Iodine

- The basic function of iodine is to participate in the synthesis of the hormone thyroxin by the thyroid gland.
- Risks associated with iodine deficiency:
- Vit.A and iron deficiencies are found universally throughout the developing world. Iodine deficiency is largely restricted to those areas where iodine concentration is low in the soil and therefore in the water and in locally produced food. The presence of so-called goitrogenic substances in some local foods (which impair the body's ability to utilize iodine) may increase the likelihood that deficiency signs will develop in areas that are low in iodine (cabbage, cauliflower and beans).

Clinical features

- When an individual's supply is deficient the thyroid gland becomes enlarged in an attempt to produce the quantities of the hormone that are needed by the body. This enlarged thyroid is called a Goiter. If the prevalence rate of goiter in a community is high; this is not, in itself, a major public health problem. **Endemic Goiter** consider as public health problem when there is a palpable enlargement of the gland in at least (30%) of the adult population in a defined geographical locality. Some (800) million people live in iodine deficient areas in under developed countries of the world.
- The prevalence rate of **endemic goiter** is associated with the incidence of **endemic cretinism and deaf mutism among newborns**. If the prevalence rate of goiter among women of childbearing age exceed (50%), as many as (10%) of newborn children will have impaired mental and physical capacity as part of the congenital iodine deficiency syndrome. The prevalence of iodine deficiency can be assessed by measuring **urinary iodine** excretion; if it is **less than 25 µg/g of creatinine, iodine deficiency exists**. As such measurement is rarely possible; indicators of iodine deficiency are needed. In practice, the prevalence rate of endemic goiter that is most commonly used in **assessing the level of iodine deficiency disease in a community by using the following:**

Classification of thyroid enlargement in the assessment of iodine deficiency disease:

Grade	Thyroid Characteristics
0	Not palpable
1a	Palpable (at least as large as distal phalanx of subject thumb) not visible with head raised.
1b	Palpable and visible with head raised.
2	Visible with head raised in normal position
3	Visible at a distance
4	Very large goiter

Most field surveys concentrate on assessing the prevalence of visible goiters.

RDA

- the recommended daily allowance for iodine intake in an adult is 80-150 µ g . If intake falls below (20 µ g) / day, iodine deficiency diseases becomes likely. Food supply about 90% of the iodine intake. And the rest from water. The sea foods are rich source of iodine such as marine fish and shell fish. The fresh water fish is a poor source of iodine, in addition to fish a common. Sources of iodine are milk products, cereals and green leafy vegetables as spinach.

Control

- The effective way of eliminating endemic goiter and endemic cretinism is by the iodization of table salt, the other control measure is the I.M injection of iodized oil, every 3-4 years (0.5 ml) infants 1.0 ml for all above 1year). This will prevent the development enlargement of endemic goiter. If given to woman before conception prevents endemic cretinism. Since it is expensive and requires such organization to inject all the vulnerable population, priority should given to women likely to become pregnant and those with large goiter who might develop complications.

Iodine
Iodine Deficiency
Iodine Deficiency Disorders (IDD)

Most preventable cause of mental retardation in the world

Keith P. West, Jr., DrPH

Center for Human Nutrition

Iodine

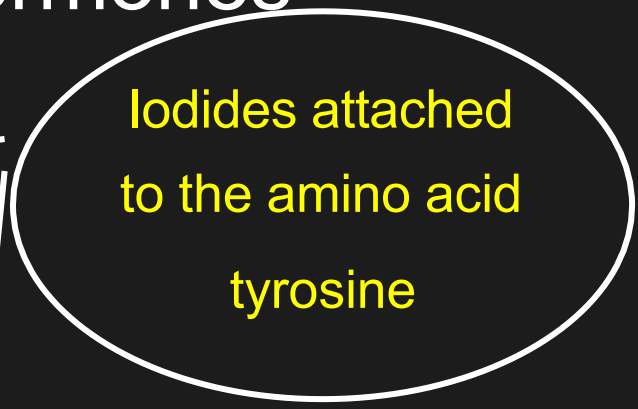
- Required to produce thyroid hormones that control cell metabolism, neuromuscular tissue growth and development, especially the fetal-perinatal brain
- Present in minute amounts (15-20 mg) in the body
- >90% of iodine stored in the thyroid

Hormones

- Endocrine: produced & circulated to distant sites of action – vs -
- Paracrine: act on neighboring cells
- Autocrine: act on same cells that produce

Iodine needed for thyroid hormones

- Thyroxine (T_4)
- Triiodothyronine (T_3)

