	5	4	2	7	4	6	9	2	5	8	4	7	6	1	8	7	5	4	8	6	9	4	3
1	8	2	9	7	6	2	5	4	7	3	6	8	5	9	4	1	6	8	9	3	7	5	1	4
9	1	5	8	7	6	9	7	8	2	4	8	3	5	6	7	1	9	4	3	6	2	7	9	3

TIME (120") \_\_\_\_\_ SCORE (NO. RIGHT) \_\_\_\_\_

The score is the number of correct matches made in 120 s.



# Digit Span

- The tests short-term memory.
- The examiner reads a series of number sequences at the rate of 1/s. The child is asked to repeat the sequence in the same order. After a correct repetition the list length is increased by 1 sequence.
- The test ends if a child fails 2 successive number sequences at a given list length.
- After digit span forward the test is repeated backwards, the list must be recalled in reverse order.

## 12. Digit Span

For both Digits Forward and Digits Backward, administer both trials of each item even if Trial 1 is passed. Discontinue after failure of both trials of any item.

Administer Digits Backward even if Digits Forward score is 0.

All ages		Digits Forward		Trial score	Trial 2/Response		Trial score	Item score
		Trial 1/Response						0,1 or 2
1	2-9				4-6			
2	3-8-6				6-1-2			
3	3-4-1-7				6-1-5-8			
4	8-4-2-3-9				5-2-1-8-6			
5	3-8-9-1-7-4				7-9-6-4-8-3			
6	5-1-7-4-2-3-8				9-8-5-2-1-6-3			
7	1-6-4-5-9-7-6-3				2-9-7-6-3-1-5-4			
8	5-3-8-7-1-2-4-6-9				4-2-6-9-1-7-8-3-5			
Digits Forward score (maximum = 16)								<input type="text"/>
All ages		Digits Backward		Trial score	Trial 2/Response		Trial score	Item score
		Trial 1/Response						0,1 or 2
	Sample	8-2			Sample	5-6		
1	2-5				6-3			
2	5-7-4				2-5-9			
3	7-2-9-6				8-4-9-3			
4	4-1-3-5-7				9-7-8-5-2			
5	1-6-5-2-9-8				3-6-7-1-9-4			
6	8-5-9-2-3-4-2				4-5-7-9-2-8-1			
7	6-9-1-6-3-2-5-8				3-1-7-9-5-4-8-2			
Digits Backward score (maximum = 14)								<input type="text"/>
Total subtest score (maximum = 30)								<input type="text"/>

## 13. Mazes



# Rapid object naming

- This measures the speed the child is able to name a series of familiar objects.
- The child is shown a card with line drawings of 20 objects. When the child has named these objects, he or she is given another card having 2 sets of the objects and asked to name them as quickly as possible.
- The score is the time taken. An adjustment is made for errors.



## Bead threading

- This measures fine motor skill and involves threading small, brightly colored beads onto a thin string.
- The child is asked to thread as many beads as possible in 60 s.
- The task is repeated 3 times and the score is the mean number of beads threaded.



# Rapid target marking

- This is a measure of the rate of information processing.
- The child is given a pencil and a target sheet. The targets are 3mm in diameter, there is an 8mm space between centers.
- The task is to strike through each target as quickly as possible.
- Following the testers demonstration and the child's practice the child is given a test sheet with 3 sets of 45 targets.

## Rapid Target Marking

Name	School / Village	Number	
DoB	Sex	Date tested	Tester

---

○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○

○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○  
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○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○ ○

After 24 weeks we repeated  
the tests



## results

- For a detailed assessment of the statistical methods used please read the paper.
- At baseline, the children were moderately to severely iodine deficient, as defined by a median urine iodine of  $44\mu\text{g/L}$  and a goitre rate of 87%
- nearly one third had low circulating Total T4 concentrations because of chronic iodine deficiency.
- Treatment produced a marked and sustained improvement in iodine status and significantly improved thyroid function

- Iodine treatment was associated with highly significant improvement in test scores on Raven's matrices, rapid target marking, symbol search and rapid naming ( $p < 0.0001$ ).
- With treatment, there was a significant gender effect with girls better on the tests of rapid target marking (1.9;  $p = 0.002$ ), symbol search (0.85;  $p = 0.04$ ), and rapid naming (1.8;  $p = 0.01$ ).
- Multiple regressions showed no significant effect of TT4, TSH or thyroid volume on any of the baseline, follow-up, or change from baseline values on the cognitive tests.

## discussion

- Iodine treatment improved information processing rates, as measured by the symbol search, rapid naming, and rapid target marking tests.
- Raven's matrices measures the ability to reason and solve problems involving new information without relying on an explicit base of declarative knowledge.
- The adjusted treatment effect of 4.7 points on Raven's matrices suggests iodine repletion was associated with a small but significant increase in intelligence.

## conclusions

- We believe this study is the first iodine supplementation trial to clearly show that the adverse effects of moderate iodine deficiency on aspects of cognitive and motor function in children are ameliorated and at least partially remedied with iodine repletion.
- Because impaired learning and reduced school performance adversely affect a region's development, these findings have particular relevance for policy makers and governments.

