
The Bioavailability of Iodine Applied to the Skin

by Guy E. Abraham, MD

I have often been asked a couple questions:

- 1) Is the application of iodine to the skin an acceptable way to supplement iodine?
- 2) Are there any data confirming the validity of the iodine skin patch test to assess body sufficiency for iodine?

The iodine skin patch test consists of applying iodine solution to a small area of the arm, leg, or abdomen. The faster the yellow color of iodine disappears from the skin, the more iodine deficient the person tested; and vice versa, if the yellow color lingers, the more sufficient in iodine the person tested.

Over 100 years ago, the application of iodine to the skin was used extensively for iodine supplementation. In 1932, Nyiri and Jannitti¹ from the Rutgers University College of Pharmacy wrote: "Iodine is being used extensively as a prophylactic and therapeutic agent by application to the outer integument, (for the reader's information, that is the skin) and has maintained its place in medicine for many decades. Its use by external application is merely on an empirical basis; very little proof of its efficacy has been obtained by experimental work. The main question as to whether or not iodine passes through the unbroken human and animal skin has not been conclusively answered."

In order to assess the bioavailability of iodine applied to the skin, these investigators used 44 rabbits and six dogs, but no human subject.

"Although the question of iodine penetration has been studied extensively especially during the second half of the last century, no satisfactory conclusion has been reached because the techniques of the various experiments were not fully reliable. Considering the increasing biological significance of the outer integument (Klose (30), Unna (31), Vollmer (32), Urbach (33)) and the widespread medicinal use of iodine on the skin, we made a series of experiments about the fate of iodine applied to the skin; thereby studying the possibility of penetration of free iodine, its fate in the body, its elimination, and its conditions of evaporation for the surface.

We carried out the experiments on six dogs and forty-four rabbits."

To summarize the results of their experiments:

- 1) Free iodine penetrates through the unbroken skin.
- 2) Approximately 88% of the iodine evaporates from the skin within three days.
- 3) Colloidal iodine evaporates somewhat more quickly than tincture of iodine; Lugol's solution is more stable than either of them.
- 4) The influence of ambient temperature on the evaporation of iodine is significant. Within the first minute, the losses of iodine by evaporation are 10-15% at 9° C; 18-25% at 24° C; and 35% at 37° C.
- 5) The remaining iodine on the skin following evaporation of 88% of the total iodine, approximately 12%, penetrates through the skin. The bioavailability of the remaining 12% of the skin iodine is very gradual.
- 6) The fate of iodine in all above experiments is the same whether iodine is applied to the skin in the form of an alcoholic solution or in colloidal suspension. (For the reader's information, the alcoholic solution is tincture of iodine and the colloidal suspension is a saturated aqueous solution of diatomic iodine, I₂).

The authors concluded:¹ "Our quantitative determinations prove that iodine which penetrates through the skin is removed only slowly from within this area into the body, thus forming an iodine depot in the skin for several days. In this prolonged retention of iodine within the skin, we see a favorable condition for a possible local prophylactic and therapeutic action."

The above conclusions apply to rabbits and dogs, but not to human subjects. The best study of the bioavailability of iodine applied to the skin in normal human subjects was reported by Miller, *et al*, in 1989.² The purpose of Miller's study was to assess the effectiveness of skin application of iodine in blocking radioiodide uptake by the thyroid gland. The subjects used in this study were 24 adult male volunteers aged from 21 to 51 years. These subjects were divided into four groups of six subjects each. One group served as control and did not receive stable iodine. The other subjects in the remaining three groups received respectively 130 mg KI orally equivalent to approximately 100 mg iodide; 80 mg iodine (tincture) on the skin; and 160 mg iodine on the

(Continued on next page)

skin. All 24 subjects ingested ^{131}I labeled NaI and radioiodide thyroid uptake was measured at 2 hours, 6 hours, and 24 hours post-ingestion of radioactive iodide. Serum inorganic iodide levels were measured at time zero, 2 hours, 6 hours and 24 hours post intervention. Twenty-four-hour radioiodide uptake by the thyroid gland as percent of dose administered was used to assess the effectiveness of iodine in blocking radioiodide uptake by the thyroid. The 24-hour percent radioiodide uptake by the thyroid gland were:

- Control: $10.9 \pm 2.9\%$ (SD)
- Oral KI: $0.34 \pm 0.26\%$
- Skin 80 mg iodine: $7.0 \pm 5.5\%$
- Skin 160 mg iodine: $2.0 \pm 2.5\%$

Prior to administration of stable iodine, the mean serum iodide in the three intervention groups were 0.024 mg/L, 0.033 mg/L, and 0.02 mg/L. The mean of the three mean values is 0.026 mg/L.