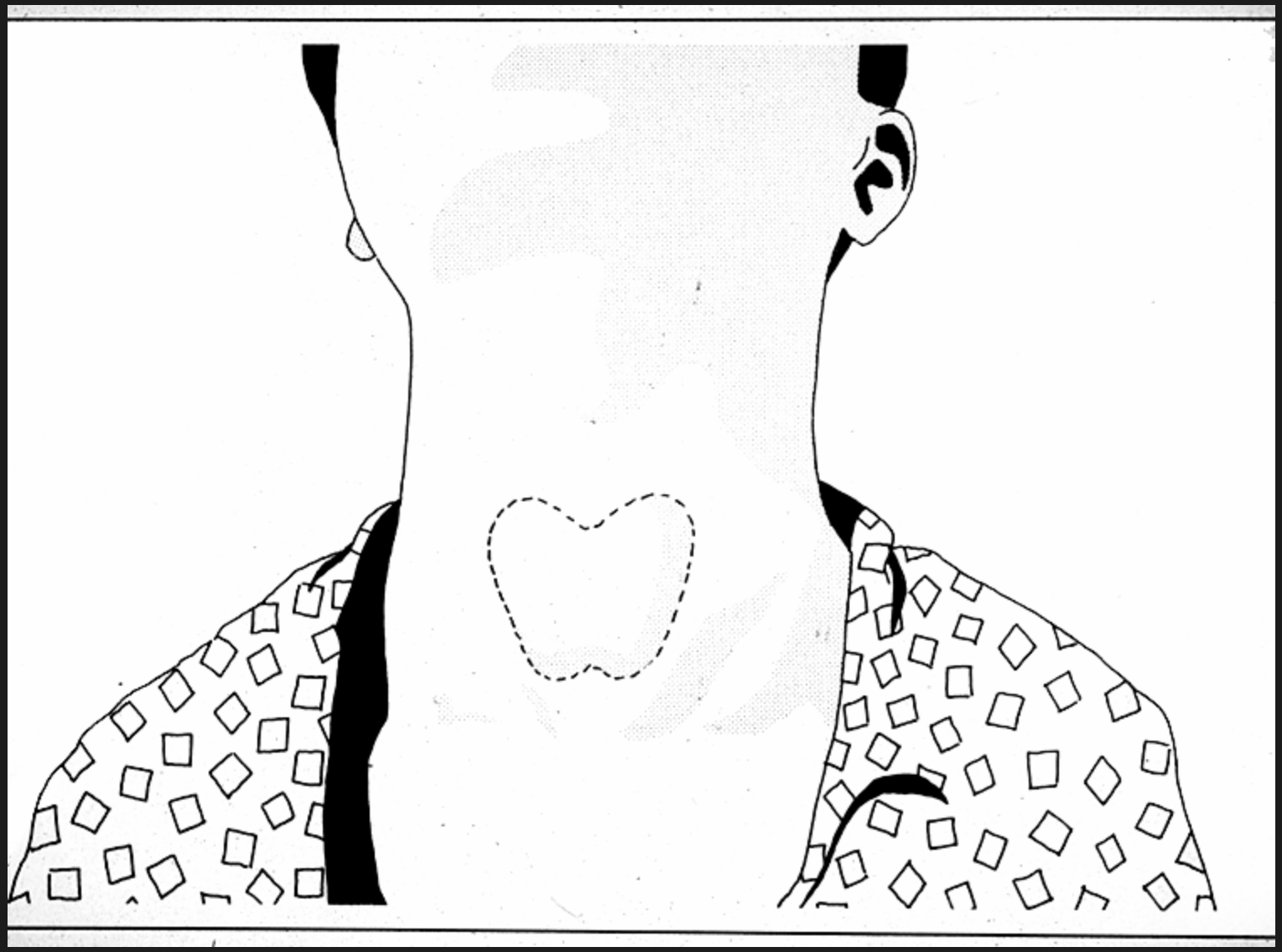


Thyroid hormones regulate numerous functions: eg

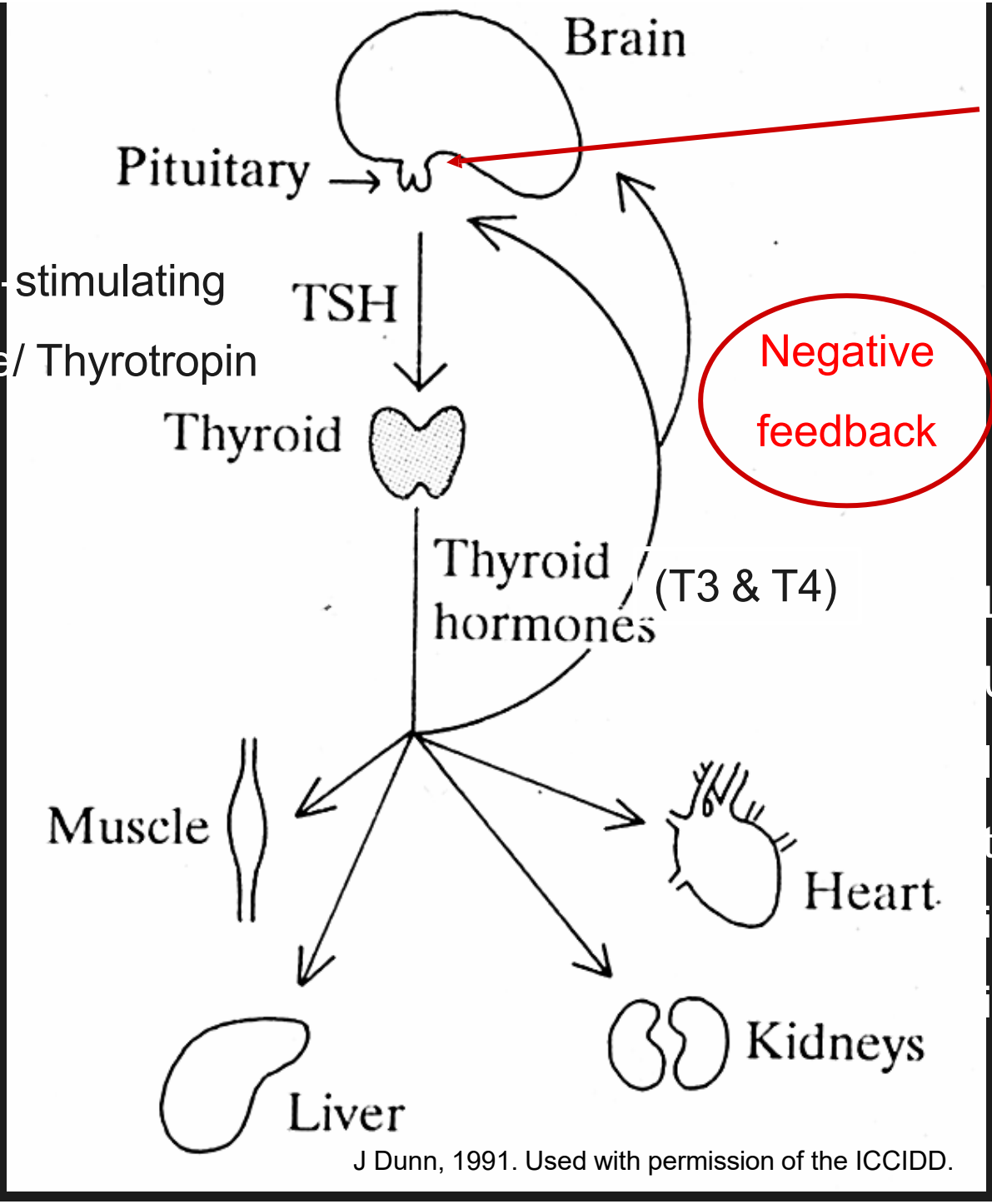
- Biochemical reactions (eg, protein synthesis, enzyme activities)
- Influence early organ development (eg, brain through 2-3 yrs of age)

Functions of Thyroid Hormones

- By influencing gene transcription, thyroid hormones regulate oxygen and energy utilization, evident through
  - Cellular metabolism (oxygen & energy utilization, ATP production)
    - Basal metabolic rate
    - Protein synthesis
    - Thermogenesis



Thyroid-stimulating Hormone/ Thyrotropin



J Dunn, 1991. Used with permission of the ICCIDD.

