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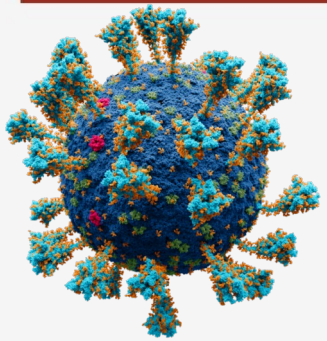

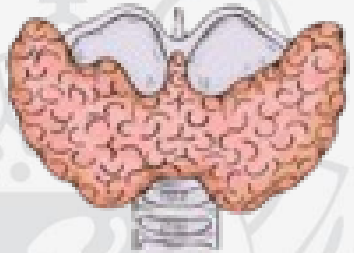

COVID-19 AND HASHIMOTO'S DISEASE

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Disclosure:

I have nothing to disclose, just say thanks to organizers, informing that the study is a basis of M.D. Thesis by Mr. D.S. Iakovlev and M.S. Thesis by Mr. M.G. Normatov

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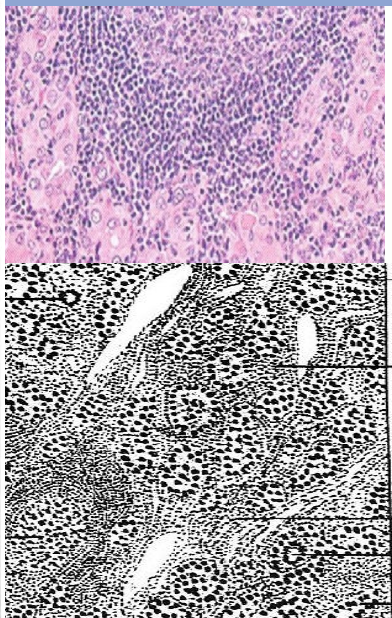
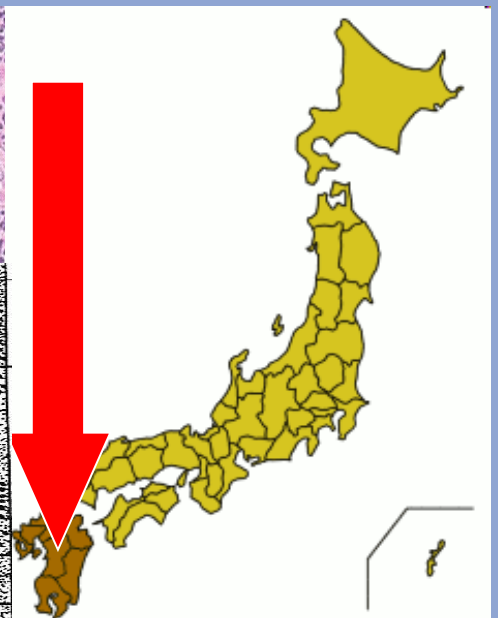
In 1912 Dr. Hakaru Hashimoto (1881-1934) has described chronic autoimmune thyroiditis (as "lymphomatous goiter") in Kyushu island, famous for its largest birthplaces of iodine-containing ores. That was the first pathohistological description of human cell-mediated autoimmune disorder in the history of Pathology.

A surgeon described 4 female cases [Hashimoto H. Zur Kenntnis der lymphomatösen Veränderung der Schilddrüse (Struma lymphomatosa). Archiv für klinische Chirurgie (Berlin) 1912; 97:219—48]



