

# Benefits and Risks of Thyroid Scintigraphy in Congenital Primary Hypothyroidism

Ivan A. Jasko, Leo V. dos Remedios, Edgar J. Schoen

Division of Nuclear Medicine and Department of Pediatrics,  
CA Kaiser-Permanente Medical Center, Oakland

A portion of the data was published in abstract form in *Clinical Research* 32:95A (1984).

*The diagnosis on the basis of low serum thyroxine level with high thyrotropin level of congenital primary hypothyroidism in newborn screening programs fails to distinguish between transient hypothyroidism and ectopic thyroid, athyrosis, dysmorphogenesis, or transient hyperthyrotropinemia. The correct use of neonatal thyroid scintigraphy aids in making a specific anatomic diagnosis. We scanned 18 of 24 infants who had congenital hypothyroidism detected from screening 116,300 newborn infants, using Tc-99m in the first 8, then I-123 in 10. Eight infants were found to be athyrotic and 2 had ectopic glands; in 8, the thyroid gland appeared normal. Probably due to initially poor technique, 1 "athyrotic" infant was later found to be normal. We suggest that before initiating long-term thyroid medication, the specific anatomic and functional diagnosis be confirmed by this low-dose thyroid scintigraphic technique which has been optimized for newborn infants.*

About 7-9 million newborn infants are annually screened worldwide for primary congenital hypothyroidism (1). In California, about 400,000 have the serum thyroxine ( $T_4$ ) level measured from blood spots on filter paper, and the lowest 5% to 10% have the serum thyrotropin (TSH) level similarly measured. Some physicians consider the initial combination of low  $T_4$  and high TSH diagnostic of hypothyroidism and commence thyroid hormone treatment without distinguishing transient hypothyroidism from inborn errors of metabolism (dysmorphogenesis) or from a dysgenetic condition (thyroid ectopia or complete athyrosis) (2). In order not to delay the initiation of thyroid therapy in severe forms of congenital hypothyroidism, infants with transient hypothyroidism must be differentiated as early as possible (3) in order to avoid thyroid hormone therapy in this group. A helpful, generally available procedure for this diagnostic purpose is thyroid scintigraphy. We have developed an effective, practical technique that consistently yields adequate thyroid images with minimal absorbed radiation dose to the infant (4-10).

## Materials and Methods

### Determination of Minimum Imaging Dose:

**Iodine-123:** We placed solutions of I-123 in 3 ml vials within a standard adult thyroid neck phantom. Scintillation imaging for 10 minutes with the thyroid pinhole collimator touching the phantom surface showed only scattered radiation with 0.01  $\mu\text{Ci}$ . An unclear image was seen at a 0.05  $\mu\text{Ci}$  dose, but the shape of the 0.1  $\mu\text{Ci}$  vial was discretely visible. The fraction of I-123 remaining after 24 hours is 0.284; consequently, a tracer dose of 5  $\mu\text{Ci}$  I-123 administered to an infant with a 24 hr radioiodine uptake of only 7% should produce a clearly visible image of the thyroid containing 0.1  $\mu\text{Ci}$ . However, commercial I-123 usually has the undesirable contaminant I-124 (half-life, 4.5 days), which may represent as much as 20% of the total radioactivity after 24 hrs. Such I-123 must be used fresh or else Tc-99m substituted as the thyroid imaging agent.

**Technetium-99m:** We performed similar phantom studies using Tc-99m and found that the 0.1  $\mu\text{Ci}$  vial in the absence of background activity can be faintly imaged. In normal adults, the 30 minute uptake of Tc-99m is only about  $1.73 \pm 0.85\%$ . In hyperthyroid patients, this value rises to  $9.3 \pm 6.2\%$  (11). In a neonate with 7% radioiodine 24 hour uptake, we estimate that the 30 minute Tc-99m uptake may be only about 0.25% and that neck background radioactivity is high. Therefore, although the 140 keV gamma rays of Tc-99m image more efficiently than the 159 keV gamma rays of I-123, we estimated that 5 to 10 times more Tc-99m thyroidal activity than I-123 activity may be necessary to achieve a recognizable thyroid image. Consequently, about 200  $\mu\text{Ci}$  of Tc-99m as pertechnetate was assumed to be the minimum that is equivalent to the 5  $\mu\text{Ci}$  of I-123 needed for adequate thyroid imaging. Our recent experience has borne this dose out.