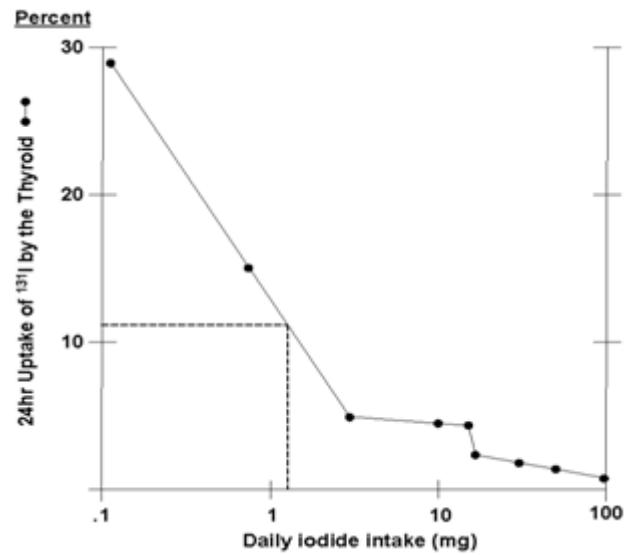
Under steady state conditions, the computed daily intake of iodine based on serum iodide is equal to the product of serum iodide times 43.5 L/day, which is the renal clearance of iodide.³ The estimated average daily intake of iodine by this group of men is $0.026 \text{ mg/L} \times 43.5 \text{ L/day} = 1.13 \text{ mg/day}$. This daily intake may be due to the iodization of bread in the 1960s and 1970s and in some states in the 1980s. The estimated daily intake of iodine during that time in the US was 1 mg.⁴ This computed daily intake in Miller's subjects is in agreement with the mean percent radioiodide uptake by the thyroid gland in this group of subjects with a mean of 10.9. By interpolation on Figure 2 of Reference 5, 10.9% uptake corresponds to an average intake of approximately 1.5 mg iodine (See Figure 1).

The two questions mentioned previously can now be answered.

To answer the first question, we will use the data in the six subjects who were exposed to 160 mg iodine via cutaneous application, because the mean serum iodide levels were relatively constant over the 24-hour period: 0.27 mg/L at 2 hours; 0.2 mg/L at 6 hours; and 0.24 mg/L at 24 hours post-intervention. The mean value of the three means is 0.24 mg/L iodide. The average amount of iodine bioavailable in these six subjects would be the product of the serum iodide levels by the renal clearance of iodide — $0.24 \text{ mg iodide/L} \times 43.5 \text{ L/day} = 10.4 \text{ mg}$. The percent of bioavailable iodine from 160 mg applied to the skin is 6.5% ($10.4 \times 100/160$). If the data reported by Nyiri and Jannitti¹ in dogs can be extrapolated to humans, (that is 12% of the

Figure 1

Percent 24-hour Uptake of Radioiodide following Intake of Increasing Amount of Iodide[†]



The dotted line represents the percent uptake by Miller's subjects and the estimated average daily intake in this group of subjects.

[†] Modified from Reference 5 (Abraham, et al. *The Original Internist*, 2002; 9(4):30-41).

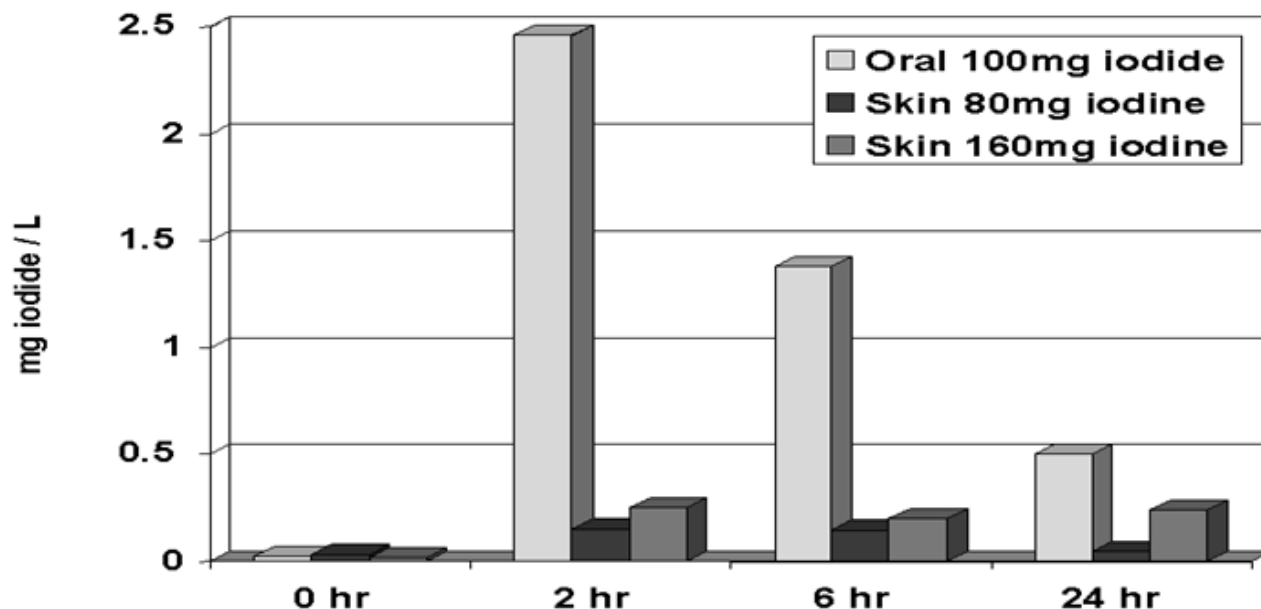
applied iodine was available for utilization by the body), then some 50% of the remaining skin depot of iodine was available during the first 24 hours following skin exposure to iodine. One can conclude that skin application of iodine is an effective, if not efficient and practical, way for supplementation of iodine with an expected bioavailability of 6-12% of the total iodine applied to the skin. The serum iodide levels were 10 times higher at 2 hours post-intervention with oral ingestion of 100 mg iodide than with 160 mg iodine applied to the skin (Figure 2).

