The involvement of the thyroid gland by tuberculosis is one of the rarest localizations of this disease [6—10, 13]. Currently, most authors believe that thyroid tuberculosis is diagnosed in 0.1—1.0 % of all known cases of tuberculosis. Clinical observations have found that the thyroid gland is more often involved in the tuberculous process with a generalized miliary process, and, as previously thought, in this case there are no clinical signs of damage to the thyroid gland. A variable clinical presentation of thyroid tuberculosis was demonstrated. It is usually presented with local symptoms associated with diffuse enlargement of the thyroid gland. It is difficult to estimate the quantity of diagnosed cases due to insufficient knowledge of the doctors about this pathology and difficulties of tuberculosis etiology diagnosis. Tuberculous etiology must be ruled out in all lesions on the median surface of the neck. Fine-needle biopsy can help to confirm the diagnosis of thyroid tuberculosis, but the final diagnosis is possible only with histological or cytological studies. The diagnosis of thyroid tuberculosis requires the use of most of all the methods used in the diagnosis of tuberculosis: from the simplest (such as X-ray or Mantoux test (with 2 international units of tuberculin) methods to modern rapid molecule-genetic tests XpertMTB/Rif that detect specific fragments of MTB DNA in serum or plasma). Ultrasound and computer tomography also help the clearing of the diagnosis. Surgical treatment in combination with antmycobacterial chemotherapy is effective.

Conclusions. Further investigations are needed to understand the definition, diagnosis and treatment of tuberculosis among other diseases of thyroid.

Keywords
Thyroid, tuberculosis, diagnosis, treatment.

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cerculosis [2, 12]. In 1878, Chiari described 7 cases of microscopically confirmed thyroid tuberculosis in an autopsy of 100 patients who died from disseminated pulmonary tuberculosis [5].

The thyroid gland is involved in the tuberculous process either hematogenously or when the infection spreads directly from the tuberculous focus to another organ, most often from the lymph nodes [20]. Some studies have shown that a paravertebral abscess can spread to the area of the thyroid gland [50]. The first description of primary thyroid tuberculosis in the form of a rapidly growing goiter with cervical lymphadenopathy without pulmonary involvement was made in 1893 by Bruns.

5 cases of thyroid tuberculosis were found in a study of 1200 cases of surgical intervention on the thyroid gland (1926) [9]. Rankin and Graham (1932) studied 20,758 cases of partial thyroidectomy at the Mayo Clinic in 1920–1930, and only 21 of them confirmed thyroid tuberculosis, which accounted for 0.1% of all thyroidectomies. Levitt (1952) found only 2 cases of thyroid tuberculosis among 2114 postoperative thyroid biopsies. Isolated cases of thyroid tuberculosis were also diagnosed by other researchers, [9, 15, 19, 32]. Bolis in Italy (1970) confirmed only 2 cases of fibrous-casous thyroid tuberculosis among 74,393 cases of postoperative biopsies. Subsequently, two fine-needle biopsy studies were conducted and 8 cases of tuberculosis were found among 1283 studies and 18 cases among 1565 cases [24].

The exact number of reported cases of thyroid tuberculosis is difficult to quantify, but to our knowledge, at least 186 cases are described in the English-language literature alone [2, 8, 33, 40, 42], four of which are diagnosed in children. In fact, it is difficult to estimate the number of diagnosed cases due to the lack of awareness of physicians about this pathology and the difficulty of ruling out a tuberculosis etiology in the diagnosis [39].

Clinical observations have found that the thyroid gland is more often involved in the tuberculous process with a generalized miliary process [40], and, as previously thought, in this case there are no clinical signs of damage to the thyroid gland [8, 30, 34, 46]. In most studies, patients with tuberculous lesions of the thyroid gland maintained clinical euthyroid status with its biochemical confirmation. However, Mosiman (1917) described 7 cases with clinical thyrotoxicosis, although its biochemical confirmation was impossible at that time. In 2010, a report from the Netherlands described a case of miliary tuberculosis with tuberculous thyroiditis (confirmed histologically and microbiologically), accompanied by thyrotoxicosis. T$_3$ level was > 309 nmol/L (control 65–110 nmol/L), T$_4$ – 4.6 nmol/L (control 1.2–3.0 nmol/L) and TSH was < 0.05 IU/L.

