

Does This Patient Have a Goiter?

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CLINICAL SCENARIOS— HOW LARGE ARE THESE THYROID GLANDS?

For each of the following patients, assessment of thyroid size is an important part of the clinical examination. In case 1, a 32-year-old woman presents with symptoms and findings consistent with hyperthyroidism, but she has no exophthalmos and has always been anxious. In case 2, a 55-year-old man has a diagnosis of Graves' disease, and the choice is made for radioactive iodine ablation therapy. In case 3, a 64-year-old man has a goiter that causes discomfort on swallowing, and thyroxine is to be administered in an attempt to shrink the thyroid gland.

WHY ASSESS THE THYROID GLAND FOR SIZE?

A goiter is simply an enlargement of the thyroid gland and may result from hormonal or immunological stimulation of gland growth or the presence of inflammatory, proliferative, infiltrative, or metabolic disorders (Table 1). A common error among those first learning about the thyroid is to associate thyroid size with function; a goiter, however, can be present in hyperthyroidism, hypothyroidism, or in a euthyroid state. Determining whether a thyroid is en-

larged can aid in diagnosis, differential diagnosis, and decisions about laboratory testing; in determining specific therapy and therapeutic dosing; and subsequently in monitoring of the clinical course. For example, when a patient presents with symptoms that could be caused by hyperthyroidism, the detection of a goiter increases the likelihood that thyrotoxicosis is present.² If the patient described in the first case had an enlarged thyroid, hyperthyroidism would be a likely diagnosis.² On the other hand, if her gland were of normal size, anxiety might be the explanation for her symptoms. Determination of thyroid size also is useful once a specific disease is diagnosed. In patients with Graves' disease, for example, thyroid size may be a factor in determining choice of treatment, since patients with smaller glands are more likely to go into immunologic remission during antithyroid drug therapy.³ If radioiodine is the chosen treatment, as in the second case, the size of the gland is often used in calculating the dose to be administered.⁴ Finally, responses to various therapies can be monitored clinically by assessing thyroid size, such as the attempt to shrink a large goiter with thyroid hormone administration in the third case.⁵

THE ANATOMIC BASIS OF THYROID EXAMINATION

Landmarks and Relation to Other Structures

The thyroid gland is located in the anterior neck and usually consists of two lobes connected at their lower midregions by a transverse isthmus (Figure 1). The most prominent structure in the anterior neck is the thyroid cartilage. Inferior to the thyroid cartilage lies the cricoid cartilage, and inferior to this lies the isthmus of the thyroid gland, as low as the level of the fourth tracheal ring. Each thyroid lobe lies against the sides of the trachea, extending up from the isthmus to the region of the cricoid and thyroid cartilages and downward toward the clavicles. The posterior portion of each lobe lies beneath the belly of the ipsilateral sternocleidomastoid muscle. Since the fascial envelope of the thyroid gland is continuous with the pretracheal fascia of the cricoid cartilage and hyoid bone, the thyroid ascends and descends along with the laryngeal structures during swallowing.

How Large Is the Normal Thyroid?

The thyroid size in a population is largely determined by the supply of iodine in the diet, with a tendency to larger glands in iodine-deficient areas.⁶⁻⁸ Consequently, studies of clinically normal thyroid glands have demonstrated sizes that span an extreme range in euthyroid individuals, differing by geographic location and varying through time within

a given region as iodine supplementation has been instituted. Until the middle of this century most authors considered a typical thyroid gland to be about 20 to 25 g, and a commonly accepted upper normal size was 35 g.⁸⁻¹¹ More recent studies in iodine-supplemented populations have reported mean weights of 10 g or less and an upper normal size of 20 g.^{12,13} While a value of 35 g may still apply in iodine-deficient areas, an upper normal weight of 20 g is probably appropriate for most parts of the Western world and will be used for this analysis. Using this definition, the prevalence of goiter is typically 2% to 5% in iodine-replete regions.^{13,14}