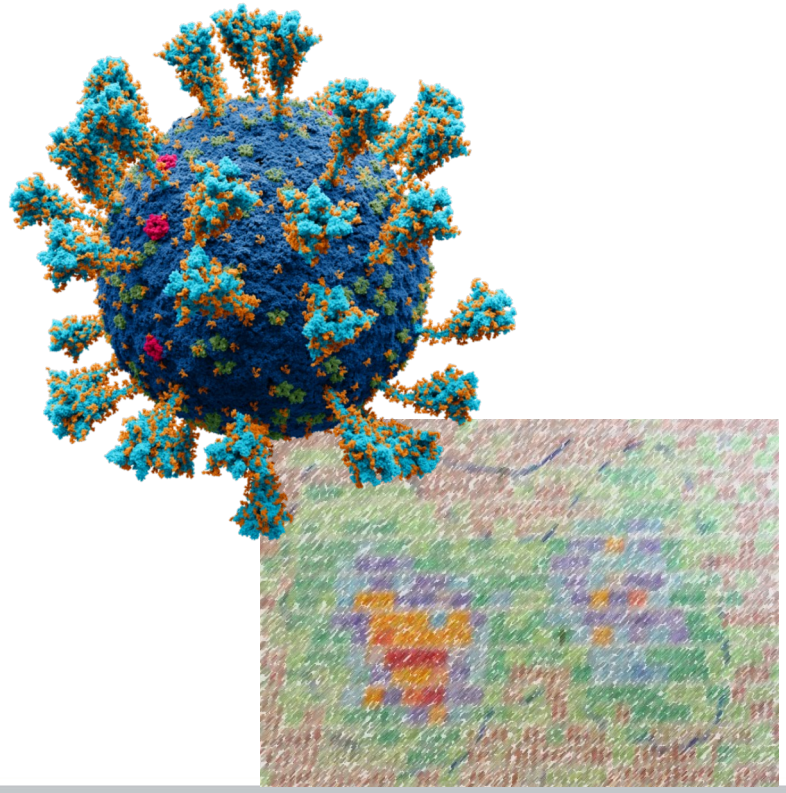


During next 100 years the prevalence of Hashimoto disease dramatically i**ncreased worldwide** (maybe due to influence of excessive **iodine and other adjuvant factors**) and it became globally **most frequent autoimmune disorder and most prevalent endocrinopathy,** a leading reason of hypothyroidism in wast areas with sufficient or excessive iodine supply.

RELEVANCE AND MATERIAL OF THE STUDY

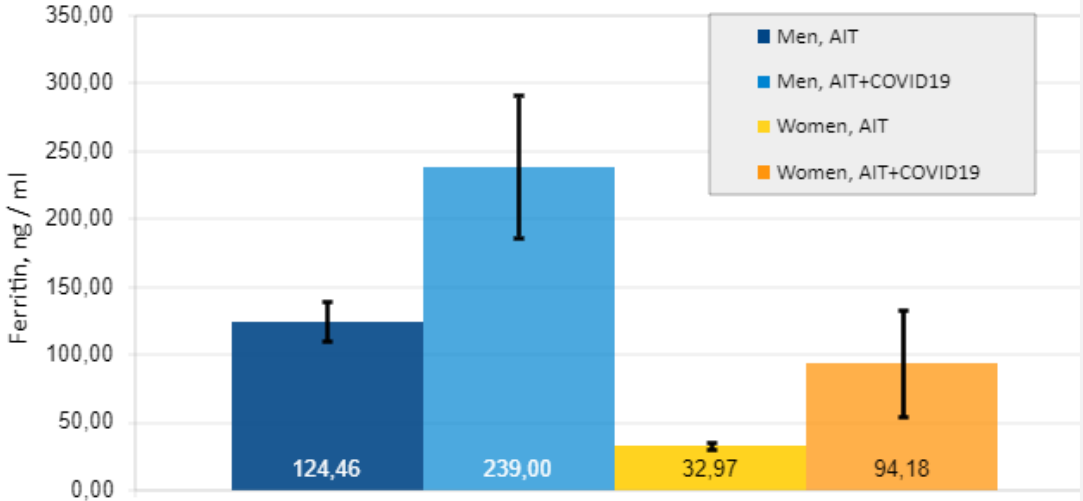
The high incidence of Hashimoto's autoimmune thyroiditis (AIT) in the global population and the spread of COVID-19 pandemic both determine the hogh incidence of their comorbidity and explain the the relevance of studying patients with combination of these diseases.