Thyrotropin-releasing hormone (TRH) produced by the hypothalamus controls TSH production in the anterior pituitary

Low T3 & T4 levels Up-regulate; high levels down-regulate the thyroid; increase in energy need increases activity

1 Follicular cells of Thyroid trap iodide ions in blood

2 Follicular cells make & secrete thyroglobulin (TG) with tyrosine amino acids

3 Iodide anions are oxidized w/ peroxidase to iodine & pass into colloid

4 Iodine attaches to TG tyrosine AAs. Binding

T1 = monoiodotyrosine

T2 = diiodotyrosine

5 Two T2s couple to make T4 = thyroxine (80% of total); or one T1 and one T2 couple to make T3= triiodothyronine (20% of total, but 4x stronger).

6 TG re-enters the follicular cell, merges w/ lysozyme and is digested. T3 & T4 are cleaved & released.

7 Lipid soluble T3 & T4 diffuse through plasma membrane into blood

8 T3 & T4 transported by thyroxine-binding globulin (TBG)

Iodine Deficiency Disorders (IDD)

Fetal Iodine Deficiency

Abortion
Stillbirth
Congenital defects
Mental retardation
Paraplegia
Deaf-mutism
Dwarfism
Psychomotor defects
Cretinism
Infant mortality

Neonatal ID

Neonatal goiter
Hypothyroidism
(too little thyroid hormone)
Infant mortality

B Hetzel Lancet 1983;2:1126;
R Semba, 2002

Materno-Fetal Iodine Deficiency: Neurological Damage

Default		CNS Site *
Intellectual deficit	→	Cerebral cortex
Deafness	→	Cochlea
Motor rigidity	→	Basal ganglia

* Probable 2nd trimester insult R. DeLong, 1994

Figure 5: Cretin in China J Dunn, 1991

Cretinism

Severe mental retardation

Severe growth deficit

Paraplegia (lower limb paralysis)

Rigidity

Deaf-mutism

Facial disturbances

The type and severity of brain, neural and musculoskeletal defects arise from timing, severity and duration of deficiency.

Effects of Iodized Oil in Pregnancy on Infant Mortality in Papua New Guinea

	No. Births	Deaths n	Deaths %	Cretins n	Cretins %
Untreated	503	97	19.3	26	5.2
Treated	478	66	13.8	7	1.5
RR			0.71		0.29

Pharoah et al, Lancet 1971;1:308

Effects of Infant Iodine Supplementation on Mortality in Indonesia

- RCT, 617 Indonesian infants, ~6 weeks of age
- 100 mg iodized oil vs placebo
- Motivation: Earlier studies lowered infant mortality when pregnant mothers' iodine status was corrected

Cobra et al. J Nutr 1997;127:574

Iodine Supplementation Reduced Early Infant Mortality in Indonesia

Follow-up	RR	(95% CI)	% Reduction
1 mo	0.20	(0.04-0.91)	80%
2 mo	0.30	(0.10-0.90)	70%
4 mo	0.52	(0.21-1.28)	48%

Cobra et al. J Nutr 1997;127:574

Iodine Deficiency Disorders (IDD)

Child/Adolescent

Goiter

Hypothyroidism

Impaired mental

and physical development

B Hetzel Lancet 1983;2:1126;

R Semba, 2002

Photo used with permission of the ICCIDD.

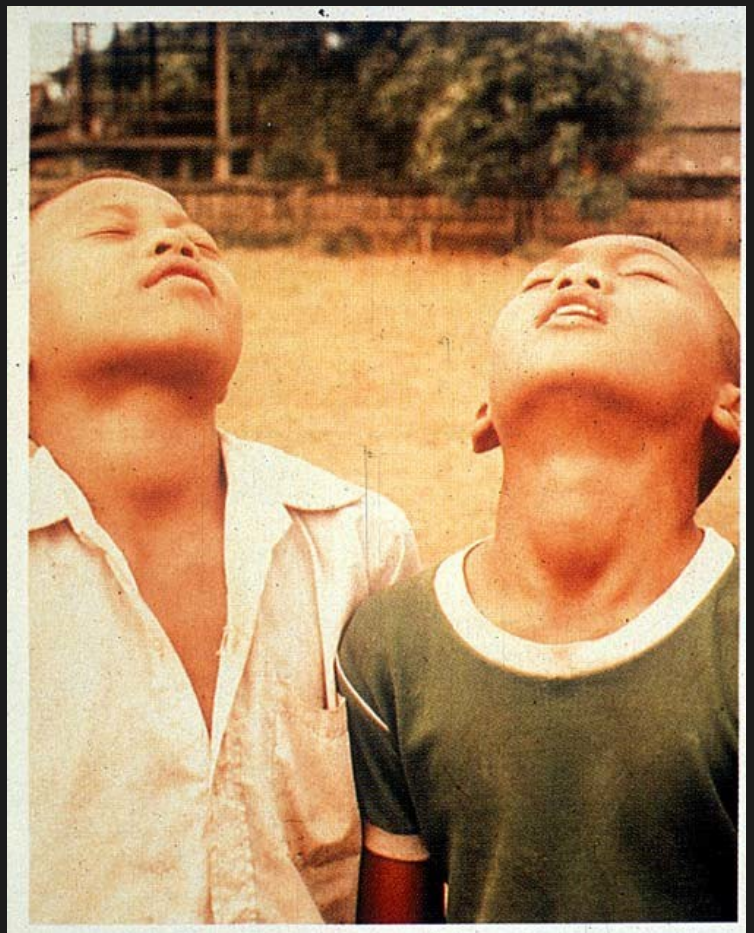


Figure 1: Goiters in children (courtesy of Romsai Suwanik and Thailand Ministry of Health)

Iodine Deficiency Disorders (IDD)

Adult

- Goiter
- Hypothyroidism
- Impaired mental function
- Iodine-induced hyperthyroidism
  (too much thyroid hormone)

B Hetzel Lancet 1983;2:1126

Photo: Keith West

Main Causes of Hypothyroidism

- Iodine deficiency
- Thyroiditis (inflammation) - autoimmune (Hashimoto's Disease)
- Surgical causes

