



Iodine and Selenium

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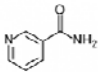
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Micronutrients

- Required by the human body in small amounts
- Body can't produce them, obtained through the diet
- Do not provide energy, yet essential for life!
- 2 types:
 - Vitamins ('vital'=life, 'amine'=nitrogen-containing compound):
 - Fat-soluble; Water-soluble
 - Minerals

Vitamins



| Fat-soluble | Water-soluble |
|---|--|
| <ul style="list-style-type: none"> • Absorption and metabolism requires dietary fat intake • Excess not easily excreted (toxicity possible) • Stored in adipose tissue | <ul style="list-style-type: none"> • Dissolve easily in water • Excess amounts are excreted • Consistent daily intake is required |

www.sciencefriday.com

Minerals

- Inorganic
- 4% of the body's weight
- 15 essential minerals (i.e. can't be synthesized in the body)
- Food sources: Meat, fish, milk, cheese, green leafy vegetables, legumes
- Higher concentration and bioavailability in animal sources
- Retain their chemical identity – not destroyed by heat, air, acid, mixing

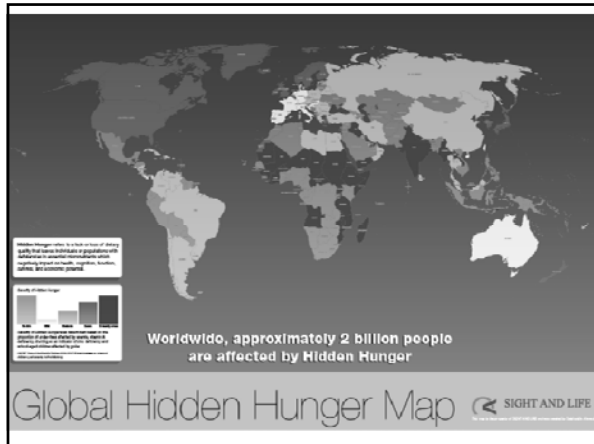
Functions

- Structure of body tissues - bones, teeth, nails, blood, nerves and muscles - Calcium
- Osmotic balance – Sodium (Na), Potassium (K)
- Nerve impulse – Calcium (Ca), Sodium (Na)
- Muscle contraction – Calcium, Sodium
- Oxygen transport - Iron
- Physical and mental development - Iron
- Maintain immune function - Zinc

Hidden Hunger

- "The chronic lack of vitamins and minerals that often has no visible warning signs so that people who suffer from it may not be aware of it"
- Can lead to mental impairment, poor health, productivity, or death
- 1 in 3 people in the world suffer from hidden hunger
- Women and children from the lower income groups in developing countries are most affected

www.micronutrient.org

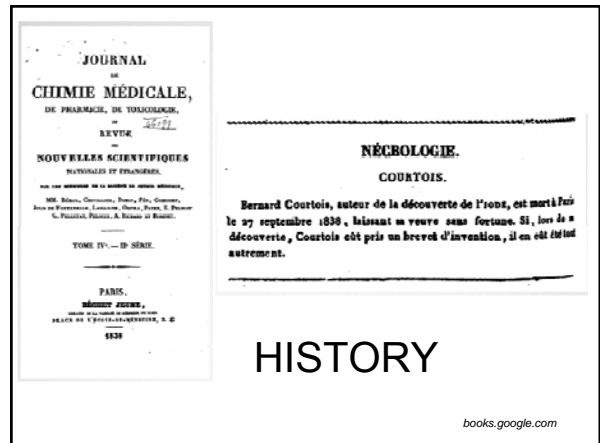


Micronutrient Deficiencies

- Iron
 - 47% of preschool-age children (293 million); 42% of pregnant women (56 million); 25% of the total population (1.6 billion) are anemic
- Vitamin A
 - 1/3 of preschool-age children (190 million) are vitamin A deficient
- Iodine
 - Nearly 2 billion people have insufficient iodine intakes

WHO, 2008. Worldwide prevalence of anemia: 1993-2005. WHO, 2009. Worldwide prevalence of vitamin A deficiency in populations at risk: 1995-2005. Andersson et al. Bulletin of the WHO, 2005

Iodine



I am satisfied. I have seen the principal features of Swiss scenery — Mount Blanc and the goiter — and now for home.

