THYROID GOITER

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THYROID GOITER

Diffuse goiter

Nodular goiter

Multinodular (polynodose) goiter
DIFFUSE GOITER

UNINODULAR GOITER

MULTINODULAR GOITER
Goiter – World Health Organisation Division (WHO)

- **Grade 0:** No goiter: hardly palpable and visible (or unpalpable or unvisible)
- **Grade IA:** clearly palpable, but unvisible with neck extension
- **Grade IB:** clearly palpable and visible with complete neck extension (head thrown). This grade involves nodular goiter, even if the thyroid itself isn’t enlarged
- **Grade II:** clearly visible when the head is in normal position (palpation isn’t neccesery for diagnosis)
- **Grade III:** thyroid seen from the distance (palpation isn’t neccesery for diagnosis)
Revised goiter division

Grade 0  Thyroid not enlarged by inspection or palpation

Grade 1  Goiter palpable, but not seen when head and neck are in normal position (thyroid isn’t enlarged visually). This category includes nodules in normal sized thyroid

Grade 2  Thyroid visible when head is in normal position, and palpatory enlarged

What is a nodule?

- Inspection: thyroid thickening, asymmetry.
- Palpation: part of the thyroid with different consistency.
- Ultrasonography: tumor of different echostructure or separated echostructure inside the thyroid.
- Scintigram: tumor of different function.
THYROID NODULES

- The most common thyroid disease (frequency 20-50%)
- Important clinical problem (thyroid cancer ~ 5%)
THE MOST COMMON CAUSES FOR THYROID NODULES

Benigne

- Folliculare adenoma
  - Macropholiculare adenoma
  - Microfoliculare (fetale)
  - Trabecullare
  - Hürthle cell

- Multinodular goiter
- Cysts (colloid and hemorrhagic)
- Thyroiditis Hashimoto
THE MOST COMMON CAUSES FOR THYROID NODULES

Malignant

- Papillary and follicular carcinoma.
- Medullar carcinoma.
- Poorly differenciated and anaplastic carcinoma.
- Primary thyroid lymphoma.
- Metastatic carcinoma: melanoma, breast carcinoma and kidney carcinoma
Prevalence of thyroid nodules

1. * around 5% (3%–8%) by palpation

2. * 10 - 76% by ultrasonography

3. * 50% by pathohistologic findings in autopsy in older people (Mortensen et al. J Clin Endocrinol Metab; 1955)

* Increase with age
* More often in women
DIFFERENTIAL DIAGNOSIS OF THYROID NODES

• 42-77% colloid nodes

• 15-40% adenomas

• 8-17% carcinomas

THYROID NODULE’S INCIDENCE (by palpation)

- Incidence of palpable nodes (in areas with iodine deficit)
  ~ 5% in female
  ~ 1% in men
## THYROID NODULE’S INCIDENCE (by palpation)

