

**ЩИТОПОДІБНА ЗАЛОЗА – ІСТОРИЧНИЙ НАРИС****Тетяна САВЧУК**

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**THYROID GLAND – HISTORICAL ESSAY****Tetiana SAVCHUK**Bukovynian State Medical University, Chernivtsi (Ukraine),  
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**Савчук Татьяна. Щитовидная железа – исторический очерк. Постановка проблемы.** Первые изображения щитовидной железы можно встретить в древнеегипетских и древнекитайских скульптурах датируемых 2700 годами до нашей эры. **Историографическая база.** Щитовидная железа была известна уже авторам древности и средних веков, которые хотя и описывали зоб и кретинизм, но еще не связывали эти заболевания с расстройством функции железы. **Цель исследования** – проанализировать исторические вехи становления тиреологии. **Основная часть.** Еще в 1600 году до нашей эры одними из первых, китайские лекари в лечении увеличенной щитовидной железы стали использовать морепродукты и водоросли, при этом они не знали, что лечебный эффект возникает от йода. Наибольший интерес к изучению щитовидной железы проявился в греко-римский период. Великий ученый греко-римского периода Галлен считал, что щитовидная железа это некий “буфер” между сердцем и головным мозгом. В византийском периоде ученые продолжили исследования в области щитовидной железы. Новый этап в осмыслении роли щитовидной железы и ее патологии связан с Эпохой Возрождения. Взлет науки и искусства в этот период происходил в приальпийских регионах, и эндемический зоб не остался незамеченным естествоиспытателями, врачами, а также художниками той поры. В XIX веке стала активно развиваться хирургия щитовидной железы, при этом основной проблемой хирургов оставалась высокая смертность. После получения искусственного тироксина в лечении гипотиреоза (недостаточности гормонов щитовидной железы) началась новая эпоха. Вторая половина 20 века ознаменовалась активным исследованием причин аутоиммунных заболеваний, таких как диффузный токсический зоб, аутоиммунный тиреоидит. **Вывод.** Безусловно, будущее развития знаний в области щитовидной железы за исследованиями в области генетики заболеваний, создание новых препаратов и методов диагностики аутоиммунных болезней щитовидной железы.

**Ключевые слова:** *эндокринология, щитовидная железа, тиреология, тироксин.*

**Formulation of the problem.** The first images of the thyroid gland can be found in ancient Egyptian and ancient Chinese sculptures dating back to 2700 BC. At that time, they did not know anything about the existence of the thyroid gland, but they already depicted people with an enlarged neck – this was a goiter or the second name - struma. A goiter or struma is an enlargement of the thyroid gland in size. Currently, the norms for the volume of the thyroid gland have been determined for both women and men. The normal volume of the thyroid gland for women is up to 18 cubic centimeters, for men up to 25 cubic centimeters. The history of studying the functions and structure of the thyroid gland stimulated the discovery of drugs for the correction of pathological conditions. These questions stimulate the analysis of historical discoveries in thyroidology<sup>1</sup>.

**Historiographic base.** The thyroid gland was already known to the authors of antiquity and the Middle Ages, who, although they described goiter and cretinism, did not yet associate these diseases with a disorder of the function of the gland. The thyroid gland was named by Thomas Wharton in 1656, based on its shape (from the Greek shield). Galen considered the thyroid gland to be part of the vocal apparatus. Morgagni, Haller and other famous scientists of the 18th century thought that it produced “lubricants” for the organs of the neck.

Given its rich blood supply, some authors viewed the thyroid gland as a vascular shunt, preventing the sudden flow of excess blood into the brain, while others considered it to be just a decoration for the neck. Modern ideas about the thyroid gland began to take shape in 1874 when Gull established the existence of “cretinoid” disease in adults. The onset of this condition after removal of the gland for goiter was first noted by Kocher and the Reverdin brothers in 1893. They called this condition cachexia strumipriva. The fact that this disease, cretinism, and myxedema, which occur spontaneously, have a common cause, was first pointed out by Semon. Baumann was the first to establish a high iodine content in iron in 1896, and Ostwald prepared an extract of thyroglobulin containing iodine in high concentration<sup>2</sup>. However, it was not until 1917 that Kendall isolated a hormone that he called thyroxine, mistakenly considering it an indole derivative. Harington in 1927 accurately established its structure and synthesized it. Unlike most hormones, thyroid hormone accumulates in the gland, and since it is stable and effective when administered orally, it is sufficient to ingest the dried thyroid gland to obtain a therapeutic effect<sup>3</sup>.