Subsequently, a variable clinical presentation of thyroid tuberculosis was demonstrated. It is usually presented with local symptoms associated with diffuse enlargement of the thyroid gland [28, 34]. Focal caseous tuberculosis of the thyroid gland is less common. It manifests itself as a local painless induration (node) with or without lymphadenopathy, mimicking thyroid cancer [1, 2, 9]. However, there is appearance of thyroiditis (painful swelling of the gland), as well as the formation of an acute or cold abscess with or without fistula formation [10, 12]. The development of fibrosis and fusion with adjacent tissues can sometimes give symptoms of compression in the form of dysphagia and dyspnea or paralysis of the recurrent laryngeal nerve [13].

A description of 5 variants of thyroid tuberculosis is proposed: multiple foci throughout the gland with miliary tuberculosis; goiter with caseosis; cold abscess, sometimes present on the anterior surface of the gland; chronic fibrosing tuberculosis (which mimics de Quervain’s thyroiditis due to the presence of giant cells, lymphocytes, and various fibrosis variants) and acute abscess formation [17]. Previously, the diagnosis of thyroid tuberculosis was made at autopsy. Currently, the diagnosis of thyroid tuberculosis is confirmed by needle aspiration biopsy [14]. Prior to the use of fine needle biopsy as a method for examining thyroid nodules, patients were subjected to surgical removal of the thyroid gland (if a tumor was suspected) and the diagnosis was made by the presence of *Mycobacterium tuberculosis* in biopsy samples [3, 32, 40, 45, 49].

Microscopically, tuberculosis of the thyroid gland is confirmed by destruction with caseous tuberculous granuloma. The histological diagnosis is based on the presence of epithelioid cell granulomas with peripheral lymphocytes, Pirogov—Langhans giant cells, and central caseous necrosis [26].

*Mycobacterium tuberculosis* is detected using the staining by Zeihl—Nelsen [4]. Epithelioid granuloma is also observed in sarcoidosis and subacute thyroiditis, but the presence of caseosis and acid-fast bacilli are specific for tuberculous thyroiditis [10, 31].

Complications of fine needle biopsy are rare and include subcutaneous hematoma, rarely tracheal trauma, and local infection [29]. Formation of a subcutaneous abscess at the site of a fine needle biopsy is rare [26].

Ultrasound and magnetic resonance studies in thyroid tuberculosis are described infrequently due to the rare pathology. Ultrasound of the thyroid gland shows heteroechogenicity with areas of hypoechogenicity, nodular and cystic formations mimicking carcinoma, multiple nodes, diffuse goiter,
or occasionally abscess. Tuberculous foci in the thyroid gland are usually hypoechoic. The abscess is anechoic and may contain internal shadows [9]. This usually results in regional lymphadenopathy.

Computed tomography (CT) can show an enlarged thyroid gland; nodes in the parenchyma have a reduced density compared to normal thyroid tissue. Swelling abscesses both inside the thyroid gland and under the skin are surrounded by a peripheral rim [26]. In addition, CT helps to determine other localizations of tuberculosis of the neck. With a tuberculous focus, a signal of medium intensity is recorded, more intense than that given by a normal thyroid parenchyma.

Contrast computed tomography can help to find caseous masses. The tomographic picture shows caseous center and a peripheral rim around due to acute inflammation, leading to compaction of the surrounding tissue («dermal sign») [21].

The results of magnetic resonance imaging in thyroid tuberculosis are described in single studies. The structure of a normal thyroid gland is homogeneous. The magnetic resonance signal coming from it is higher compared to that coming from the neck muscles [16]. In thyroid tuberculosis, histologically and microbiologically confirmed, the thyroid gland showed an average signal in both T1 and T2 modes, and the signal intensity was higher than in normal thyroid parenchyma.

Nevertheless, the clinical and radiological features of thyroid tuberculosis are nonspecific and histological examination is necessary for an accurate diagnosis. Tuberculosis of the thyroid gland is an uncommon disease and primary involvement of thyroid is even more rare. It is a rare disease even in countries in which tuberculosis is endemic. The diagnosis is often difficult as the clinical presentation has no distinct characteristics.