Hence, 214 individuals (160 females) suffered from AIT and acute COVID-19 of varying severity between January 2020 and October 2021 were studied. Two of the patients experienced an extremally severe cytokine storm.



Because low levels of iron and ferritin are associated with hypothyroidism [Rayman MP, 2018] and due to role of ferritin in COVID-associated immunopathology [Shoenfeld Y. et al., 2021] we studied ferritin in AIT and in AIT+COVID:

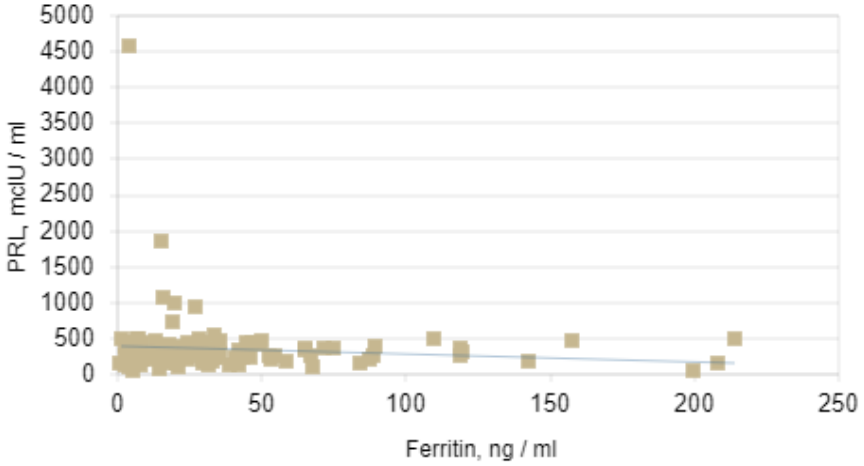
- In AIT without COVID-19, the **ferritin** level was **124.5 ± 14.6 ng/ml** in men and much lower (**33.0 ± 2.8 ng/ml**) in women ($p<0.01$), which is below optimum (60 ng/ml). In the acute phase of COVID-19, the **ferritin** level definitely increased depending on the severity of the COVID-19, and in severe pneumonia it reached **2939.8 ng/ml**.

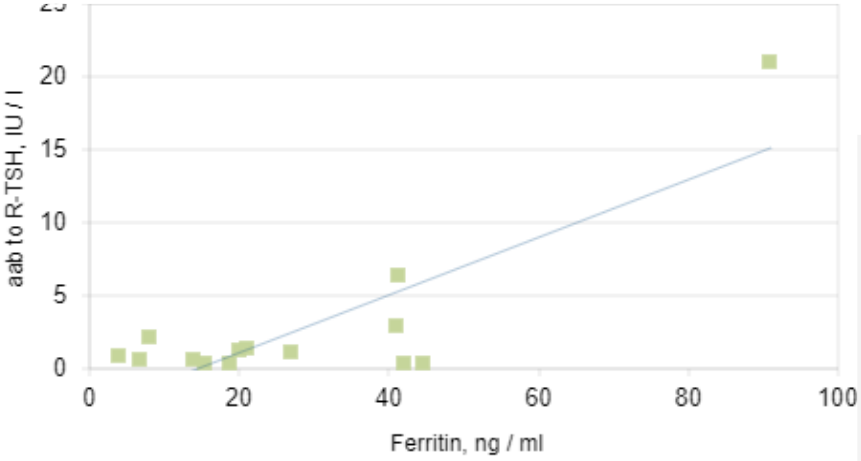


Analysis of the **ferritin** level in long term of post-COVID rehabilitation period showed that its return to normal values proceeded very slow.