HOW TO EXAMINE THE THYROID GLAND TO DETERMINE SIZE

The normal thyroid, due to its relatively small size, partial concealment by the sternocleidomastoids, and soft texture, is rarely visible and may be marginally palpable.^{5,9,15} Enlargement is initially noted as an increase in the size of the lateral lobes to palpation.^{5,8} Further growth results in a gland visible in the anterior neck on careful inspection from the side^{16,17} and from the front with the neck extended.^{5,7,15,18} With increasing size, the gland becomes even more prominent on inspection from the side and visible from the front with the head in a normal position. Ultimately, a very large goiter is easily palpable, has prominence from the side of greater than 1 cm, and is visible from the front at a distance.^{5,17,18}

As a result of observations on these patterns of enlargement, various systems have been described to size a thyroid gland based on (1) the estimated weight¹⁹⁻²¹; (2) the volume relative to the size of normal glands^{5,8}; (3) the presence or absence of palpable or visible enlargement^{8,18,22}; (4) the degree of visible prominence when the neck is viewed laterally¹⁷; (5) neck circumference determined by tape measure^{23,24}; (6) the surface area of the gland projected onto the skin^{22,25};

See also p 808.

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Table 1.—Conditions That May Present With an Enlarged Thyroid Gland*

Endemic/iodine deficiency goiter
Multinodular goiter
Graves' disease
Hashimoto's thyroiditis
Subacute thyroiditis
Painless/postpartum thyroiditis
Familial goiter
Malignancy
Goitrogens
Iodine excess

*Adapted from Eastham.¹

and (7) the maximum width of the lower poles using a ruler or calipers.²⁶ Many of these rating scales were developed for epidemiologic studies of goiter in endemic areas and were intended to classify significant goiters rapidly (with examination time in some studies averaging only 18 seconds per subject).⁵ As a result, many are of little use for the smaller thyroid glands seen in regions without significant levels of endemic goiter. Most studies from which data for accuracy and precision of goiter determination can be derived do not report specifics of thyroid examination technique. Consequently, there is no objective evidence to support the use of one examination method over another.^{23-25,27,28} Many of the variations are minor, though, and shared features will be described.

The patient should be comfortably positioned, either standing or seated, with the neck in a neutral position or slightly extended. The region of the neck below the thyroid or cricoid cartilage should be observed from the front, with good cross-lighting to accentuate shadows and highlight masses. If an abnormality is suspected, the neck should be moved as appropriate to alter the prominence of the area under suspicion. A particularly useful maneuver is fully extending the neck for inspection. This position stretches superficial tissues over the thyroid gland, which is pressed against the relatively unyielding trachea, and visibility of the gland is enhanced. Another aspect of thyroid inspection that is often neglected is to observe the neck from the side, looking for a prominence protruding from the normally smooth and straight contour between the cricoid cartilage and the suprasternal notch.¹⁷ The amount of prominence should be measured using a ruler (Figure 2). This requires a certain degree of guesswork in deducing where the normal neck contour would lie, but the measurement can provide information useful for ruling in the presence of a goiter, as will be discussed herein. There is no particular spot to place the ruler—it merely serves as a visual guide to estimating the degree of protrusion.

Following inspection, the gland is pal-

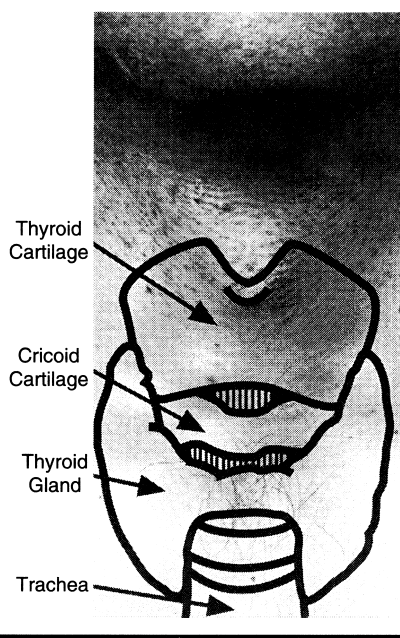


Figure 1.—The location of the thyroid gland.