### Imaging Techniques:

We found that the scintillation camera with the low-energy converging collimator is best for covering the field from the base of the tongue to the upper chest, so that even with 7% 24 hour radioiodine uptake the thyroid should be localized in a 10 minute image using either I-123 or Tc-99m. The pinhole collimator touching the skin of the neck gives better resolution,

For reprints contact: L.V. dos Remedios, Nuclear Medicine, Kaiser-Permanente Medical Center, 280 W. MacArthur Blvd., Oakland, CA 94611.

**TABLE 1. Absorbed Radiation Dosimetry\* in Normal and Hypothyroid Newborn Infants (rem)**

Technique	Normal (RAIU 50–70%)		Hypothyroid (RAIU ≤ 7%)	
	Thyroid	Whole Body	Thyroid	Whole Body
5 $\mu$ Ci I-123	1.5	0.003	0.15	0.005
200 $\mu$ Ci Tc-99m	0.5	0.05	0.05	0.05
Chest x-ray (14)	0.007	0.009	0.007	0.009

RAIU = 24 hr radioactive iodine uptake

\*Absorbed doses extrapolated from Medical Internal Radiation Dose (MIRD) adult data to infants (11–13)

and a simultaneous 24 hour radioiodine uptake may be obtained. However, a lingual thyroid gland will be missed, motion artifact may be a problem, and greater intrathyroidal detail is not required for diagnosis. Rectilinear dot scanning should not be used, as it is too slow and inefficient because of the low photon flux from the minimal doses necessary in neonates.

#### Absorbed radiation dosimetry:

Because of its smaller size (1.3–3g) and normally elevated radioiodine uptake (50–70%) (4–10), the neonatal thyroid receives a disproportionately higher radiation dose (12,13) from any given amount than does the adult thyroid (Table 1).

#### Subjects:

Between September 1, 1978 and April 30, 1983, 116,300 newborn infants born at hospitals of the Northern California Kaiser-Permanente Medical Care Program were screened by us for congenital hypothyroidism. Full-term infants with  $T_4$  levels more than two standard deviations below the mean on filter paper blood spot tests also had TSH tested from these spots. In infants with TSH greater than 25  $\mu$ IU/ml, testing was repeated. In following up presumptive positive tests for  $T_4$  and TSH, fresh serum specimens were used. In the early stages of screening, few infants with congenital hypothyroidism received scintigraphy and the dosages and techniques used at the different Kaiser hospitals varied due to unfamiliarity with neonatal thyroid imaging. On the basis of this experience, we have optimized neonatal thyroid scintigraphy. Preferably when available fresh, 5  $\mu$ Ci of I-123 is given orally. The next day, the neck area is imaged using the scintillation camera with the low-energy converging collimator. The infants are swaddled without sedation and the head held still during the mandatory 10 minute imaging time. If necessary, the pinhole collimator may be used to obtain a 24 hr radioiodine uptake using the I-123 standard in a phantom. Athyrotic, lingual, or normal thyroids are readily distinguished. Our second choice is 200  $\mu$ Ci of Tc-99m injected intravenously with the converging collimator used after 20 minutes in a similar manner. Clinical and laboratory follow-up was monitored regionally by a single medical director (E.J.S.) and a full-time nurse specialist.

#### Results

Of the 116,300 infants screened for  $T_4$ , 8,031 (6.9%) were tested for TSH. Presumptive positive tests (low  $T_4$ , initial TSH

more than 25  $\mu$ IU/ml) were found in 183 neonates, 24 of whom (1:4,800) were diagnosed as having primary congenital hypothyroidism by demonstrating persistently high TSH levels at repeat serum testing. Eighteen of these 24 patients had thyroid scintigraphy, nine had normal thyroid scintigrams, seven showed absence of the thyroid gland, and two had ectopic glands. One "athyrotic" infant was shown later to have normal thyroid function at age two years. The initial diagnosis was erroneous due to faulty technique (poor positioning, too large a field of image, and inadequate total counts). There was no statistically significant correlation between the initial  $T_4$  and TSH values and scintigraphic results.