Symptoms of Hypothyroidism

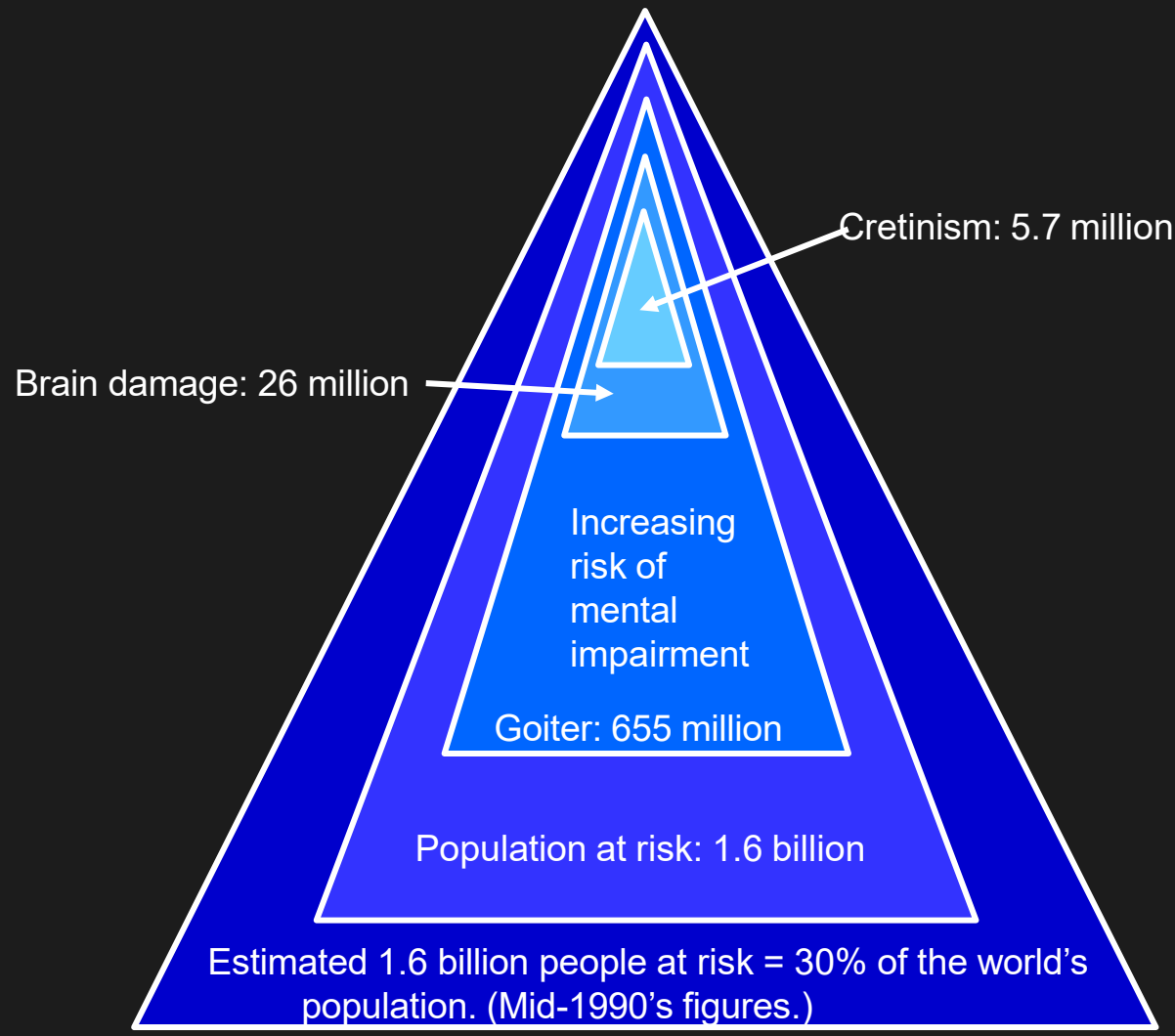
http://www.endocrineweb.com

- Fatigue ;Weakness
- Weight gain or increased difficulty losing weight
- Coarse, dry hair
- Hair loss
- Dry, rough pale skin
- Cold intolerance
- Muscle cramps/aches
- Constipation
- Depression
- Irritability
- Memory loss
- Abnormal menstrual cycles
- Decreased libido

IDD Globally (WHO, 1994)

	Total Millions Affected	% All Regions
At-risk	1,572	29
Goitrous	655	12
Cretinism	11	2

Iodine Deficiency Disorders



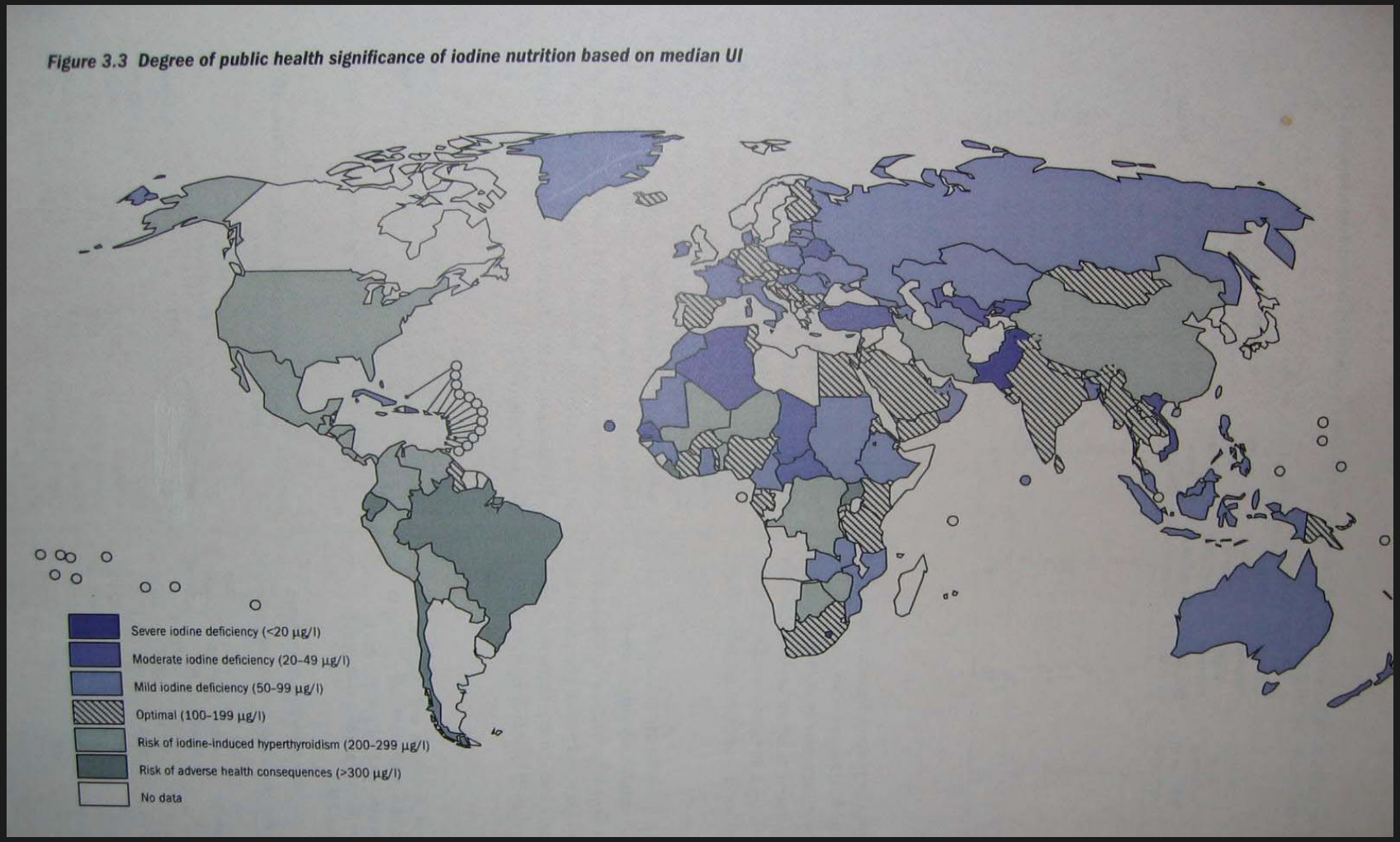
Adapted from a British Geological Survey diagram.