pated, and this is where the greatest differences in methods arise. Authors vary as to whether they prefer palpation using fingers or thumbs, an approach from the front or from behind the patient, and whether each lobe is palpated by the ipsilateral hand or the opposite hand. In the absence of data to support a specific method, though, examiners should use the approach with which they are most comfortable. Regardless of the technique used, it is often useful to first attempt to locate the thyroid isthmus by palpating between the cricoid cartilage and suprasternal notch. An isthmus may not be felt, but if it is, this can help locate the gland. When palpating the lobes, it is beneficial to relax the sternocleidomastoids. To better feel the left lobe, for example, the neck can be slightly flexed and rotated to the left, both to relax the left sternocleidomastoid and to make space for the palpating fingers or thumb between the sternocleidomastoid and trachea. There are certain additional maneuvers that may be useful, such as measuring neck circumference or the dimensions of a lobe using calipers, but no information is available to assess accuracy or precision of these techniques. Other elements of the thyroid examination that are carried out concomitantly with size assessment include determining gland texture, gland mobility, tenderness, and the presence of nodularity. Auscultation also may be performed for the presence of bruits. These features have their own implications but are not central to determining the presence of a goiter, so are beyond

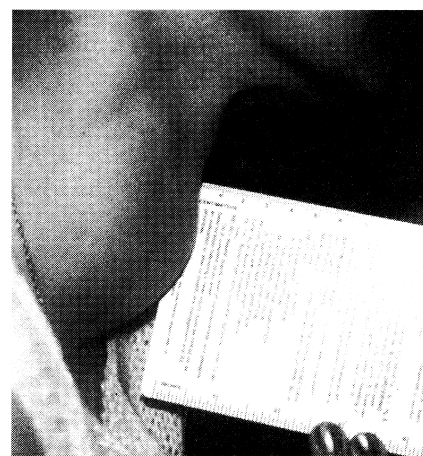


Figure 2.—Estimating lateral thyroid prominence.

the scope of this discussion. If no thyroid is detected in the neck, it may be maldescended or intrathoracic. Methods of examining for these variants will not be discussed here, since, again, no information is available to analyze the reported techniques.

Dogma holds that the thyroid examination is improved by having the patient swallow during both inspection and palpation. Indeed, it has been stated that swallowing increases sensitivity of inspection alone to that of inspection combined with palpation.²⁸ No study, however, has actually analyzed whether a swallowing maneuver is of benefit, although most examiners believe it is. The movement resulting from swallowing accomplishes several things. First, it changes the shadowing of any mass, enhancing visual detection of a bulge in the neck contour that may be too subtle to be detected otherwise. Second, movement of the thyroid raises a low-placed gland up from below the sternal notch or lower sternocleidomastoid, making it accessible when it may not have been previously. Third, as in any palpation technique, movement of the object against the palpating hand increases definition. Finally, since only the larynx, upper trachea, and thyroid gland move with swallowing, this maneuver can aid in anatomical localization.²⁹ Swallowing has thus become an integral part of the thyroid examination, based on common sense and experience but no formal study. One final point is that the degree of excursion of the thyroid on swallowing is proportional to the size of the bolus swallowed, so the patient should be given a sip of water.³⁰

When examining the thyroid to determine the presence of a goiter, the goal is estimating gland size. Most endocrinologists express findings in absolute mass or as relative to an upper normal-sized

gland, such as “normal” or “two to three times normal size.” Many nonendocrinologists have some difficulty quantifying thyroid mass, but this ability is crucial in accurately classifying a gland, as will be seen later in the analysis of accuracy.