Mark Twain, 1880

A REVIEW OF THE INTERNATIONAL
CONFERENCE ON ENDEMIC GOITRE
HELD AT BERNE, SWITZERLAND*

By R. R. FITZGERALD,
Montreal

To Switzerland belongs the rather dubious honour of leading the list of the countries in which goitre is endemic. In this small country, goitre and cretinism, deaf-mutism and idiocy not only blight the lives of a high percentage of the people but also leave the remaining apparently healthy population under the stigma of borderline physical and mental deficiency.

The Swiss Goitre Commission has been in existence many years. It has seen surgery gain some of its most brilliant triumphs in the cure of goitre. It is now in the midst of a great experiment in prophylaxis with iodized salt.

Berne Conference 1932

Fitzgerald RR. The Canadian Medical Association Journal December 1932

Sources of Iodine

- Concentration in food reflects the soil in which plants are grown or on which animals graze
- Plentiful in the ocean
- Needed in tiny amounts, but this amount is critical

Dietary Iodine

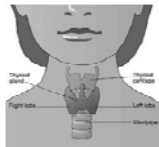
| Life Stage Group | Recommended Iodine Intake (µg/day) |
|------------------|------------------------------------|
| Infants | |
| 0-6 months | 110* |
| 7-12 months | 130* |
| Children | |
| 1-8 years | 90 |
| Males & Females | |
| 9-13 years | 120 |
| 14+ years | 150 |
| Pregnant women | 220 |
| Lactating women | 290 |

Institute of Medicine

Dietary Sources in the US

- Vegetables and grains
 - Iodine content relatively low and highly variable depending on the soil content
- Table salt (not mandatory)
- Bread
 - Iodate dough conditioners
- Dairy products
 - Iodine supplementation of cattle feed
- Use of iodophor sanitizing agents for udder washes, teat dips, and cleaning milking equipment (->nondeliberate)

Functions of Iodine

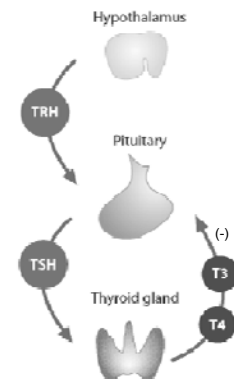


- An essential part of thyroxin
- Thyroxin is a hormone produced in the thyroid gland
- Thyroxin stimulates basal metabolism, oxygen use and heat production
- Essential for function and development of the brain and nervous system

Hypothalamic

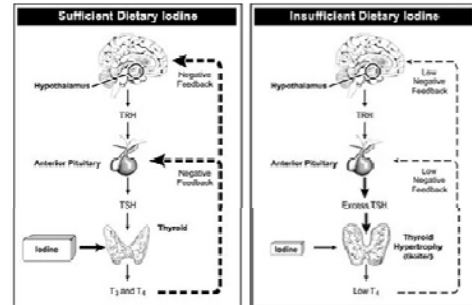
Pituitary

Thyroid Axis



| HYPOTHYROIDISM | HYPERTHYROIDISM |
|--------------------------|--------------------------|
| Cold intolerance | Heat intolerance |
| Bradycardia (slow pulse) | Tachycardia (fast pulse) |
| Constipation | Increased defecation |
| Fatigue | Anxiety, Tremor |
| Weight gain | Weight loss |

Thyroid Function



Iodine Intake and Thyroid Function

Linus Pauling Institute, OSU



Iodine Deficiency

- Median Urinary Iodine (<100 µg/L)
- Iodine excreted primarily through urine
- Indicator of iodine intake, not thyroid function

Table 2.1 Epidemiological criteria for assessing iodine nutrition based on median UI concentrations in school-age children

| Median UI (µg/L) | Iodine intake | Iodine nutrition |
|------------------|--------------------|---|
| < 20 | Insufficient | Severe iodine deficiency |
| 20-49 | Insufficient | Moderate iodine deficiency |
| 50-99 | Insufficient | Mild iodine deficiency |
| 100-199 | Adequate | Optimal iodine nutrition |
| 200-299 | More than adequate | Risk of iodine-induced hyperthyroidism within 5-10 years following introduction of iodized salt in susceptible groups |
| > 300 | Excessive | Risk of adverse health consequences (iodine-induced hyperthyroidism, auto-immune thyroid diseases) |

Source: WHO et al. (17)

Symptoms?