Iodine Deficiency: Global & Regional WHO 2004

UN Region	% Countries	Low I Intake (millions)	% of popn	Goiter (millions)	% of popn
Africa	42	324	43	202	27
Asia	50	1,239	36	505	15
Europe	53	331	53	102	16
LAC	11	47	10	22	5
N Am	0	28	10	-	-
Oceania	75	19	65	4	13
Global	42	1,989	35	893	16

West et al, Intl Pub Hlth Nutr, 2005

Iodine Deficiency Disorders
WHO 2004



54 countries with IDD as public health problem based on urinary iodine concentration

"Europe is iodine deficient"

Vitti et al., Lancet 2003

Sufficient (UI ≥ 100 µg/L)

- Austria, Bosnia, Bulgaria, Croatia, Cyprus, Czech Rep., Finland, Macedonia, Netherlands, Poland, Portugal, Slovak Rep., Serbia, Switzerland, UK, *Iceland, *Luxembourg, *Norway, *Sweden

Deficient (UI < 100 µg/L)

- Belgium, Denmark, France, Germany, Greece, Hungary, Italy, Ireland, Montenegro, Romania, Slovenia, Spain, Turkey, #Albania

* Likely sufficient;

Likely deficient

Iodine Status Assessment

- Goiter classification
- Urinary iodine concentration
- TSH (thyroid stimulating hormone) concentration
- Other common clinical measures:
  - Ultrasonoagraphy of thyroid volume
  - Serum concentrations: thyroxine, TBG, many other analytes

Goiter

This Ecuadorian boy is exhibiting signs of a goiter, an enlargement of the thyroid gland, due to an iodine deficiency.

Photo courtesy of CDC PHIL:
http://phil.cdc.gov/

Simplified Goiter Classification

Grade	Thyroid Size
0	Not palpable / not visible
1	Palpable in normal position
2	Visible in normal position

Poor response indicator to Universal Iodization of Salt (USI)

WHO, 1994

Epidemiological Criteria for Assessing Severity of IDD Based on Median Urinary Iodine Levels (WHO, 1994)

Median Value (µg/l)	Severity of IDD
< 20	Severe IDD
20-49	Moderate IDD
50-99	Mild IDD
≥ 100	No deficiency

Sensitive indicators of iodine intake, not thyroid function

IDD: As a Public Health Problem (WHO, 1994)

Indicator	Mod/Severe Cut-off (% of population)
Goiter grade > 0	≥ 20%
Median urinary iodine	< 50 µg/L
TSH > 5 mU/L blood (best in newborns)	≥ 20%
Thyroid volume > 97%ile	≥ 20%

Best IDD Indicators by Target Group (WHO, 1994)

Goiter grade >0	School children
Cretinism	Children/adults
Median **UI** (µg/L)	School children
TSH >5 mU/L blood	Neonates
Thyroid volume >97% ile	School children
Thyroglobulin (DBS)	Children

Iodine Interventions

Universal Iodization of Salt
Iodization of other “Vehicles”
Iodized Oil Supplementation

RDA for Iodine

Infants 0-6 mo:	100 ug
7-12 mo	120 ug
Children 1-8 yr:	90 ug
Adolescents:	120-150 ug
Pregnant/lactating women:	200 ug

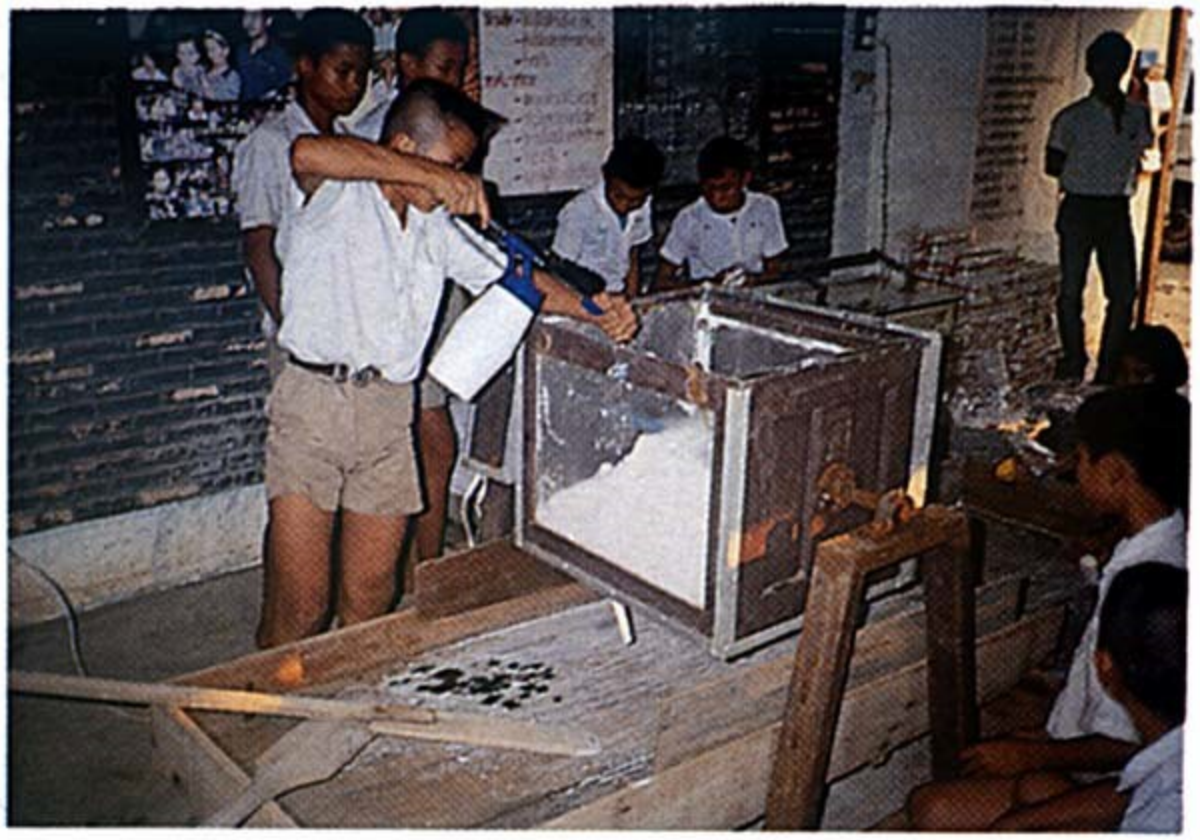
Dietary Reference Intakes, Institute of Medicine, National Research Council, Wash DC, 2001