FALSE-POSITIVE AND FALSE-NEGATIVE GOITERS

Finding a goiter when one is not present may simply be an error in detection. There are, however, several common causes of a false-positive goiter or pseudogoiter. One is simply an easily palpable gland in a thin individual.⁵ Since the entire thyroid is so accessible, the tendency is to interpret this accessibility as being due to an enlarged gland rather than the true reason, a decrease in interfering tissues that normally block access to the gland. A second cause is a variant of the normal placement of the thyroid gland in the neck. In some individuals, the gland is higher than usual, and this prominence is again attributed to enlargement.³¹ A third anatomical variant has been termed “Modigliani syndrome.”³² This is where the thyroid actually lies in normal position below the cricoid cartilage, but such individuals possess long, curving necks that enhance the prominence and palpability of the gland. A fourth condition producing pseudogoiter is a fat pad in the anterior and lateral neck.²⁴ While this may be more common in obese individuals, it can also be found in those of normal weight, particularly young women. With experience, examiners can learn to differentiate this from true thyroid tissue by the differing textures and shapes and the lack of movement of a fat pad with swallowing. Another cause involves the thyroid being pushed forward by lesions behind it, making it more easily palpable.^{5,33} Finally, any enlargement in the vicinity of the thyroid gland may be mistaken for an enlarged thyroid gland, particularly if it is adherent to the thyroid or larynx and so moves with swallowing.²⁹

There are three principle causes of false-negative goiter detection in addition to true misclassification. The first and probably most common cause, of course, is an inadequate physical examination. In some circumstances an imperfect examination is unavoidable, as when a patient is intubated. In most cases, however, with a little effort, a good examination can be performed on virtually all patients. Second, some individuals, particularly the obese, the elderly, or those with chronic pulmonary disease, have very short and thick necks, obscuring the thyroid.^{5,24,34} Some patients also have an atypical thyroid placement, such as a retrosternal location, or lobes that are lateral and obscured by the sternocleidomastoids, making palpation difficult.³⁵

Table 2.—Interobserver Precision in Assessment of Thyroid Size or Presence of Goiter

Reference	Agreement		κ	
	All Categories*	Goiter Only†	All Categories*	Goiter Only†
Trotter et al ^{36,†}	0.67	0.83	0.48	0.50
Kilpatrick et al ^{8,§}	0.86	0.95	0.74	0.77
Dingle et al ^{37,}	0.85	0.87	0.47	0.38
Trowbridge et al ^{7,§}	Not available	0.96	Not available	0.58
Combined (95% confidence interval)	0.86¶ (0.82-0.90)	0.92 (0.90-0.94)	0.70¶ (0.68-0.72)	0.77 (0.76-0.79)

*Analysis of all size categories used by authors.

†Analysis of presence or absence of goiter only, based on authors' definitions.

‡Agreement between two observers, three categories of staging, after an unspecified time.

§Agreement between one observer and one or two others, four categories of staging, after an unspecified time.

||Agreement between one observer and two others, four categories of staging, after 2 years.

¶Raw data combined from Kilpatrick et al⁸ and Dingle et al³⁷ only, since they are the only two with the same rating scales.

Table 3.—Comparison of Interobserver Precision for Thyroid Inspection and Palpation

Reference	Agreement		κ	
	Inspection	Palpation	Inspection	Palpation
Kilpatrick et al ⁸	0.95	0.89	0.77	0.76
Dingle et al ³⁷	0.87	0.89	0.38	0.60
Combined (95% confidence interval)	0.93 (0.90-0.96)	0.89 (0.85-0.92)	0.65 (0.62-0.69)	0.74 (0.67-0.82)

Table 4.—Intraobserver Precision in Assessment of Thyroid Size or Presence of Goiter

Reference	Agreement		κ	
	All Categories*	Goiter Only†	All Categories*	Goiter Only†
Hennessy ^{6,‡}	0.83	0.90	0.70	0.79
MacLennan et al ^{22,§}	0.79	0.82	0.41	0.47
Combined (95% confidence interval)	0.81 (0.77-0.84)	0.85 (0.82-0.88)	0.59 (0.52-0.65)	0.65 (0.63-0.67)

*Analysis of all size categories used by authors.