<table>
<thead>
<tr>
<th>State</th>
<th>Nodule incidence</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAD (Salt Lake City)</td>
<td>2.3% (young adults) 0.46% (school children)</td>
<td>Rallison ML, 1991</td>
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<tr>
<td>England (Whickham)</td>
<td>3.2%</td>
<td>Turnbridge WMG, 1977</td>
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<tr>
<td>SAD (Massachusetts)</td>
<td>4.2%</td>
<td>Vander JB, 1968</td>
</tr>
<tr>
<td>Italy (Sicily)</td>
<td>5.1%</td>
<td>Belfiore A, 1987</td>
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<tr>
<td>Denmark</td>
<td>6.5% (middle age women)</td>
<td>Christensen SB, 1984</td>
</tr>
<tr>
<td>State</td>
<td>Nodule incidence</td>
<td>Author</td>
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<tr>
<td>SAD (Stanford)</td>
<td>13.4%</td>
<td>Caroll et al.; 1982</td>
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<tr>
<td>Japan (Tokushima)</td>
<td>19.7%</td>
<td>Miki et al.; 1993</td>
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<tr>
<td>Finland (Hyvinkaa)</td>
<td>21.3%</td>
<td>Brander et al.; 1991</td>
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<tr>
<td>Germany</td>
<td>23.4% (18-65 years)</td>
<td>Reiners et al.; 2004</td>
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<tr>
<td>Italy (Pescopagano)</td>
<td>28.5% (56-65 years)</td>
<td>Aghini-Lombardi et al.; 1999</td>
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<td>Danmark (Copenhagen)</td>
<td>32% (41-71 years)</td>
<td>Knudsen et al.; 2000</td>
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<td>Italy (Palermo)</td>
<td>33%</td>
<td>Bartolotta et al.; 2006</td>
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<tr>
<td>SAD (San Francisco)</td>
<td>40% (patients with hyperparathyroidisam)</td>
<td>Stark et al.; 1983</td>
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<tr>
<td>SAD</td>
<td>46%</td>
<td>Horlocker et al.; 1985</td>
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# Thyroid Nodule’s Incidence (by Autopsy)

<table>
<thead>
<tr>
<th>State</th>
<th>Nodule Incidence</th>
<th>Author</th>
</tr>
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<tbody>
<tr>
<td>SAD</td>
<td>13% (soldiers age 18-39 years)</td>
<td>Oertel, Klinck 1965</td>
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<tr>
<td>Hungary</td>
<td>27.1% sufficient iodine intake</td>
<td>Kovacs et al. 2005</td>
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<td>44.6% insufficient iodine intake</td>
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<tr>
<td>SAD</td>
<td>50.5%</td>
<td>Mortensen JD et al. 1955 (Mayo clinic)</td>
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<tr>
<td>Belarussia</td>
<td>60%</td>
<td>Furmanchuk et al. 1993</td>
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DIAGNOSIS AND TREATMENT OF PATIENTS WITH THYROID NODES

- Inspection and palpation
- TSH serum level
- Ultrasonography of the thyroid
- Thyroid scintigraphy (\(^{99m}\text{TcO}_4^-, \, ^{123}\text{I}, \, ^{131}\text{I}\))
- Fine needle aspiration citology and Tg and Ct in aspirate
- RTG, CT, MR
Inspection and palpation
ULTRASONOGRAPHY

• Introduced in 1967. by Fujimoto as thyroid imaging method

• The most precise method for detection of thyroid nodes

• Detection of nodes larger then 2 mm

• Mandatory in palpable nodes.

• Ultrasound guided fine needle aspiration.
NODULAR CHANGES: Number, size, echostructure, position in the thyroid
1. Cysts and cystic - degenerative noduleses
2. Single nodul - isoechochogenic, hypoechogenic, degeneratively changed (benigne goiter)
3. Multinodular (polynodular) goiter
4. Nodul in lymphatic goiter
5. tumors- adenomas, cancers
Ca. papillare
Ca. papillare
Panoramic US image, coronal section: solitary nodule in the right lobe
Metastatic lymph nodes
Echographic criterion of malignancy

- Hypoechogenic
- Microcalcification
- Absence of hypoechogenic edge, irregular borders
- Intranodular vascularisation
- Regional lymphadenopathy
Flow grades in CD (Color Doppler)

*Color Doppler can help to determine which nodules require FNAC*
Neck examination

Reactive lymph node

Metastatic lymph node
Scintigraphy

Scintigraphic “cold” node

Scintigraphic “hot” node
Scintigraphic “cold” node  Scintigraphic “warm” node
Ultrasound guided fine needle aspiration citology (FNAC)
CARCINOMA RISK IN THE NODULE

~5% solitary nodule

~5% nodes in multinodular goiter

~5% small unpalpable nodes detected by ultrasound
CARCINOMA RISK IN THE NODULE

Risk factors:

• Age < 20 years.
• children < 14 years – around 50% nodes are cancer
• Male gender (2 times more often)
• Scintigraphic nonfunctional “cold” nodes
• Quick growth of the nodule
• Nodes > 4 cm
Clinical findings suggesting thyroid carcinoma:

1. Quick growth of the nodule,
2. Hard and irregular by palpation,
3. Vocal cord paralysis,
4. Enlarged neck lymph nodes,
5. Family history for medullary carcinoma,
6. Distant metastasis.
Scintigraphically “warm” or “hot” nodules (Autonomously functioning thyroid nodule-AFTN) have very low malignancy risk (0.2-0.5%).

Fine needle aspiration citology is indicated only in those nodules with clinically (quick grow, hard consistency) and ultrasound characteristics suspected for malignancy.
Importance of thyroid nodule detection

* Most of the patients don’t have any symptoms
* Most are euthyroid
* Some patients have palpable nodule, neck pressure or other discomfort
* For thyroid carcinoma detection (5% of all nodes)

* Carcinoma risk is similar in solitary nodules and inside multinodular goiter
  • Cancer are found equally in small and large nodes
  • Microcancer can be aggressive
  • **Aim** of diagnostic procedure is to reduce number of unnecessary operations of benign thyroid diseases and early diagnosis of malignant tumors
Microcarcinoma < 1 cm

- Thanks to ultrasound significant number of detected thyroid cancers today are less then 1 cm in diameter
- **Occult** microcarcinomas can be found as source of neck lymphnode metastasis or distant metastasis
- **Incidental** papillary microcarcinomas are detected as pathohistological finding in thyroid tissue after surgery for other reasons
- **Latent** microcarcinomas which are incidental finding in autopsy
Goiter

1. **endemic goiter**: more than 5% of inhabitants or school children have goiter.
2. **sporadic goiter**: diffuse and nodular (multinodular) goiter.

Endemic stands for expansion in the population, because clinical manifestation, pathohistological finding and biochemical parameters are same in endemic and sporadic goiter.
Endemic goiter
Endemic goiter
Endemic cretinism
Croatia-1950.

- 2,000,000 people with goiter
- Frequency 10 - 90%
- 20,000 endemic cretinism
- 2 - 4,000 deaf-mute
- Male to female children with ratio was 1:1
Home of the family with goiter, Rude, 1950'

Cretin’s destiny was closely related with their mother’s life...
IODINE PROPHYLAXIS IN CROATIA

• 1930. – 1941. sporadic iodine prophylaxis

• 1953. First low about mandatory table salt iodination
  
  10 mg KI/kg NaCl

• Ten years later three times reduction in goiter frequency in Croatia with loss of cretinism
In the beginning of the 1990’s goiter frequency in Croatia was 8%-35%
1996.

MILD TO MODERATE IODINE DEFICIENCY IN SPITE SALT IODINATION WITH 10 mg KI/kg NaCl
1996.
NEW LEGISLATION ABOUT SALT IODINATION
25 mg KI/kg NaCl
RESULTS:
Thyroid volumes measured in four main geographic regions were within normal range for school children who receive sufficient amount of iodine.

ZAGREB__________ 7,2 mL
STOCKHOLM_______ 4 mL
MÜNCHEN__________ 9 mL

THYROID VOLUME, age 12, 2002.

ZAGREB__________ 4,8 mL
<table>
<thead>
<tr>
<th>Satisfactory (≥100 µg/L)</th>
<th>Probably sufficient</th>
<th>unsatisfactory (&lt;100 µg/L)</th>
<th>Probably unsatisfactory</th>
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<tbody>
<tr>
<td>Austria</td>
<td>Island</td>
<td>Belgium</td>
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<td>Bosna and Hercegovina</td>
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<td>Switzerland</td>
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<td>United Kingdom</td>
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<td>Turky</td>
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Lancet, 2003; 361: 1226
Recommended daily intake of iodine

- 90 μg for preschool children (0 to 59 months);
- 120 μg for schoolchildren (6 to 12 years);
- 150 μg for adults (above 12 years); and
- 200–250 μg for pregnant and lactating women.