Iodization of Salt

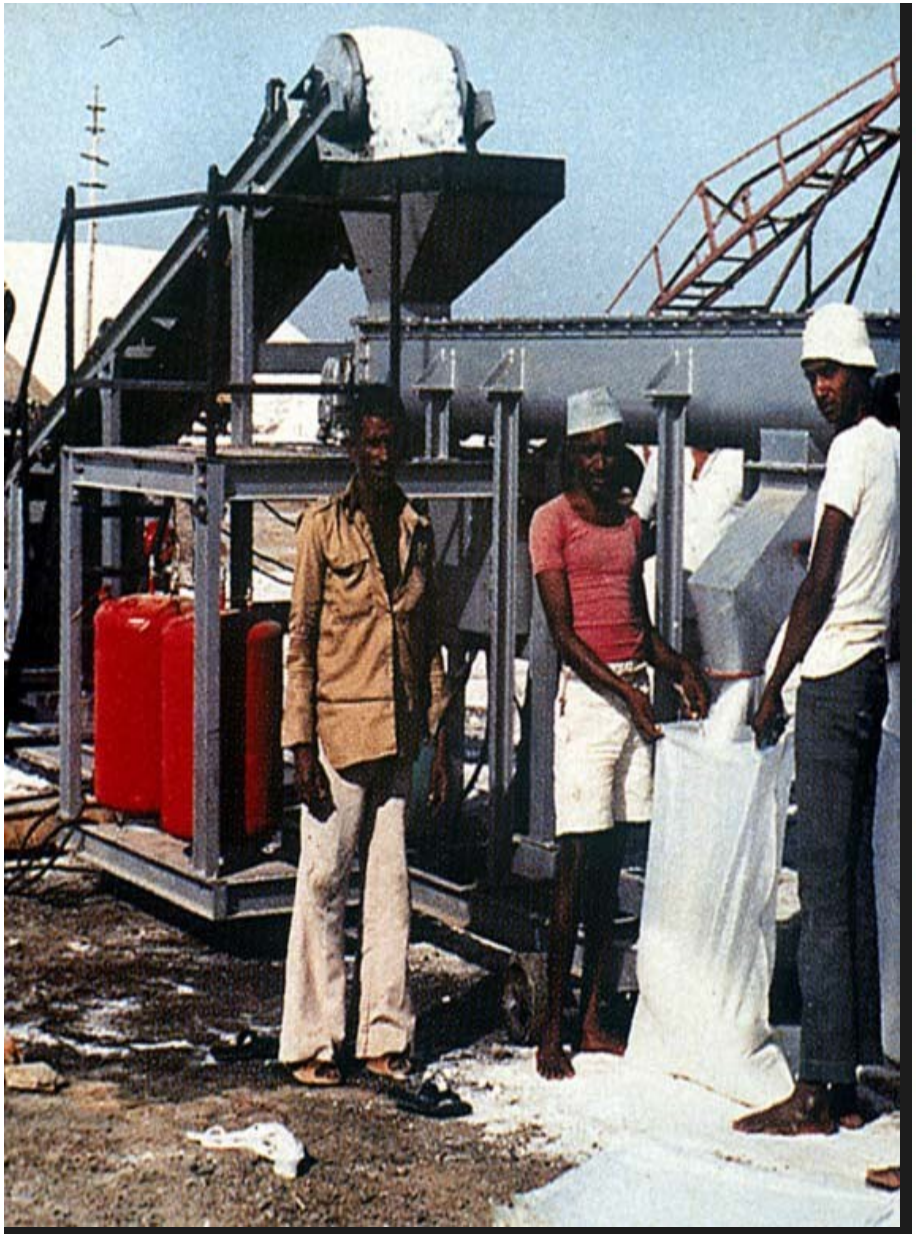
At a level that assures

150 ug/day is safe for all populations

WHO, UNICEF, FAO, ICCIDD, IAEA

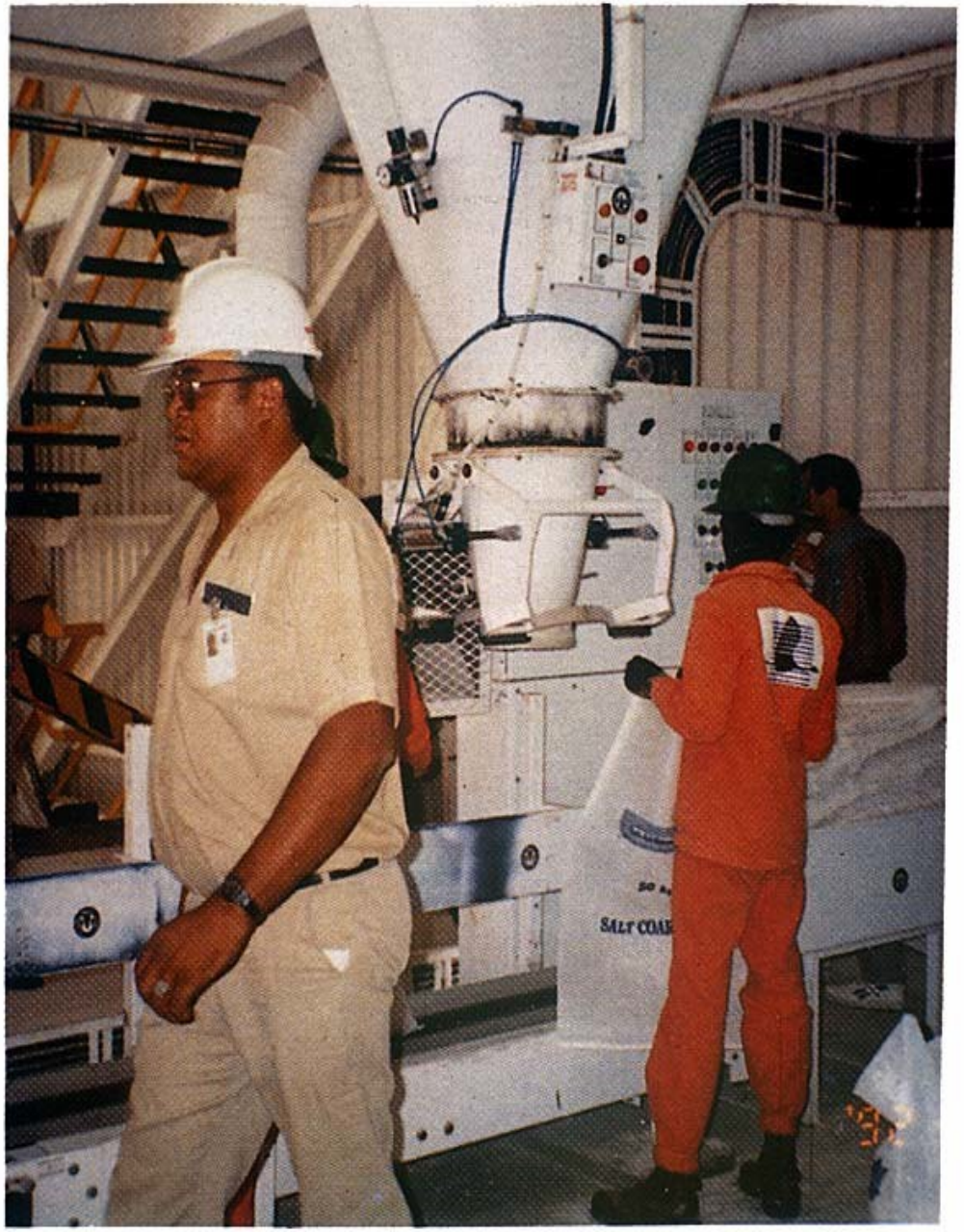


(Chapter 8) - Simple iodization in a village school, using hand spraying of iodate