†Presence or absence of goiter only, based on authors' definitions.

‡Four categories of staging, reexamined within 44 days.

§Three categories of staging, examined 12 days later.

PRECISION OF ESTIMATING THYROID SIZE

Interobserver Variability

Data on interobserver precision in estimating thyroid size are available both for rating scales that attempted to place glands in one of three or four categories based on palpability and visibility and for simple estimation of the presence or absence of a goiter (Table 2). Agreements were good to very good in both cases. When placing glands in categories, κ ranged from 0.47 to 0.74, with a value from combined data of 0.70 (95% confidence interval [CI], 0.68 to 0.72).^{7,8,36,37} (The κ statistic and other statistical measures are defined in the introductory paper to this series.³⁸) For determination of goiter, κ ranged in these four studies from 0.38 to 0.77, with a value for combined data of 0.77 (95% CI, 0.76 to 0.79). Similar numbers were reported in another study³⁹ in which observers determined whether individual lobes were enlarged, with κ from 0.32 to 0.62, and in yet another report⁴⁰ that determined the presence of a goiter, κ was 0.10 to 0.54. Due to the nature of the rating scales

used in two of these studies,^{8,37} we can specifically compare interobserver variability for the techniques of inspection ($\kappa=0.65$; 95% CI, 0.62 to 0.69) and palpation ($\kappa=0.74$; 95% CI, 0.67 to 0.82). These techniques did not differ significantly in the level of agreement, and both were very good (Table 3).

As might be expected, the majority of disagreements between observers involved smaller glands and those near the cutoff for goiter determination, and most disagreed by only one stage in classifications.^{7,8,36,37} Agreement may be better between examiners with greater experience than between those with differing levels of training.⁴⁰

Intraobserver Variability

In two studies,^{6,22} examiners placed thyroid size in categories of enlargement, and repeated the examination on a separate occasion (Table 4). These data produced a κ from combined numbers of 0.59 (95% CI, 0.52 to 0.65) for placement in all categories of the rating scales used by the examiners. For simply determining the presence or absence of goiter, κ

Table 5.—Comparison of Intraobserver Precision for Inspection and Palpation

Reference	Agreement		κ	
	Inspection	Palpation	Inspection	Palpation
Hennessy ⁶	0.93	0.90	0.82	0.79
MacLennan et al ²²	0.95	0.82	0.18	0.47
Combined (95% confidence interval)	0.94 (0.92-0.96)	0.85 (0.82-0.88)	0.73 (0.71-0.76)	0.65 (0.63-0.67)

Table 6.—Accuracy of the Clinical Assessment for the Presence of a Goiter*

Reference	Sensitivity	Specificity	Likelihood Ratio	
			Positive	Negative
Silink et al ¹⁷ †	0.64	0.89	5.8	0.40
Tannahill et al ²¹ ‡	0.93	0.75	3.7	0.09
Hegedus et al ⁴⁴ §	0.43	1.00	Infinity	0.57
Hegedus et al ⁴⁵ §	0.60	1.00	Infinity	0.40
Hegedus et al ⁴⁶ §	0.77	0.80	3.9	0.29
Berghout et al ¹⁸	1.00	0.62	2.6	0.00
Perrild et al ⁴⁷ ¶	0.64	1.00	Infinity	0.36
Hintze et al ¹² #	0.66	0.74	2.5	0.46
Jarlov et al ⁴⁸ ‡	0.80	0.80	4.0	0.25
Combined (95% confidence interval)	0.70 (0.68-0.73)	0.82 (0.79-0.85)	3.8 (3.3-4.5)	0.37 (0.33-0.40)