Fetal Effects

- Maternal iodine deficiency
- Decreased placental transfer of thyroxine
- Impaired brain development
 - (cretinism, poor motor/cognitive performance)

Iodine and Evolution

The Geographical Review

VOLUME 88 January 1998 NUMBER 1

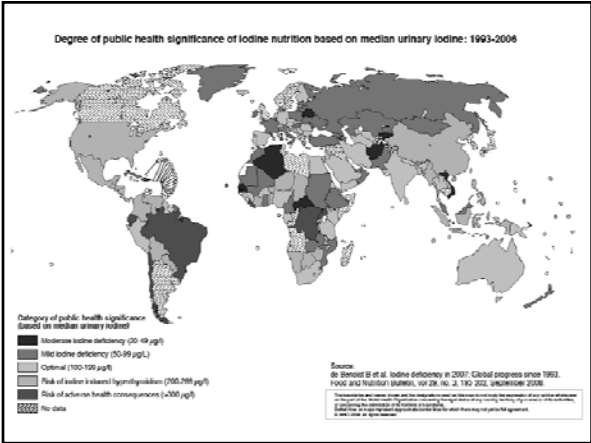
THE IODINE FACTOR IN HEALTH AND EVOLUTION*

BY FRANK E. DOBSON

ABSTRACT. Iodine is essential for modern humans and may have been essential for Neanderthals as well. Today about 20 percent of the world's population is at risk of iodine deficiency (diets with less than 100 µg iodine per day), 200 million people suffer from goiters, 40 million have cretinism (brain damage and mental retardation), and 100 million are afflicted by congenital, the most severe form of cretinism. Neanderthal skeletal finds are identical to those of modern humans who suffer from cretinism. Cre-Magnon Venus figurines also exhibit distinctive traits associated with cretinism among modern humans. This new evidence coupled with recent archaeological evidence suggests that a single genetic alteration, which improved the ability of the thyroid gland to concentrate iodine, underlies the differences between Neanderthals and modern humans. Late Pleistocene human evolution, consequently, may be explained by several alternative interpretations involving iodine pathology and/or biological adaptation. Speculation may have resulted from the geographical isolation of island populations. Keywords: cretinism, Cre-Magnon, Europe, evolution, iodine, medical geography, Neanderthal, Venus figurine.

Iodine Deficiency

| PHYSIOLOGICAL GROUPS | HEALTH CONSEQUENCES OF IODINE DEFICIENCY |
|----------------------|---|
| All ages | Goitre Hypothyroidism Increased susceptibility to nuclear radiation |
| Fetus | Spontaneous abortion Stillbirth Congenital anomalies Perinatal mortality |
| Neonate | Endemic cretinism including mental deficiency with a mixture of mutism, spastic dipleggia, squint, hypothyroidism and short stature Infant mortality |
| Child and adolescent | Impaired mental function Delayed physical development Iodine induced hyperthyroidism (IiH) |
| Adults | Impaired mental function Iodine induced hyperthyroidism (IiH) |



Global Burden

- Nearly 2 billion people worldwide have insufficient iodine intake
- Single greatest preventable cause of mental retardation
- Serious consequences of deficiency:
 - People have impaired mental function, less vigorous, harder to educate & motivate
 - Mild maternal deficiency can ↓ child's IQ by 10-15 points
 - Implications on economic productivity

1. Andersson et al. Bulletin of the WHO, 2005

Vulnerable Groups

- 40 million infants are born without the protection that iodine offers the growing brain, and a full 18 million are mentally impaired as a result
- 50 countries could prevent the loss of intellectual capacity by as much as 10 to 15 percentage points if young children, newborns, and pregnant mothers received enough iodine

Micronutrient Initiative

UNICEF global databases 2010, from Multiple Indicator Cluster Surveys (MICS), DHS and other national surveys

Pregnancy and Lactation

- Iodine Supplementation for Pregnancy and Lactation: Recommendations of the American Thyroid Association
- '...', the American Thyroid Association recommends that women receive 150 µg iodine supplements daily during pregnancy and lactation and that all prenatal vitamin/mineral preparations contain 150 µg of iodine'