The results are generalizable in that the degree of iodine deficiency in our study population is present in many regions worldwide.

The results also support current recommendations from WHO for regional distribution of oral iodized oil capsules to school children in areas of moderate iodine deficiency, as an interim measure, until salt iodization can be implemented .

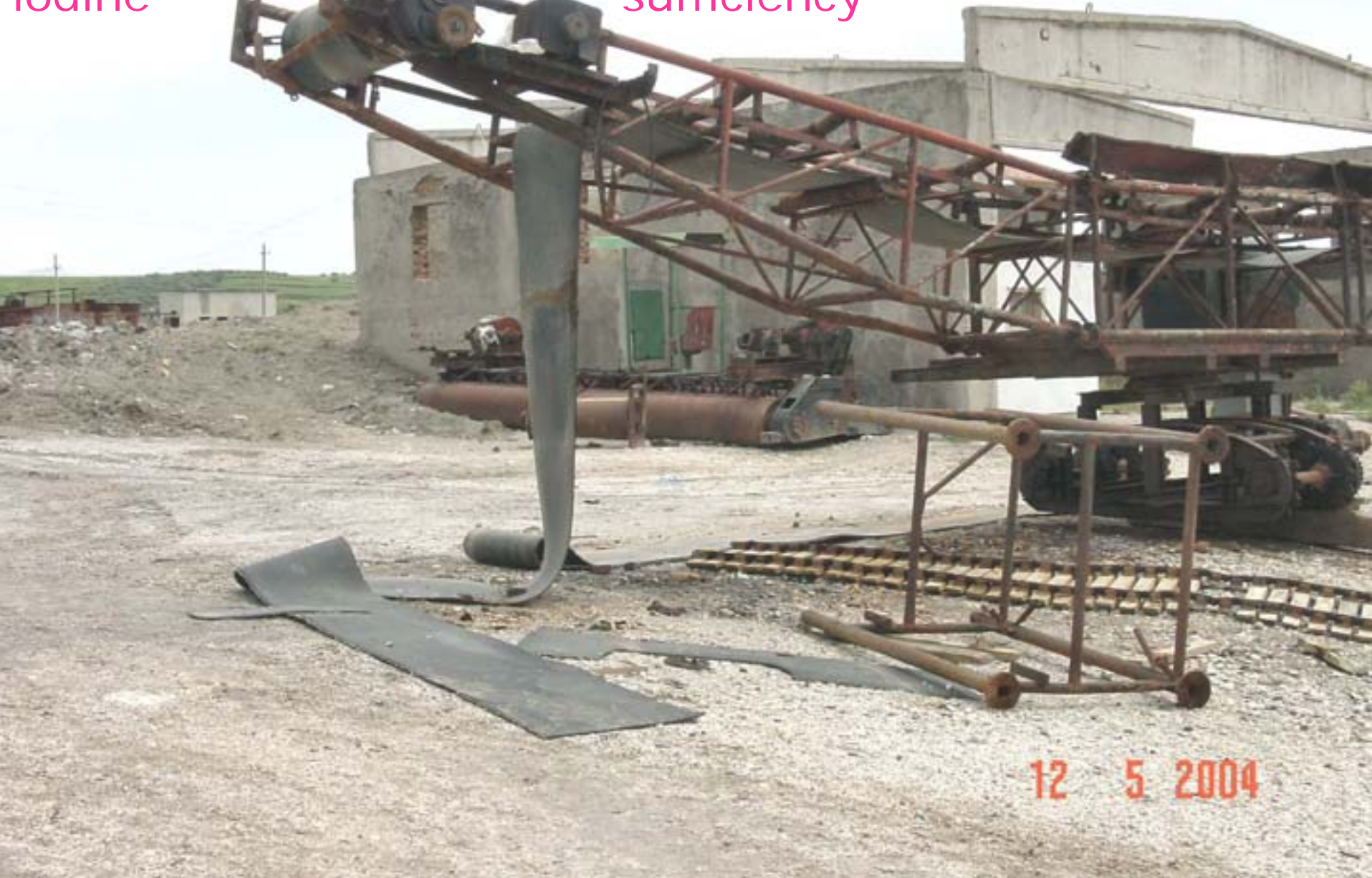
The Mara Foundation is a Dutch NGO  
They purchased 40,000 iodised oil capsules



We have distributed these to school  
children in the affected areas.

29 9 2004

Fortification of salt with iodine is recognized as the most effective and cost efficient strategy to achieve iodine sufficiency



12 5 2004



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### Albania begins production of iodized salt

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The first production of iodized salt in Albania began today with the inauguration of the iodization line at the Vlora Salt Factory. Local production of iodized salt will help prevent iodine deficiency disorders (IDD), which currently put at risk the mental capacities and academic achievements of 63% of school children in Albania, who don't have enough iodine in their diets.

This is the equipment with which the salt is iodised and packed.