*Goiter defined as thyroid gland size greater than 20 g, except by Silink et al,¹⁷ in which goiter was defined as gland size greater than 22 g and by Hintze et al,¹² in which male gland size was greater than 25 g and female gland size was greater than 18 g.
†Graded degree of lateral prominence, goiter being any prominence, with criterion standard of autopsy weight.
‡Directly estimated weight, with criterion standard of ultrasound.
§Goiter defined as visible or palpable gland, with criterion standard of ultrasound.
||Graded five stages of thyroid size based on palpability and visibility, with criterion standard of ultrasound.
¶Two observers had to agree on the presence of goiter, which was undefined, using ultrasound as the criterion standard.
#Graded five stages of thyroid size based on palpability, with criterion standard of ultrasound.

Table 7.—Accuracy in Assessing Grades of Thyroid Gland Weight

Thyroid Size, Reference*	Positive Likelihood Ratio
Normal, 0-20 g	
Williams et al ¹⁹ †	0.00
Smith et al ²⁰ †	0.00
Tannahill et al ²¹ ‡	0.10
Jarlov et al ⁴⁸ ‡	0.26
Combined (95% CI)	0.15 (0.10-0.21)
1-2 times normal, 20-40 g	
Williams et al ¹⁹ †	Infinity
Smith et al ²⁰ †	0.32
Tannahill et al ²¹ ‡	2.22
Jarlov et al ⁴⁸ ‡	2.65
Combined (95% CI)	1.9 (1.1-3.0)
>2 times normal, >40 g	
Williams et al ¹⁹ †	Infinity
Smith et al ²⁰ †	Infinity
Tannahill et al ²¹ ‡	Infinity
Jarlov et al ⁴⁸ ‡	12.7
Combined (95% CI)	25.0 (3.6-175)

*CI indicates confidence interval.
†Directly estimated thyroid weight, with postsurgical weight as the criterion standard.
‡Directly estimated thyroid weight, with ultrasound as the criterion standard.

ranged from 0.47 to 0.79, with a κ from combined data of 0.65 (95% CI, 0.63 to 0.67), which is very good. Similar values were reported in a study of patients with various thyroid diseases, in which κ ranged from 0.54 to 0.74.³⁹ Intraobserver agreement was slightly better for the inspection component of the examination (κ=0.73; 95% CI, 0.71 to 0.76) than for palpation (κ=0.65; 95% CI, 0.63 to 0.67) (Table 5).

Table 8.—Accuracy in Assessing Thyroid Size by Categories

Stage, Size	Positive Likelihood Ratio (95% Confidence Interval)
Method of Silink et al ¹⁷ *	
0, not visible	0.41 (0.34-0.49)
1, 0-2 mm	3.4 (1.8-6.3)
2, 2-10 mm	Infinity
3, >10 mm	Infinity
Method of Berghout et al ¹⁸ †	
0A	0.00
0B	0.00
1	1.00 (0.42-2.4)
2	3.9 (1.8-8.2)
3	Infinity

*Graded degree of lateral prominence with goiter being any prominence, using autopsy weight as a criterion standard.
†Graded stages 0 to 3 based on palpability and visibility, with goiter being 1 to 3, using ultrasound as a criterion standard: 0A indicates lobes smaller than size of thumb terminal phalanx, thyroid not visible with neck extended; 0B, lobes bigger than size of thumb terminal phalanx, thyroid not visible with neck extended; 1, easily palpable, visible with neck extended; 2, visible with neck in normal position; and 3, easily visible.