solution. The entire operation is carried out by schoolchildren under the supervision of the head master, and provides iodized salt for their village.

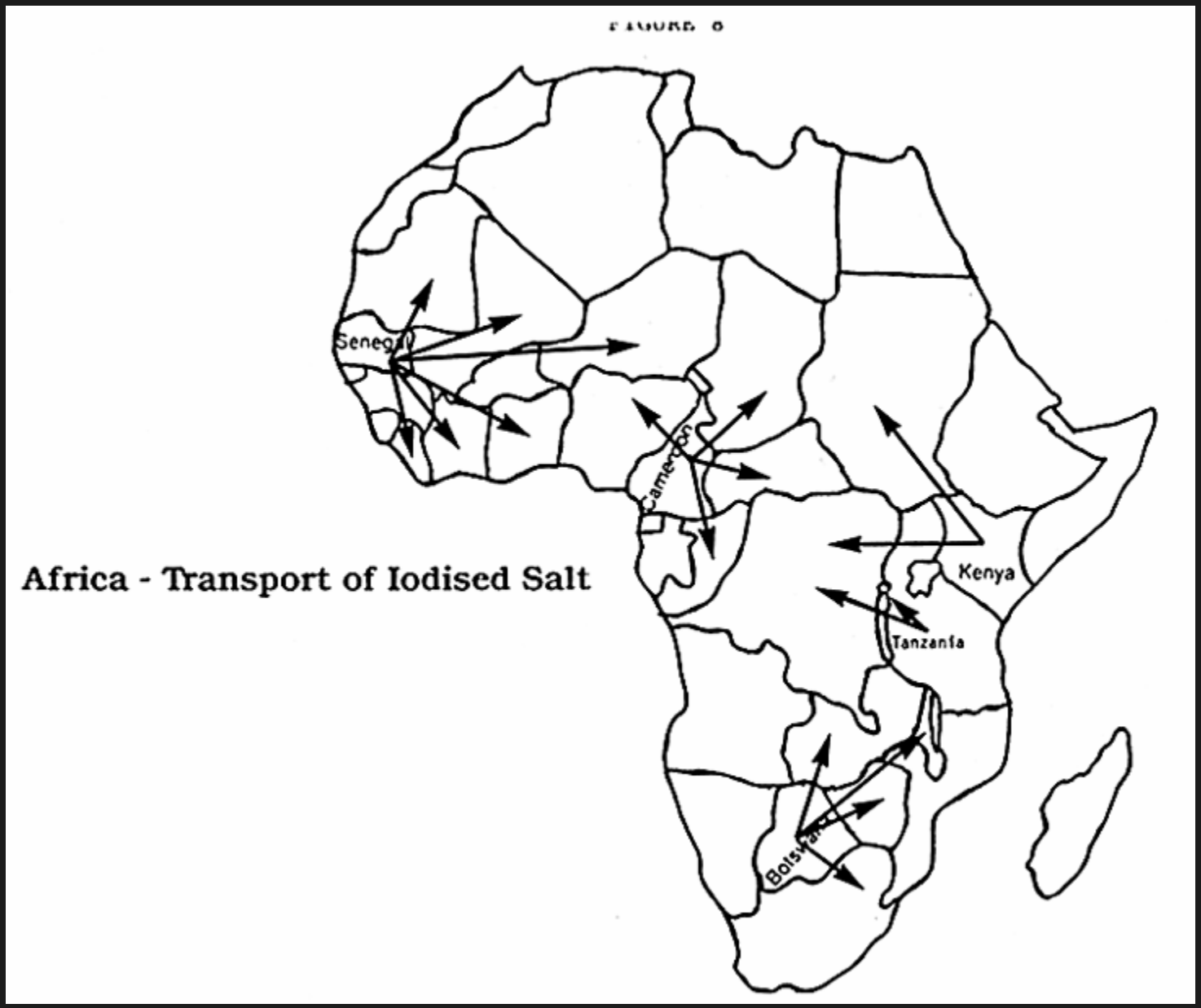


Different levels of sophistication for producing salt

Photos used with permission of the ICCIDD.