**Clinical case.** A 21-year-old man is admitted to the hospital because of painless swelling on the anterior surface of the neck, fatigue, malaise without fever and hemoptysis for 1 month. He was BCG vaccinated in the past. On examination: a dense swelling abscess in the left lobe of the left thyroid lobe with an exophytic component shows hypoechoic nodule at the lower pole of the thyroid gland. There is no clinical manifestations when swallowing, presumably originating from the formation on the anterior surface of the neck, mobile. Thyroid function tests: total T4 — 8.63 mg/dL (normal limits — 5.1—14.1), TSH — 0.51 μIU (normal limits — 0.27—4.2). Chest X-ray is normal. Ultrasound of the neck shows hypoechoic nodule at the lower pole of the left thyroid lobe with an exophytic component extending to the thymus; in the left lobe of the thyroid gland, calcifications are determined. The lymph nodes of the jugular chain are enlarged bilaterally. The changes described suggested thyroiditis. Ultrasound-guided fine-needle biopsy shows large areas of necrosis, epithelioid cell granuloma, and isolated cells of thyroid follicles. *Mycobacterium tuberculosis* is microscopically detected in the aspirate. A week after the biopsy, the tumor-like formation on the neck rapidly increased in size, pain and fluctuation appeared. Magnetic resonance imaging shows a low-intensity shadow in the trachea.

Several small lymph nodes in the neck are also noted. A subcutaneous nodule is observed in the zone corresponding to the thyroid gland. In addition, there is a focus in the C6 vertebra. The spinal cord is not changed. Abdominal ultrasound is normal. No other localizations of tuberculosis were found. ELISA analysis did not detect HIV. Final diagnosis: multifocal tuberculosis involving the cervical vertebrae and thyroid gland. Subcutaneous abscess drained. The patient underwent a course of anti-tuberculosis chemotherapy. After 6 months from the start of treatment, the tumor-like formation on the neck disappeared, the patient’s general state is satisfactory [27].

In a study comparing clinical and paraclinical symptoms and signs of tuberculosis in thyroid lesions among 26 patients, thyroid tuberculosis was confirmed in 7 cases and thyroid tuberculosis was only suspected in 19 cases. Acid-fast bacilli were found in 4 patients (57.1 %) in the aspirate obtained by fine-needle biopsy. A positive tuberculin skin test was observed only in 3 patients with confirmed tuberculosis (42.9 %). Microscopically, an epithelioid cell granuloma, Pirogov—Langhans giant cells and, in one case, signs of carcinoma were found. The majority of patients (63.2 %) with confirmed tuberculosis were observed to be euthyroid [3, 45].

The most common lesions in the medial anterior neck include thyroid-glossal dust cyst, lipomas, thyroid cancer, and occasionally median lymph nodes, especially lymph nodes just above the thyroid. Thyroid tuberculosis should be differentiated from various types of thyroiditis, including subacute (giant cell) thyroiditis [17], diffuse toxic goiter, and nodular goiter. Thyroid tuberculosis is also differentiated from sarcoidosis [22]. The diagnosis of tuberculosis is made in the presence of caseosis and acid-fast bacteria. Chronic fibrosis of the thyroid gland is associated with tuberculosis, mainly by European authors, although a clear relationship of sclerosing thyroiditis with tuberculosis remains doubtful [5].

It is especially important to differentiate thyroid tuberculosis from thyroid cancer in order to avoid unnecessary surgical intervention [2].
Sometimes the diagnosis of the thyroid gland is made erroneously when miliary tuberculosis and papillary thyroid carcinoma are combined, or previously diagnosed thyroid tuberculosis later turns out to be medullary thyroid cancer [1, 3, 18]. The differential diagnosis of tuberculous thyroiditis depends on the presence or absence of localized pain. If pain is the dominant clinical symptom, the differential diagnosis is performed between infectious thyroiditis (bacterial, fungal, viral) or subacute granulomatous thyroiditis (de Quervain, thyroid sarcoidosis, etc.). Due to the rarity of cases of tuberculous lesions of the thyroid gland, tuberculosis was suspected in patients suffering from pulmonary tuberculosis when they developed significant destruction of the thyroid gland with the formation of fistulas [25, 28]. Most patients present with diffuse enlargement of the thyroid gland [8, 28].