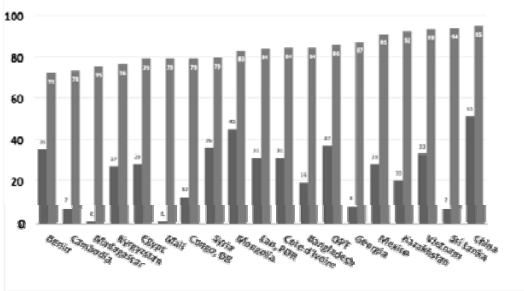
Thyroid 2006, 16(10): 949-951

Interventions

- Fortification of salt:
 - Universal Salt Iodization
- Iodized oil capsules for pregnant women in areas with a high prevalence of iodine deficiency & access to iodized salt is limited

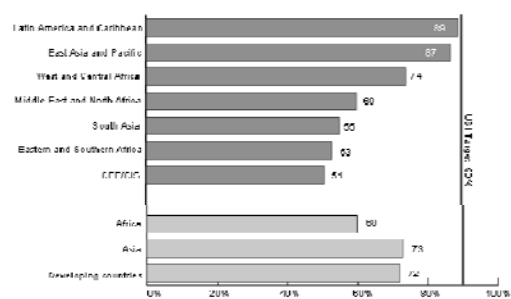
Why Fortification?

- Salt is consumed by everyone and generally stable throughout the year
- Safe and inexpensive
- Accessible fortification technology
- Limited number of producers
- Sensory/cooking properties
- Ease of program implementation



Change (1995-2008)

Source: UNICEF Global Database, Nov 2009



Household Iodized Salt Consumption

UNICEF global databases 2010, from Multiple Indicator Cluster Surveys (MICS), DHS and other national surveys

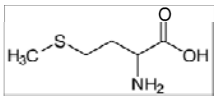
SELENIUM

History

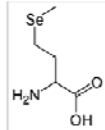
- Discovered in 1817 by Jons Jacob Berzelius
- Schwarz and Foltz in 1957
 - Dietary Se prevents liver necrosis in rats
- 1960s-70s
 - Identified as a critical component of a number of enzymes

Sources of Selenium

- Plants take up selenium from the soil & incorporate into selenomethionine (Se is incorporated in place of S during methionine biosynthesis, dependent on Se/S ratio in soil)

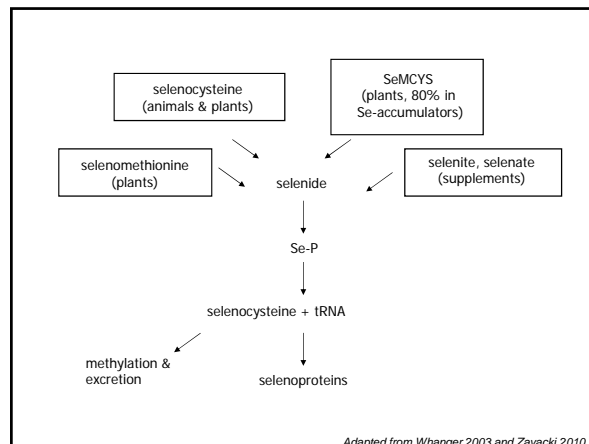


Methionine $C_5H_{11}NO_2S$



Selenomethionine $C_5H_{11}NO_2Se$

- Selenomethionine is incorporated non-specifically in plant proteins in place of methionine



Adapted from Whanger 2003 and Zavacki 2010

Table 2: Recommended Dietary Allowances (RDA) for Selenium for Children and Adults [12]

| Age (years) | Males and Females ($\mu g/day$) | Pregnancy ($\mu g/day$) | Lactation ($\mu g/day$) |
|-------------|-----------------------------------|---------------------------|---------------------------|
| 1-3 y | 20 | N/A | N/A |
| 4-6 y | 30 | N/A | N/A |
| 9-13 y | 40 | N/A | N/A |
| 14-18 y | 55 | 60 | 70 |
| 19 y + | 55 | 60 | 70 |

Table 3: Adequate Intake for Selenium for Infants [12]

| Age (months) | Males and Females ($\mu g/day$) |
|--------------|-----------------------------------|
| 0-6 months | 15 |
| 7-12 months | 20 |