**The aim of the research** is to analyze the historical milestones in the development of thyroidology.

**Main part.** Back in 1600 BC, one of the first Chinese

<sup>1</sup> Churilov L.P., Stroev Yu.I. “Rytsari shchita: istoriya idey v troidologii. Prodolzheniye i: antichnost', srednevekov'ye i renessans” [The knights of a shield: history of ideas in thyroidology. Proceeding i: antiquity, the middle ages and renaissance], *Translational Medicine*, 2014, N 1, P. 105–112, URL: <https://doi.org/10.18705/2311-4495-2014-0-1-105-112> [in Russian].

<sup>2</sup> Slater S.D. “The discovery of thyroid replacement therapy”, *JLL Bull., Commentaries on the history of treatment evaluation*, 2010, P. 1–12 [in English].

<sup>3</sup> Lyuyshi chun'tsyu [Mr. Liu's Spring and Autumn], *Per. s kit. G. A. Tkachenko, Moskva, Mysl'*, 2001, P. 90 [in Russian].

healers in the treatment of an enlarged thyroid gland began to use seafood and algae, while they did not know that the healing effect arises from iodine. For the first time, goiter is mentioned in Chinese texts approx. 2700 BC A.D. 85<sup>4</sup>. The ancient Chinese physician Cui Chindi divided neck tumors into hard, incurable and soft, curable. The Qin dignitary Li Buwei (291–235) wrote in the famous text “The Spring and Autumn of Mr. Liu” in 239 BC: “Where the water is light, there are many bald and goiter”. The Chinese alchemist Kou Hong in 340 recommended the alcoholic extract of algae as a remedy for goiter. The legendary Sun Simyao (581–682), a classic of Chinese medicine, a doctor of the Tang dynasty, “Buddha of Healing”, the creator of a 30-volume clinical encyclopedia, which was the basis of traditional medicine in China until the beginning of the 20th century, in the treatise “Beiji Qianjin Yaofang – The Most Important Recipes worth a thousand bars of gold for each urgent case” (652) recommended not only for goiter, but – most surprisingly – for the treatment of children with developmental delay – raw or dried cervical gland (in Chinese: “e”) sheep, deer or buffalo, as well as its juice! Consequently, the ancient Chinese knew about the connection between cretinism and goiter and that the drawing of the thyroid glands also helps with “unpleasant” developmental delay! In this they are centuries ahead of the medicine of Europe. The emperor of the Qing dynasty Kangxi (1654–1722) ordered each inhabitant of Mukden to eat 2 kg of seaweed per year<sup>5</sup>. And for three hundred years this decree has been strictly implemented in Mukden. Thanks to him, the inhabitants of Mukden, despite the geochemical deficiency of iodine in the non-coastal regions of Manchuria, do not suffer from endemic goiter<sup>6</sup>.

The greatest interest in the study of the thyroid gland manifested itself in the Greco-Roman period. The prominent representatives of this period were Aelius Celsius (25 BC 50 AD), who was one of the first to distinguish various types of thyroid tumors. He described thyroid tumors depending on their content: liquid or thick component. Currently, this means a cyst in the thyroid gland, the contents of which can be liquid or thick (colloid). Celsius suggested either removing the cysts of the thyroid gland, or, if this is not possible, injecting destructive substances into them. It is important to note that the method of reducing thyroid cysts using alcohol (ethanol) is currently working very well. Today, if a patient has a cyst in the thyroid gland that interferes cosmetically, presses or makes it difficult to swallow food, ethanol sclerotherapy (“Thyroid nodule sclerotherapy”) is a good and effective method<sup>7</sup>.

No less great scientist of the Greco-Roman period Gallen (130–200 AD) actively studied the thyroid gland. Gallen believed that the thyroid gland is a kind of “buffer” between the heart and the brain. In this case, the cartilage in the larynx, in front of which the thyroid gland lies, was called “thyroid” or “oblong shield”. Gallen believed that the thyroid gland secretes a substance that

lubricates the cartilage of the larynx, followed by movement and sound. The doctor of the gladiatorial school and the ancient pathologist Claudius Galen of Pergamon – believed that the function of the thyroid gland is absorption, he considered the goiter to be a protrusion of the larynx, but he knew about the pituitary gland, its choroid plexuses, the role of the recurrent laryngeal nerve in voice formation and developed a coherent theory about the transport of vital heat from the pituitary gland to nerves and thyroid gland, reminiscent of the provisions on the pituitary-thyroid regulation of the basal metabolism<sup>8</sup>.

In the Byzantine period, scientists continued research in the field of the thyroid gland.

So the healer Aetios (527–665 AD), approximately, in 550 A.D. one of the first to describe the connection between the enlargement of the thyroid gland and changes in the eyes (the so-called ophthalmopathy) (“Thyrotoxicosis – ophthalmopathy”). Aetios (527–665) described both simple goiter and exophthalmic, referring to the Greco-Roman surgeon Leonidas of Alexandria, who warned of the possibility of aphonia in case of damage to the laryngeal nerve due to surgical treatment of these ailments, similar descriptions of goiter as “bronchocele” were given by Pavel Eginat (665–690), which apparently differentiated its hyperthyroid – “hyperemic” forms.