Bacteriological examination of the punctate and subsequent histological examination confirm the diagnosis of tuberculosis. De Quervain’s thyroiditis may resemble the histopathological features of thyroid sarcoidosis and mimic thyroid tuberculosis, however, caseous masses are absent in these diseases, unlike tuberculosis. In the absence of pain, thyroid tuberculosis may be mistaken for a malignant neoplasm; at the same time, these diseases can be combined [41].

We present our own clinical observations. Observation N 1 (subacute tuberculous thyroiditis in a patient with infiltrative pulmonary tuberculosis). A 46-year-old woman was treated in Kharkiv TB dispensary N 1 with a diagnosis: new case of infiltrative tuberculosis of the right upper lobe with destruction and bacterial excretion, drug resistance to isoniazid, streptomycin and ethionamide. She was admitted because of weakness, fatigue, weight loss of significant severity. There was swelling of the anterior surface of the neck. On examination, a formation was found on the anterior surface of the neck to the right of the midline, 3 · 2 cm in size, mobile when swallowing, hoarseness for 3 weeks. On palpation, the thyroid gland is sharply painful, enlarged to 1 degree. From disease history, it was established that the patient fell ill three weeks before admission, when the body temperature increased to 40—42 °C, she took antipyretic drugs, the body temperature decreased to 37.5—38.0 °C. Tuberculous contact has not been found. She made chest X-ray annually, last year it was normal. The patient's general state was of moderate severity. There was swelling of the anterior surface of the neck. The percussion sound was shortened above the right lung. Auscultation showed weakened breathing above the right lung, dry whistling rales.

Sputum tests showed MTB microscopically and subsequently on culture, resistant to isoniazid, streptomycin and ethambutol. Complete blood count: moderate leukocytosis (14.2 · 10^9/l), increased ESR (45 mm/hour). Urine test was within normal limits. Mantoux test was close to hyperergic (20 mm pappule). Chest X-ray showed an enrichment of the pulmonary pattern; small focal shadows of medium and low intensity in the right upper pulmonary lobe, destruction cavity 4.5 · 4.0 cm at the apex; the pulmonary root in the upper section is expanded.

Clinical symptoms of thyroid dysfunction were not identified.

Ultrasound of the thyroid gland: the volume of the thyroid gland is increased to 23.47 cm³, there are 2 nodes in the left lobe (7 · 5 and 5 · 4 mm). An ultrasound scan of the thyroid gland also revealed its heterogeneity, the presence of nodules, and cystic degeneration.

Fine-needle biopsy of the thyroid gland under X-ray control revealed epithelioid cells, giant multinucleated cells of the Pirogov—Langhans.

Thus, a patient with new case of infiltrative tuberculosis of the right upper pulmonary lobe with destruction and bacterial excretion was diagnosed with tuberculous thyroiditis, a diffuse-nodular form with an increase in the thyroid gland up to 1 degree, euthyroid.

The patient was prescribed a standard 5-component anti-tuberculosis treatment with correction after receiving data on the drug resistance of mycobacteria, as well as vitamins of group «B», hormone therapy (prednisolone according to a 10-day regimen, starting with 20 mg), calcium gluconate 10 % 10.0 ml intravenously N 10.

After 5 days, the patient’s body temperature returned to normal, pain in the thyroid gland significantly decreased. After 10 days, the pain and hoarseness disappeared. After 2 months, the patient stopped bacterial excretion. After 6 months, the cavity healed, a fibrous cord formed at the site of the cavity. In the upper lobe of the right lung, single intense foci, elements of linear foci were observed.