#### Discussion and Conclusion

A recent Scandinavian study (15) showed that most parents have strong adverse emotional reactions to the diagnosis of congenital hypothyroidism. To avoid misdiagnosis in normal newborn infants, we have found thyroid scintigraphy an accurate technique for obviating a false-positive diagnosis. The levels of the initial serum  $T_4$  and TSH are not reliably predictive of permanent hypothyroidism. Scintigraphy need not delay diagnosis and treatment, as our mean infant age at scintigraphy was 12 days and therapy was begun at a mean of 14 days.

The whole-body absorbed radiation dose for scintigraphy is comparable to that of chest x-ray films (14). The dose to the thyroid is somewhat higher but acceptable.

We believe that the 90% incidence of dysgenesis as a cause of primary congenital hypoplasia reported at the Second International Congress of Neonatal Thyroid Screening (1) is too high and that the true incidence is closer to 50% (15). An accurate early diagnosis at the screening center is important, as most of these infants are managed by primary physicians whose expertise in the diseases of the neonatal thyroid gland may be limited.

#### References

1. Fisher DA: Second international conference on neonatal thyroid screening: progress report. *J Pediatr* 1983;102:653–54.
2. Fisher DA, Klein AH: Thyroid development and disorders of thyroid function in the newborn. *N Engl J Med* 1981;304:702–12.
3. Schoen EJ, dos Remedios LV, Backstrom M: Thyroid scintigraphy in congenital primary hypothyroidism. *Clinical Research* 1984;32:95(A).

4. Van Middlesworth L: Radioactive iodide uptake of normal newborn infants. *Am J Dis Child* 1954;88:439-42.
5. Martmer EE, Corrigan KE, Charbeneau HP, et al: A study of the uptake of iodine (I-131) by the thyroid of premature infants. *Pediatrics* 1956;17:503-9.
6. Oliner L, Kohlenbrener RM, Fields T, et al: Thyroid function studies in children: normal values for thyroidal I<sup>131</sup> uptake and PBI<sup>131</sup> levels up to the age of 18. *J Clin Endocrinol Metab* 1957;17:61-75.
7. Ogborn RE, Waggener RE, VanHove E: Radioactive-iodine concentration in thyroid glands of newborn infants. *Pediatrics* 1960;26:771-76.
8. Kearns JE, Philipsborn HF Jr: Values for thyroid uptake of I-131 and protein-bound iodine in "normal" individuals from birth to twenty years. *Quarterly Bulletin of Northwestern University Medical School* 1962;36:47-50.
9. Fisher DA, Oddie TH, Burroughs JC: Thyroidal radioiodine uptake rate measurement in infants. *Am J Dis Child* 1962;103:738-49.
10. Heyman S, Crisler JF Jr, Treves S: Congenital hypothyroidism: I thyroidal uptake and scintigraphy. *J Pediatr* 1982;101:571-74.
11. Atkins HL: Technetium-99m pertechnetate uptake and scanning in the evaluation of thyroid function. *Semin Nucl Med* 1971;1:345-55.
12. Wellman HN, Anger RT Jr: Radioiodine dosimetry and the use of radioiodines other than <sup>131</sup>I in thyroid diagnosis. *Semin Nucl Med* 1971;1:356-78.
13. Kereiakes JG, Rosenstein M: *CRC Handbook of Radiation Doses in Nuclear Medicine and Diagnostic X-ray*. Boca Raton, Florida, CRC Press, 1980.
14. Singleton EB: Radiologic considerations of intensive care in the premature infant. *Radiology* 1981;140:291-300.
15. Bodegard G, Fyro K, Larsson A: Psychological reactions in 102 families with a newborn who has a falsely positive screening test for congenital hypothyroidism. *Acta Paediatr Scand* 1983;suppl 304:3-21.