In the seventh century AD, the Greek physician Paul of Aegina was one of the first to describe the technique of removing the thyroid gland. Moreover, in 990, Ali-ibn-Abbas was one of the first to report the surgical removal of a goiter<sup>9</sup>.

During the Renaissance, the thyroid gland was not only interested in doctors, but also artists and anatomists.

In 1475, the Chinese physician Wang Hei proposed the use of dried pig thyroid gland to treat an enlarged thyroid gland. Of course, at present such methods are not used in the treatment of thyroid diseases<sup>10</sup>.

The great Leonardo da Vinci (1452–1519) was one of the first to depict the thyroid gland, describing in detail its vessels and nerves<sup>11</sup>.

A new stage in understanding the role of the thyroid gland and its pathology is associated with the Renaissance. The rise of science and art during this period took place in the Alpine regions, and the endemic goiter did not go unnoticed by naturalists, doctors, and also artists of that time. It has repeatedly happened in history that medical science helped art, and art helped scientific medicine. This is exactly what happened in the thyroidology of the Renaissance: the first anatomically and topographically accurate description of the human thyroid gland, its sketch, which was dozens of years ahead of the development of the anatomy of that era, one of the first hypotheses about its role in the body – does not belong to a doctor or a professional anatomist. and the great Leonardo da Vinci (1452–1519).

In the 17th and 18th centuries, more and more researchers

<sup>4</sup> Stroyev Yu. I., Churilov L. P. “Istoriya zoba” [Goiter history], *Aktual'n. probl. transportn. med.* [Actual. probl. transport medicine], Odessa, 2012, N 2(28), P. 149–155 [in Russian].

<sup>5</sup> Khan Niazi A., Kalra S., Ilfan A., Islam A. “Thyroidology over the ages”, *Ind. J Endocrinol. Metab.*, 2011, Vol. 15 (Suppl. 2), P. 121–126 [in English].

<sup>6</sup> Hamdy R. C. “Editorial. The Thyroid Gland: Brief Historical Perspective”, *South. Med.J.*, 2002, URL: <https://pubmed.ncbi.nlm.nih.gov/12005002> [in English].

<sup>7</sup> Ignjatovic M. “The thyroid gland in works of famous old anatomists and great artists”, *Langenbecks Arch. Surg.*, 2010, Vol. 395, P. 973–985 [in English].

<sup>8</sup> Leoutsakos V. A. “Short history of the thyroid gland”, *Hormones*, Athens, 2004, Vol. 3, N 4, P. 268–271 [in English].

<sup>9</sup> Nere Zh. Mikelandzhelo 1475–1564 [The Michelangelo 1475–1564], Moskva, ArtRodnik, 2004, 96 p. [in Russian].

<sup>10</sup> Stroyev Yu. I., Churilov L. P., Agapov M. M. “Klinicheskaya patofiziologiya yuvenil'nogo metabolicheskogo sindroma: rol yunosheskogo dispituitarizma, displazii soyedinitel'noy tkani i autoimmunnogo tiroidita” [Clinical pathophysiology of juvenile metabolic syndrome: the role of juvenile dyspituitarism, connective tissue dysplasia and autoimmune thyroiditis], *Patol. fiziol. eksperim. terap.* [Patol. fiziol. experimental therapist.], 2011, N 3, P. 3–15 [in Russian].

<sup>11</sup> Ahmed A. M., Ahmed N. H. “History of disorders of thyroid dysfunction”, *East Mediterr. Health J.*, 2005, Vol.11, N 3, P. 459–469 [in English].

began to pay attention to the function of the thyroid gland. After the discovery of iodine in 1811 by Bernard Courtois, researchers from all over the world began to study its therapeutic effect on the thyroid gland. One of the first Austrian physician Jean-François Coindet (1821) and other scientists of that time described the therapeutic effect of iodine on an enlarged thyroid gland. In 1877, the great German surgeon Theodor Billroth noted that the therapeutic effect of iodine is maximum in the early stages of an increase in the volume of the thyroid gland, while with a large thyroid gland, the therapeutic effect of iodine is minimal. The well-known Lugol's solution (iodine solution), which was invented by the French chemist Jean Lugol in 1829. Initially by the author, Lugol's solution was intended for the treatment of tuberculosis, but later, the solution began to be used for more effective treatment of thyrotoxicosis, a condition in which the thyroid gland produces excessive hormones<sup>12</sup>.