Observation N 2 (thyroid tuberculosis). A 22-years-old patient, who is a medical student, gradually developed swelling of the right side of the anterior surface of the neck. On examination, a formation was found on the anterior surface of the neck to the right of the midline, 3 · 2 cm in size, mobile when swallowing. The surface of the formation is smooth, the consistency is dense. The edges of the formation are unclear on palpation. Formation is associated with the right lobe of the thyroid gland. There were no clinical symptoms of thyroid dysfunction (hyper- or hypothyroidism). Nodular euthyroid goiter was previously diagnosed. ESR — 55 mm/hour, other parameters of complete blood count were normal. Chest X-ray showed no pathological changes. The levels of
Thus, the diagnosis of thyroid tuberculosis requires the use of most of all the methods used in the diagnosis of tuberculosis: from the simplest (such as X-ray or Mantoux test (with 2 international units of tuberculin) methods to modern molecular-genetic tests XpertMTB/Rif that detect specific fragments of DNA of Mycobacterium tuberculosis in serum or plasma). Ultrasound and computed tomography also contribute to clarifying the diagnosis. Ultrasound shows heterogeneous hypoechoic masses, and computed tomogram reveals a low-intensity shadow of a «swelling» around the formation and regional lymphadenopathy [38].

Tuberculous etiology must be ruled out in all lesions on the median surface of the neck [28]. Fine-needle biopsy [10] can help to confirm the diagnosis of thyroid tuberculosis, but the final diagnosis is possible only with histological or cytological studies. Surgical treatment in combination with antitubercular chemotherapy is effective [43, 44, 50]. Further research will contribute to a better understanding of the definition, diagnosis and treatment of tuberculosis among other thyroid diseases.
Туберкульоз щитоподібної залози: рідкісна локалізація чи рідкісна діагностика? Огляд літератури

Мета роботи — вивчення частоти, клінічної картини, діагностики та лікування туберкульозу щитоподібної залози.

Матеріали та методи. Аналіз даних світового досвіду та власних спостережень.

Результати та обговорення. Туберкульоз щитоподібної залози є рідкісною локалізацією цього захворювання. На сьогодні більшість авторів вважають, що туберкульоз щитоподібної залози діагностується в 0,1—1 % всіх відомих випадків туберкульозу. Клінічними спостереженнями встановлено, що щитоподібна залоза частіше втягується в туберкульозний процес при генералізованому міліарному процесі, і, як вважалося раніше, в цьому випадку відсутні клінічні ознаки ураження щитоподібної залози.

Огляд даних світового досвіду та власних спостережень. Незважаючи на рідкісність туберкульозу щитоподібної залози, її діагностика є важливою. У контексті боротьби з туберкульозом необхідно зосередитися на розумінні та ефективному лікуванні цього захворювання.

44. Tabacu E, Galie N, Galbenu P, Mitrea M. Thyroid tuberculosis — a clinical case // Pneumologia.— 2000.— Vol. 49 (1).— P. 41—44.
47. Terzidis K, Tourni P, Kakepoku E, Elevizaki M. Thyroid tuberculosis // Hormones (Athens).— 2007.— Vol. 6 (1).— P. 75—79.
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наї залози. Продемонстровано різну клінічну картину туберкульозу щитоподібної залози. Зазвичай виявляється місцевими симптомами, пов’язаними з дифузним збільшенням щитоподібної залози. Оцінити кількість виявлених випадків важко через недостатню поінформованість лікарів про цю патологію та труднощі діагностики етиології туберкульозу. При всіх ураженнях середньої поверхні щитоподібної залози необхідно виключити туберкульозну етиологію. Тонкоголкова біопсія може допомогти підтвердити діагноз туберкульозу щитоподібної залози, але остаточний діагноз можливий тільки за допомогою гістологічного або цитологічного дослідження. Діагностика туберкульозу щитоподібної залози вимагає використання більшості методів діагностики туберкульозу: від найпростіших (наприклад, рентгену чи проби Манту (з 2 міжнародними одиницями туберкуліну) до сучасних експрес-молькулярно-генетичних тестів XpertMTB /Rif, які виявляють специфічні фрагменти ДНК мікобактерій туберкульозу у сироватці або плазмі). Ультразвукова діагностика і комп’ютерна томографія також допомагають уточнити діагноз. Ефективним є хірургічне лікування в поєднанні з антимікобактеріальню хіміотерапією.

Висновки. Необхідні нові дослідження для зрозуміння дефініції, діагностики та лікування туберкульозу серед інших захворювань щитоподібної залози.

Ключові слова: щитоподібна залоза, туберкульоз, діагностика, лікування.

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