ACCURACY OF ESTIMATING THYROID SIZE

Three criterion standards have been used in assessing the accuracy of thyroid size determination: weight measured after surgical or postmortem removal, ultrasound assessment, and nuclear scintigraphy. Ultrasound assessments of thyroid weight correlate well with true gland weight as determined following excision

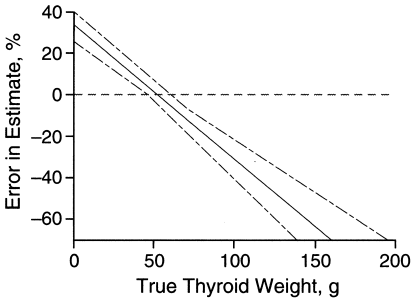


Figure 3.—Error in estimating thyroid mass, described by the following formula: percentage of error=(−0.656×mass)+34.8, where thyroid mass is in grams (r=0.41; P<.001). The 95% confidence interval is indicated by the broken lines.

(r=0.88 to 1.00), although there is lack of agreement as to the best formula to use for estimating size.^{18,21,41} Nuclear scan determination is a little less reliable but acceptable (r=0.77 to 0.98).^{9,42,43} Again, different formulas have been used to translate the scintigraphic profile to thyroid volume.^{9,42,43}

Combining data from nine studies of detection of goiter by physical examination,^{12,17,18,21,44-48} the sensitivity from combined data was 0.70 (95% CI, 0.68 to 0.73) with a specificity of 0.82 (95% CI, 0.79 to 0.85) (Table 6). If a goiter was clinically detected, the positive likelihood ratio of one being present was 3.8 (95% CI, 3.3 to 4.5). Conversely, if a goiter was not felt to be clinically present, the negative likelihood ratio was 0.37 (95% CI, 0.33 to 0.40). These likelihoods are comparable with, or better than, those for many other physical signs^{49,50} and were not affected by the presence of single or multiple nodules.⁴⁸ Experienced examiners were somewhat more accurate in their assessments than more junior colleagues.⁴⁸

Some authors have defined specific stages of thyroid enlargement, based on the usual sequence of changes that occur as the thyroid gland increases in size. Since some of these staging classifications incorporate observations not normally used in simply estimating thyroid mass, they can significantly enhance the predictive abilities of the clinician (Table 7). In the combined data from four studies,^{19-21,48} when a clinician felt that a thyroid gland was of normal size, the positive likelihood ratio of goiter being present was 0.15 (95% CI, 0.10 to 0.21). If classified as one to two times normal size, the positive likelihood ratio was 1.9 (95% CI, 1.1 to 3.0), and for greater than two times normal, the positive likelihood ratio was 25.0 (95% CI, 3.6 to 175).

Certain staging methods for thyroid enlargement can help clarify the true status of some of the patients with glands felt to be in the range of one to two times

normal size after routine inspection and palpation.^{14,17} The amount of prominence of the thyroid on lateral inspection, for example, resulted in a high likelihood of goiter if it was greater than 2 mm (Table 8). Of further utility was finding that a gland was not visible with the neck extended, a result that effectively ruled out a goiter.

BIAS IN ESTIMATING THYROID SIZE

When the results from four different studies^{19-21,48} estimating thyroid gland weights were combined, a regression line was produced describing the tendency to bias in gland size determination (Figure 3). This clearly shows that smaller glands are routinely overesti-

mated in size, while larger glands are underestimated. The size at which this crossover occurs corresponds to about 2½ times upper normal size. The practical application of this finding is that glands in the one to two times normal size category fall in the range in which size is typically overestimated.

THE BOTTOM LINE

To determine whether a goiter is present, follow these steps:

1. Examine the thyroid gland by inspection and palpation.

2. Categorize thyroid size as normal or goiter. Subcategorize goiter as small goiter (one to two times normal) or large goiter (greater than two times normal).

3. If you placed the thyroid in the small goiter category, consider whether you overestimated the size; determine whether there is any prominence in the profile of the neck in the region of the thyroid when viewed laterally (classify the prominence as ≤ 2 mm or > 2 mm); and determine if the gland is not visible from the front with the neck extended.

4. Place your patient in one of the following categories: "goiter ruled out": normal thyroid size or thyroid considered to be not visible with neck extended; "goiter ruled in": large goiter present or lateral prominence greater than 2 mm; or "inconclusive": all other findings.

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