- Thus, in men with AIT+COVID-19, the **ferritin** level during the rehabilitation period remained at the upper limits of the norm and amounted to **239.0 ± 52.7 ng/ml** (the difference with the male AIT patients without COVID-19 was statistically significant, **p <0.001**),
- and in women with AIT+COVID-19, in long rehabilitation period it was: **94.2 ± 39.4 ng/ml** (the difference with female AIT group without COVID-19 was also significant, **p <0.01**).
- Generally those AIT patients with anemia and lowest ferritin had tendency to lower thyroid function and stronger autoimmunity.

The level of ferritin in individuals with AIT who did not suffer from COVID-19 fluctuated within the normal range with a tendency to its lower limit and inversely correlated with prolactin level (r=-0.11).





But ferritin in AIT strongly positively correlated with the level of autoantibodies to TSH- receptors (r=0.82); even stronger than with hemoglobin (r=0.47), and weakly posiitively correlated – with body mass index (r=0.23), freeT3 (r=0.13), and with iron levels (r=0.07).

THYROID STATUS AFTER COVID-19 IN AIT PATIENTS IN FACT DID NOT SIGNIFICANTLY CHANGE, AND LEVELS of anti-TG and anti-TPO autoantibodies even tended (P<0.1) to decrease

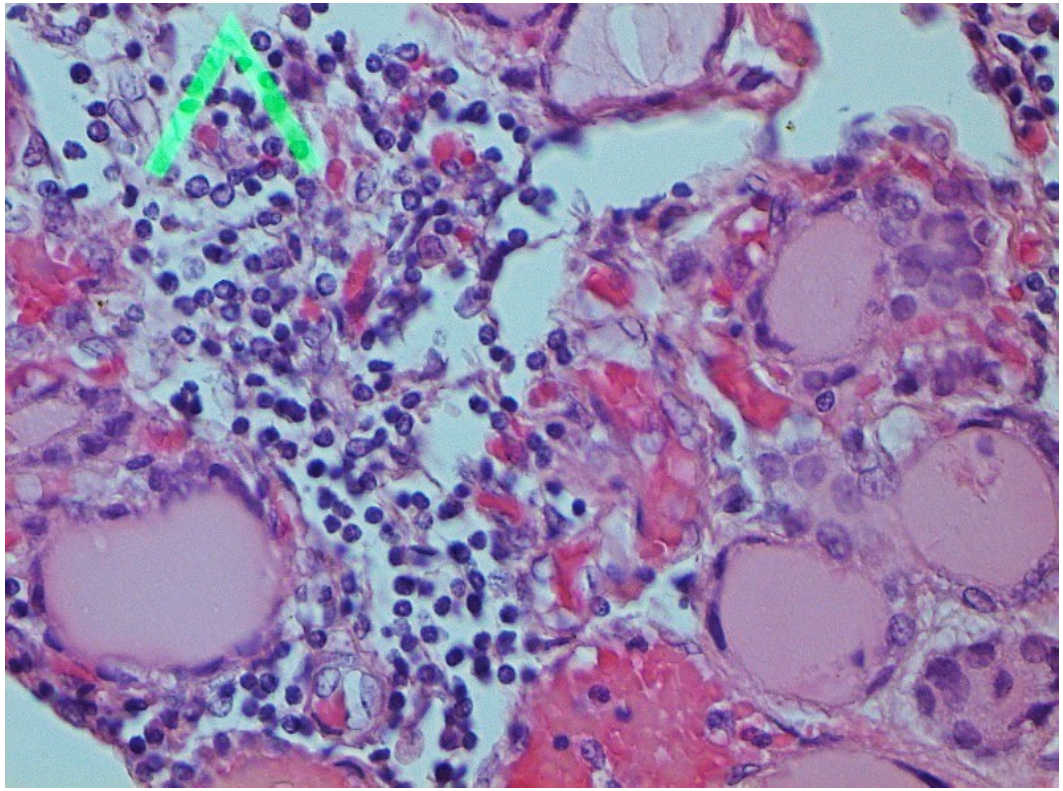
Immunoendocrine parameter	BEFORE COVID-19	AFTER RECOVERY + 6.5 months
TSH, μIU/ml	1.81±0.22	1.50±0.17
Free T4, pM/l	14.90±1.24	14.51±0.70
Free T3, pM/l	4.48±0.51	5.02±0.32
Anti-TG, IU/ml	**71.93±33.30**	**7.69±1.87***
Anti-TPO, IU/ml	**136.4±26.0**	**37.6±22.7***
Anti-TSHR, IU/l	2.79±1.62	1.66±0.90
Prolactin,μIU/ml	359.8±84.5	303.0±35.4
Cortisol, nM/l	417.8±43.2	419.3±44.9