<http://ods.od.nih.gov/pdf/factsheets/selenium.pdf>

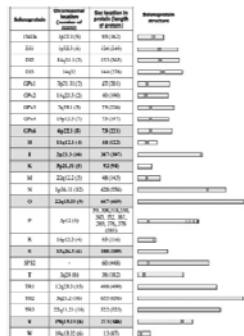
Table 1: Selected Food Sources of Selenium [11]

| Food | Micrograms (μg) | Percent DV* |
|--|------------------------|-------------|
| Brazil nuts, dried, unblanched, 1 ounce | 544 | 700 |
| Tuna, light, canned in oil, drained, 3 ounces | 63 | 95 |
| Salmon, wild, 3oz chunks | 25 | 50 |
| Spaghetti w/ meat sauce, frozen, 1 serving | 34 | 50 |
| Cod, cooked, 3 ounces | 32 | 45 |
| Turkey, light meat, roasted, 3oz ounces | 32 | 45 |
| Beef ribeye roast, lean only, roasted, 3 ounces | 23 | 35 |
| Chicken breast, meat only, roasted, 3oz ounces | 20 | 30 |
| Noodles, enriched, boiled, 1/2 cup | 17 | 25 |
| Macaroni, elbow, enriched, boiled, 1/2 cup | 15 | 20 |
| Egg, whole, 1 medium | 14 | 20 |
| Cottage cheese, low fat 2%, 1/2 cup | 12 | 15 |
| Cornmeal, instant, fortified, cooked, 1 cup | 12 | 15 |
| Rice, white, enriched, long grain, cooked, 1/2 cup | 12 | 15 |
| Rice, brown, long-grained, cooked, 1/2 cup | 10 | 15 |
| Bread, whole wheat, commercially prepared, 1 slice | 10 | 15 |
| Wheat, whole, 1 ounce | 8 | 8 |
| Bread, white, commercially prepared, 1 slice | 8 | 6 |

<http://ods.od.nih.gov/pdf/factsheets/selenium.pdf>

Functions of Se

- Selenoproteins contain Selenocysteine (Sec) and mediate Se function
- Knocking out the Sec gene is lethal to the fetus
- 25 Selenoproteins have been identified



Kryukov et al., Science 300, 1439 (2003)

Glutathione Peroxidases

- GPx 1-4, 6
- Destroys Hydrogen Peroxide
 - H_2O_2 generates free radicals, which can damage DNA, lipids, and proteins
- GPx 4 is a structural protein necessary for the integrity of the sperm midpiece
 - Se deficiency can lead to male infertility

Iodothyronine Deiodinases

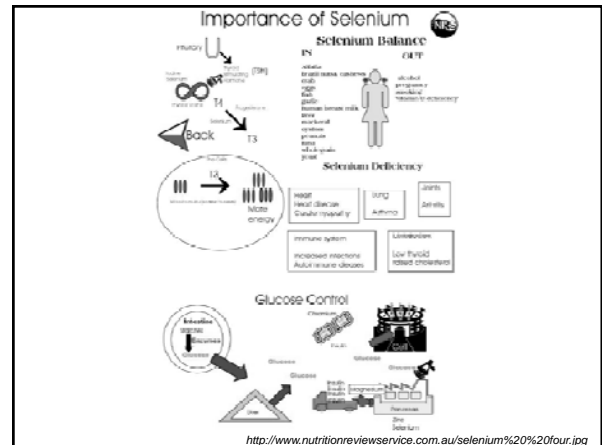
- Family of 3 selenoenzymes
- Needed for the peripheral conversion of thyroid hormone to its active form

Thioredoxin Reductases

- Provide reducing equivalents for ribonucleotide reductase
 - Needed for DNA synthesis
- Over-expressed in many cancers

Selenoprotein P

- Probably protects the cardiovascular system against oxidant damage
- Very efficient at binding heavy metals



Selenium Status

- Hair
- Toenails
- Plasma levels (99% US adults have Se levels < 95 ng/ml)
- Glutathione peroxidase activity



Selenium in the US

Regions of SE Deficiency

- China
- New Zealand
- Central Africa
- Finland
- *Western Europe*
- *Northwestern US*