(Chapter 11) - A salt packaging machine



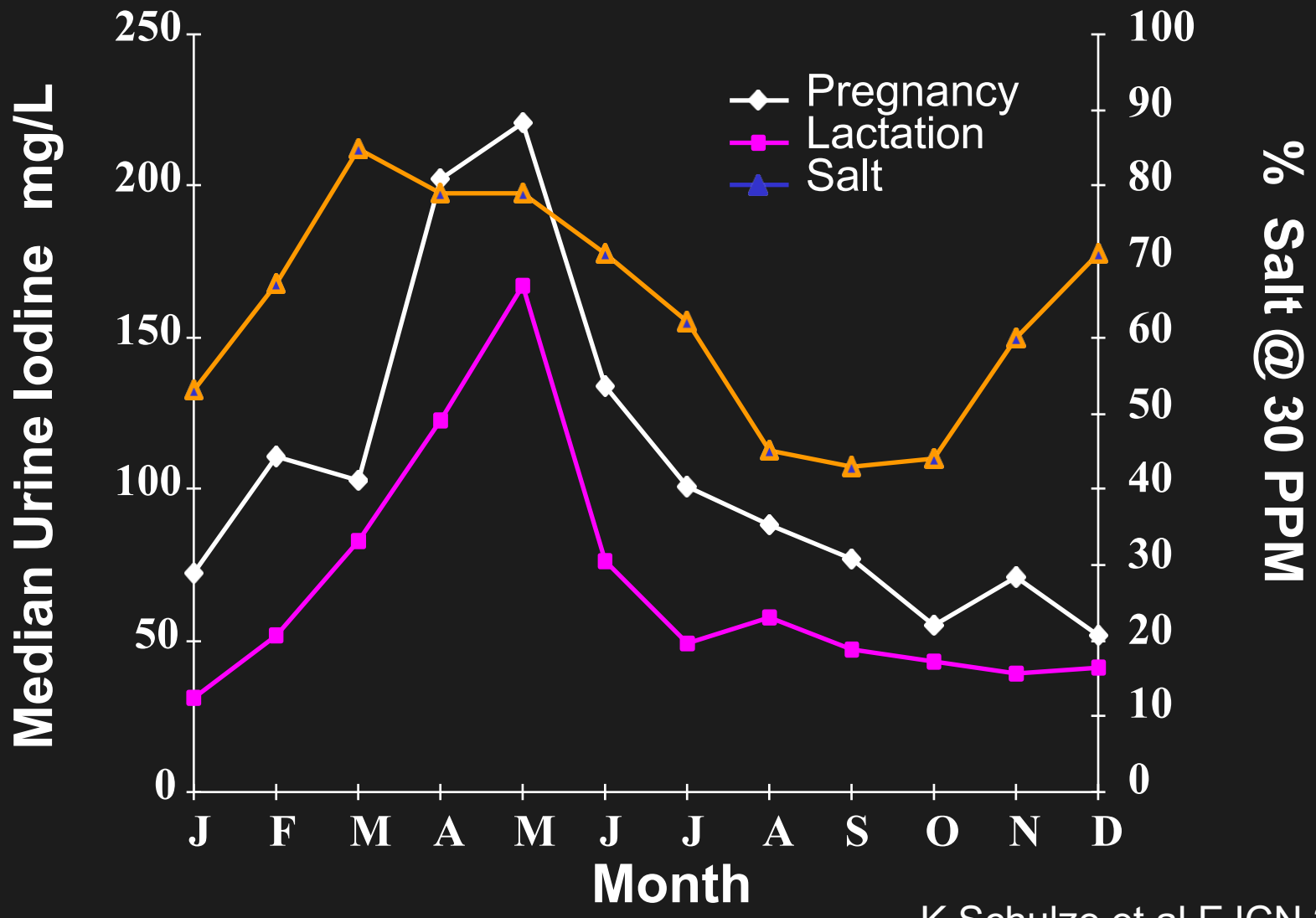
Map used with permission of the ICCIDD.

Prevalence of Goiter Before/After Salt Iodization Programs

	Columbia		Guatemala	
	Year	%	Year	%
Before	1945	82	1952	39
After	1952	37	1962	15
	1965	3	1965	5

Scrimshaw, 1994

Salt Iodine and Urinary Iodine Concentration during Pregnancy & Lactation by Month, Nepal



K Schulze et al EJCN 2003

Iodizing Irrigation water in Xinjiang, China

- Area of severe iodine deficiency
- Potassium iodate added to irrigation water in 3 villages; control areas supplied by different irrigation system
- Maternal urinary iodine increased from <10 to 55 ug/L
- “iodinated water could reduce infant mortality by approximately half”

DeLong et al, Lancet, 1997; Semba, 2001

Effect of Iodination of Water Supply in Sarawak, Malaysia

	Before Iodination	9 Mo After Iodination
Goitre (%)	61	30
Serum T_4 (nmol/L)	80	109
Urinary iodine (g/L)	20	178
Serum TSH (U/L)	12	< 4

Maberly, et al, 1981

Iodized Oil Supplementation

Target Group: Women during pregnancy and 1st year post-partum; Children

When/Where:

- IDD moderate-severe
- Cretinism/neonatal hypothyroidism
- No universal salt iodization for 1-2 yr

Effect of Iodized Oil in Tanzanian School Children

	Before	After 1 Yr
Urine iodine (ug/g Cr.)	2.6	39.0
% children with TSH >5 mU/L	61.0	2.0

Source: TFNC, Tanzania

Iodized salt

- Universally and regularly consumed
- Costs ~$0.04/yr/person
- Simple technology

Iodized oil

- Effective in high risk groups
- Administered every 6 to 12 months

Animals will probably

Receive widely (universally)

distributed iodized salt;

but not iodized oil

Goitrogens

eg, Thiocyanate found in cassava

- Insufficient soaking or cooking
- SCN decreases I uptake by thyroid
- Suppresses circulating T_4
- Problem where I intake is marginal

Photo: Keith West

Photo: Keith West

Successful advocacy

- Every year China loses 60-70 million IQ points due to IDD
- Newton's IQ was 190
- China is losing 368,000 Newtons every year

PRC Ministry of Health Endemic Disease Control Office, 1997

Virtual Elimination of IDD

1985	ICCIDD founded
1990	World Summit for Children
1991	Conference on Ending Hidden Hunger (Montreal)
1992	ICN, Rome
1994	UN Committee on Health Policy Statement on USI

Web resources

- Thyroid Manager
  - www.thyroidmanager.org/
- ICCIDD – International Council for the Control of Iodine Deficiency Disorders
  - www.people.virginia.edu/~jtd/iccidd/
- PAMM – Program Against Micronutrient Malnutrition
  - www.sph.emory.edu/PAMM/iodine.htm