To answer the second question, the skin iodine patch test is not a reliable method to assess whole body sufficiency for iodine. Many factors play a role in the disappearance of the yellow color of iodine from the surface of the skin. For example, if iodine is reduced to iodide by the skin, the yellow color of iodine will disappear because iodide is white. In order to regenerate iodine on the skin, one needs to apply an oxidant such as hydrogen peroxide, complicating the test further. The evaporation of iodine from the skin increases with increased ambient temperatures and decreased atmospheric pressure. For example, the yellow color of iodine will disappear much

(Continued on next page)

Figure 2

Serum Iodide Levels following Oral Ingestion of 100 mg Iodide and Skin Application of 80 and 160 mg Iodine^{††}



Each bar represents the mean of six subjects.

†† Compiled from Reference 2 (Miller, et al. *Health Physics*, 1989; 56:911-914).

faster in Denver, Colorado at 5,000 feet above sea level than in Los Angeles, California at sea level, irrespective of the amount of bioavailable iodine. The iodine/iodide loading test⁴ is much more accurate, and it is now available from three laboratories participating in the proficiency testing of Optimox Corporation: FFP Laboratories in Hendersonville, North Carolina; Hakala Research in Lakewood, Colorado; and Labrix Clinical Services Inc. in Oregon City, Oregon.

About the Author

Guy E. Abraham, MD, is a former Professor of Obstetrics, Gynecology, and Endocrinology at the UCLA School of Medicine. Some 35 years ago, he pioneered the development of assays to measure minute quantities of steroid hormones in biological fluids. He has been honored as follows: General Diagnostic Award from the Canadian Association of Clinical Chemists, 1974; the Medaille d'Honneur from the University of Liege, Belgium, 1976; the Senior Investigator Award of Pharmacia, Sweden, 1980. The applications of Dr. Abraham's techniques to a variety of female disorders have brought a notable improvement to the understanding and management of these disorders.

Twenty-five years ago, Dr. Abraham developed nutritional programs for women with premenstrual tension syndrome and post-menopausal osteoporosis. They are now the most commonly used dietary programs by American obstetricians and gynecologists. Dr. Abraham's current research interests include the development of assays for the measurement of iodide and the other halides in biological fluids and their applications to the implementation of orthoiodosupplementation in medical practice.

REFERENCES

- 1) Nyiri W and Jannitti M. "About the fate of free iodine upon application to the unbroken animal skin. An experimental study." *J Pharmacol Exp Ther*, 1932; 45:85-107.
- 2) Miller KL, Coen PE, et al. "Effectiveness of skin absorption of tincture of I in blocking radioiodine from the human thyroid gland." *Health Physics*, 1989; 56:911-914.
- 3) Abraham GE. "The concept of orthoiodosupplementation and its clinical implications." *The Original Internist*, 2004; 11(2):29-38.
- 4) Abraham GE. "The safe and effective implementation of orthoiodosupplementation in medical practice." *The Original Internist*, 2004; 11(1):17-36.
- 5) Abraham GE, Flechas JD, and Hakala JC. "Orthoiodosupplementation: Iodine sufficiency of the whole human body." *The Original Internist*, 2002; 9(4):30-41. ♦