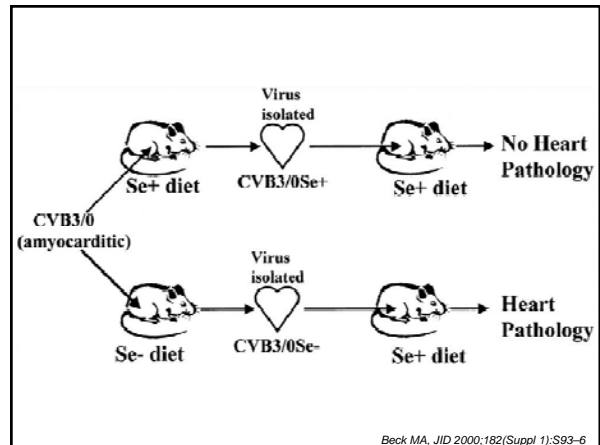
Se Deficiency



- Kashin-Beck Disease
 - Degenerative Osteoarticular disorder - still occurs in parts of China, Korea, and Siberia
 - Se supplementation does not eliminate this disease - likely due to concomitant iodine deficiency
- Keshan Disease
 - Endemic cardiomyopathy - largely been eliminated
- Total Parenteral Nutrition
 - General muscle wasting, flaky skin, problems walking

Se Deficiency

- Epidemiological studies show that Se may be linked to:
 - Cancer
 - Bronchopulmonary disease and Sudden Infant Death Syndrome in Premature Infants
 - Impaired immunity - reduced T-cell counts and impaired lymphocyte activity
 - HIV disease progression
- Thyroid Disease
 - Se deficiency can lead to Goiter
 - Combined Se and I deficiency - Myxedematous Cretinism



Se and Coxsackie Virus

- Coxsackie virus in selenium deficient mice mutates from an avirulent to virulent strain because of a 6 bp change in its genome.
- Se deficiency - Low GPx - More oxidative damage from free radicals
- Similar phenomena occurs with influenza in Se-deficient mice

Se and Cancer

- Observational Studies
 - Death from Lung, Colorectal, and Prostate Cancers lower among people with higher blood levels or intake of Se
- SUVIMAX in France
 - Supplement (vitamins A and C, beta-carotene, zinc, and Se) lowered risk of Prostate CA by half in those who had normal PSA at baseline
- SELECT (Se and Vitamin E Cancer Prevention Trial) in the US
 - Se and/or vitamin E did not prevent prostate cancer

Se and HIV

- Associated with increased risk of disease progression and death
- Trial in Tanzania among HIV-infected women

| Outcome | Mean Placebo | Mean Change Selenium Group | P |
|------------------------------------|--------------|----------------------------|------|
| CD4 cell count (/mm ³) | 486±278 | 1 (22, 19) | 0.72 |
| CD3 cell count (/mm ³) | 1635±630 | 10 (38, 58) | 0.86 |
| CD8 cell count (/mm ³) | 1048±439 | 12 (21, 44) | 0.91 |
| Viral load (log) | 4.12±1.03 | 0.02 (0.11, 0.06) | 0.71 |

Kupka, AJCN 2006;87:1802

Se Toxicity

- Dr. Gregory House: You idiot.
- Dr. Samira Terzi: Who are you calling an idiot?
- Dr. Gregory House: Whoever knew that John was stationed in Brazil, not Bolivia.
- Dr. Samira Terzi: Brazil?
- Dr. Gregory House: [House turns and faces Agent Smith] Well, then, I guess, I'm talking to you, idiot.
- CIA Agent Smith: It's the same region. It's the same parasite, same diseases.
- Dr. Gregory House: But not the same language. In Bolivia, chestnuts are chestnuts. Brazil, on the other hand, has Castanhas-do-Pará, literally, "Chestnuts from Pará." Because it would be stupid for people from Brazil to call them Brazil Nuts.
- CIA Agent Smith: So he ate Brazil Nuts. Big Deal.
- Dr. Gregory House: No, he ate a lot of Brazil Nuts, which is a big deal, because they contain selenium. Which, in high doses, causes fatigue, vomiting, skin irritation, discharge from the fingernail beds, and hair loss. Any of this sound familiar?

<http://www.imdb.com/title/tt1123416/quotes>

Selenosis

- Se toxicity
- GI upsets, hair loss, white blotchy nails, garlic breath odor, fatigue, irritability, and mild nerve damage

<http://ods.od.nih.gov/pdf/factsheets/selenium.pdf>

Acknowledgments

- Julia L. Finkelstein
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