From WHO/UNICEF/ICCIDD (2), WHO
Epidemiological criteria for assessing iodine nutrition based on median urinary iodine concentrations in school-aged children

<table>
<thead>
<tr>
<th>Median urinary iodine</th>
<th>Iodine intake (μg/L)</th>
<th>Iodine nutrition</th>
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<tbody>
<tr>
<td>&lt; 20</td>
<td>Insufficient</td>
<td>Severe iodine deficiency</td>
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<tr>
<td>20-49</td>
<td>Insufficient</td>
<td>Moderate iodine deficiency</td>
</tr>
<tr>
<td>50-99</td>
<td>Insufficient</td>
<td>Mild iodine deficiency</td>
</tr>
<tr>
<td>100-199</td>
<td>Adequate</td>
<td>Optimal</td>
</tr>
<tr>
<td>200-299</td>
<td>More than adequate</td>
<td>Risk of iodine-induced hyperthyroidism within 5-10 years following introduction of iodized salt in susceptible</td>
</tr>
<tr>
<td>&gt; 300</td>
<td>Excessive</td>
<td>Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)</td>
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The natural course of multinodular goiter’s development

• Gradual growth of the goiter and nodules.
• Development of multiple nodes with age.
• Variation in size and architecture of the nodes.
• Appearance of cysts, fibrosis, necrosis, hemorrhage, calcifications.
• Variable growth flow – possible longtime phases of inaction.
• Appearance of autonomic nodes with TSH supression – transit to multinodular toxic goiter (common form of hyperthyroidism in insufficient iodine intake).
Clinical manifestation

- Asymptomatic small goiter
- Large multinodular, retrosternal or intrathoracic goiter with symptoms of compression: in 10-20% patients
  - Dysphagia
  - Dyspnea
  - Dysphonia
  - Stridor
  - Pemberton’s sign
  - Syndroma Horner
- Pain (nodule hemorrhage)
- Thyreotoxic symptoms
Frequency of multinodular goiter

- High frequency in areas with iodine deficit (endemic goiter) up to 30%.

- Eradication of endemic goiter in countries which implemented mandatory iodine prophylaxis.

- In areas with sufficient iodine intake goiter frequency is around 4% (sporadic goiter).

- Increase of thyroid nodule frequency with age
Causes of nontoxic goiter

1. Iodine deficit (compensatory thyroid enlargement)

2. Strumogenic substance (tiocionats, thyreostatic preparations, lithium, different vegetables)

3. Enzymatic disorders
Multinodular goiter: Clinical problem

1. Compression

2. Hyperthyroidism, hypothyroidism

3. Malignancy
Diagnostics treatment

- Inspection and palpation
- TSH
- Thyroid ultrasonography
- Thyroid scintigraphy
- Fine needle aspiration cytology
- RTG, CT, MR, SPECT
TSH

- Inversly relationship between goiter size and serum TSH level.
- Longtime goiter – development of autonomic nodes with TSH suppression.
- Suppressed TSH: determination of FT3, FT4.
- Antibodies.
Thyroid ultrasonography

- Nodule frequency (US):
  - Up to 50% population has multiple nodules which aren’t palpable
  - Up to 50% persons with single palpable nodule have multiple nodes registered on ultrasound

- Ultrasound guided fine needle aspiration cytology

- Objective follow up of goiter and nodule size
Multinodular goiter: multiple nodes in the thyroid
Multinodular goiter: panoramic US image, cross section, multiple nodes in the thyroid
Multinodular goiter: panoramic US image, cross section, enlarged thyroid with multiple nodes
Fine needle aspiration citology (FNAC)