In the early 19th century, scientists such as Karl Adolph von Basedow (1799–1854) and Robert James Graves (1796–1853) described the link between excess thyroid hormone production and changes in the heart and eyes. The so-called “Merserburg Triad” proposed by Besed. Currently, when detecting thyrotoxicosis, in addition to the name diffuse toxic goiter, experts often use the phrase “Graves' disease” or “Basedow's disease”. In the Russian-language literature, one can often find the name of diffuse toxic goiter as “Graves' disease.”<sup>13</sup> The great Russian surgeon was the first in Russia to perform thyroid surgery and anatomist Nikolai Ivanovich Pirogov. Since 1877, only 1 patient has died of complications in Billroth. At the same time, special hemostatic clamps were described to them.

An invaluable contribution to the development of thyroid surgery was made by such doctors as Sergei Petrovich Fedorov, Vladimir Andreevich Opiel, Oleg Vladimirovich Nikolaev and Elizaveta Semenovna Drachinskaya.

In 1906, the American surgeon Cryle reported 132 radical lymph node dissections (removal of affected lymph nodes) of the neck for thyroid cancer. The operation included removal of the affected lymph nodes of the neck, sternocleidomastoid muscle and internal jugular vein. Currently, the Kraille operation is rarely performed, due to its high trauma and a pronounced unsatisfactory cosmetic result. After receiving artificial thyroxine in the treatment of hypothyroidism (thyroid hormone deficiency), a new era. Artificial thyroxine is identical to human thyroxine, which means that when a thyroxine tablet is received, the patient's body does not recognize it as foreign or “not his own”. Thyroxine has become widely used by endocrinologists in the treatment of hypothyroidism, surgeons were able to more safely perform operations in the amount of complete removal of the thyroid tissue, without fear of exposing the patient to hypothyroidism<sup>14</sup>. The second half of the 20th century was marked by active research into the causes of autoimmune diseases, such as diffuse toxic goiter, autoimmune thyroiditis. Revealed antibodies to

thyroperoxidase, antibodies to thyroglobulin, antibodies to TSH receptors. By the end of the 20th century, the cycle of synthesis of thyroid hormones was most fully described with a detailed description of their movement inside the cell, followed by secretion into the general bloodstream and effects on the body.

**Conclusion.** Undoubtedly, the future of the development of knowledge in the field of the thyroid gland lies in research in the field of genetics of diseases, the creation of new drugs and methods for diagnosing autoimmune diseases of the thyroid gland.

**Савчук Тетяна. Щитоподібна залоза – історичний нарис. Постановка проблеми.** Перші зображення щитоподібної залози можна зустріти в давньоєгипетських і старокитайських скульптурах датуються 2700 роками до нашої ери. **Історіографічна база.** Щитоподібна залоза була відома вже авторам давнини і середньовіччя, які хоча і описували зоб і кретинізм, але ще не пов'язували ці захворювання з розладом функції залози. **Мета дослідження** – проаналізувати історичні віхи становлення тиреології. **Основна частина.** Ще в 1600 році до нашої ери одними з перших, китайські лікарі в лікуванні збільшеної щитоподібної залози стали використовувати морепродукти і водорості, при цьому вони не знали, що лікувальний ефект виникає від йоду. Великий вчений Галлен вважав, що щитоподібна залоза це якийсь “буфер” між серцем і головним мозком. У 19 столітті стала активно розвиватися хірургія щитоподібної залози, при цьому основною проблемою хірургів залишалася висока смертність. У 1881 році Більрот один з перших в Європі доповів про 48 успішних операцій на щитоподібній залозі. Після отримання штучного тироксину в лікуванні гіпотиреозу (недостатності гормонів щитоподібної залози) почалася нова епоха. Друга половина 20 століття ознаменувалася активним дослідженням причин аутоімунних захворювань, таких як дифузний токсичний зоб, аутоімунний тиреїдит. Виявлено, антитіла до тиреопероксидази, антитіла до тиреоглобуліну, антитіла до рецепторів ТТГ. **Висновок.** Безумовно, майбутнє розвитку знань в області щитоподібної залози за дослідженнями в галузі генетики захворювань, створення нових препаратів і методів діагностики аутоімунних захворювань щитоподібної залози.

**Ключові слова:** ендокринологія, щитовидна залоза, тиреологія, тироксин.

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<sup>12</sup> Pozilli P. “Blessed with exophthalmos in Michelangelo's Last Judgement”, *Open Journal of Microphysics*, 2003, Vol. 96, N 9, P. 688–690 [in English].

<sup>13</sup> Stroyev Yu. I., Churilov L. P. “Samyi tyazhelyi element zhizni. K 200-letiyu otkrytiya yoda” [The hardest element of life. To the 200th anniversary of the discovery of iodine], *Biosfera* [The Biosphere], 2012, T. 4, N 3, P. 343–372 [in Russian].

<sup>14</sup> Toni R. I., Ghigo E., Roti E., Lechan R. M. “Endocrinology and art. Acromegaly and goiter in the Pre-Columbian, Mesoamerican population”, *J. Endocrinol. Invest.*, 2007, Vol. 30, N 2, P. 169–170 [in English].