- Indicated in:
  - fast growing goiter with dominant nodule
  - clinically suspected nodes
  - ultrasound suspected nodes
  - unpalpable nodes larger then 1 cm – guided by ultrasound (4-6% malignant)

- Risk for carcinoma development in nodes smaller then 1 cm is same as in large nodes - around 5%
- Not routinely indicated
Thyroid scintigraphy

Multinodular goiter
Scintigraphy with $^{99m}$ Tc-pertechnetate

Multinodular toxic goiter
Scintigraphy with $^{131}$I
Intrathoracic goiter-planar scintigraphy with I-131-
Pemberton’s sign
Radiological examinations

- X-ray of thorax
- X-ray of trachea and esophagus
- CT
- MR

- Indications:
  - large multinodular goiter
  - retrosternal goiter
  - intrathoracic goiter
X-ray of the trachea and neck soft tissue
- deviation and/or compression of the trachae, tracheomalatia
- thyroid calcification
Planar scintigraphy with I-131-intrathoracic goiter
SPECT/CT

Patient ID: 0206201103111952  Study Name: Thyroid Scan  Series Date: 02-Jun-2011
Series Time: 10:05:41
CT, MR
Ectopic- intratracheal thyroid
Clinical problem: Carcinoma in multinodular goiter

• 4 - 17% cancer are found in the surgically removed multinodular goiters.
• 4 - 24% thyroids on the autopsy have carcinoma.
• Incidentaly found unpalpable nodes have 4-6% cancer on US guided fine needle aspiration.
• Higher risk:
  - in patient who had head and neck area radiated during childhood.
Cancer problem

- Up to 5% nodes have carcinoma regardless whether they are solitar nodul or multinodular thyroid

- 4% of population have solitar nodule (40 000 per 1 000 000)
- 4% persons with nodule have carcinoma (1600 per 40 000)
- 1 600 cancers per 1 000 000 habitants
- 30 - 60 cancers a year per 1 000 000 habitants
- 6 patients die per 1 000 000 habitants

- Clinical treatment of dominant and/or suspected nodes in multinodular goiter
Treatment of multinodular goiter

- There is no simple or optimal therapy – individual approach
- Follow up without therapy
- Surgery
- Radioiodine therapy
- Suppression therapy with thyroxine
- Percutane injection of ethanol
- Laser therapy
Surgical treatment of multinodular goiter

• Indications:
  – Carcinoma finding by FNAC
  – Goiter and nodes growth with symptoms of compresion
  – Cosmetic large goiter
  – Hyperthyroidism

• Therapy of choice in young patients
• Subtotal thyroidectomia
• Near total or total thyroidectomia (relapse in up to 60% )
Therapy with I-131

• Indications:

- Scintigraphic “hot” nodes – multinodular toxic goiter or just suppressed TSH, especially in elderly patients

- malignant tumor excluded

- large and/or retrosternal goiter

- older patients with increased risk for surgery – especially cardiopathes
Radioiodine therapy of euthyroid goiter

- 40% reduction in goiter size during the first year, and 60% reduction during 3–5 years period
- Weaker effect in large goiters
- Recombinant hTSH.

- Significantly more effective and easier to endure in regard to suppression therapy with thyroxine
- No significant side-effects (hypothyroidism).
- No increase in cancer risk in patients treated with $^{131}$I.
Thyroxine suppression therapy

- Possible reduction of small non-toxic multinodular goiter

- Not indicated with suppressed TSH.

- Individual access (not recommended in cardiopaths and older patients).

- Relapse after discontinuation of therapy.
Follow up without therapy

• Goiter stable for many years.

• Cytology: benign.

• Ultrasound follow up of goiter and nodule’s size every 6 -12 months with TSH level follow up.

• In case of growth of either goiter or nodes and/or appearance of suspected nodes repeat FNAC.

• In case of appearance of TSH suppression: determine FT3, FT4 and do the thyroid scintigraphy.