BLOOD LYMPHOCYTES IN AIT AND IN AIT+COVID-19

Patients with Hashimoto's autoimmune thyroiditis		Average content of lymphocytes, ×10^9/l	Average lymphocyte count, %
Non-COVID-19 AIT sufferers		2.32±0.04	35.57±0.47
COVID-19 +AIT sufferers	Acute phase of the disease	1.88±0.14	32.02±2.37
	Convalescence period	2.27±0.09	36.27±0.85

Blood lymphocyte absolute count and relative % was high-normal in AIT, but in acute COVID-19 decreased with subsequent normalization. This can be related not only to viral effects, but also to emigration of lymphocytes from the blood to the involved tissues during acute COVID-19 and may play a part in multi-organ post-covid autoimmune disorders.

Thyroid definitely is among the places of lymphocytic infiltration during COVID-19 and is altered by SARS-CoV-2:

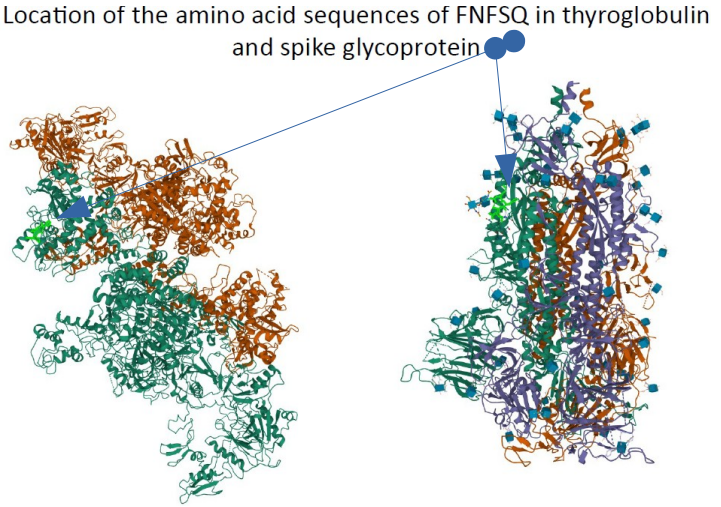


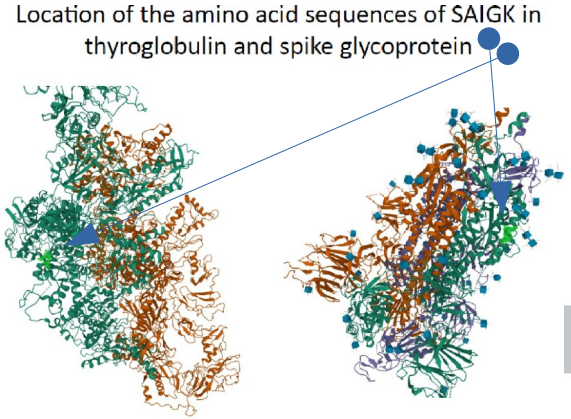
Micrograph of a section of the thyroid gland. H&E staining, ×200. Female patient X., aged 34, died of subtotal COVID-19 pneumonia with generalization of the process after caesarean section at 27–28 weeks of pregnancy. **She had not AIT in anamnesis;**
In the preparation: uneven small follicles of thyroid gland; lining of epithelial cells with large clear nuclei (possibly virus-induced); ^ marks focal lymphocytic infiltration (courtesy of Prof. Vsevolod A. Zinserling)

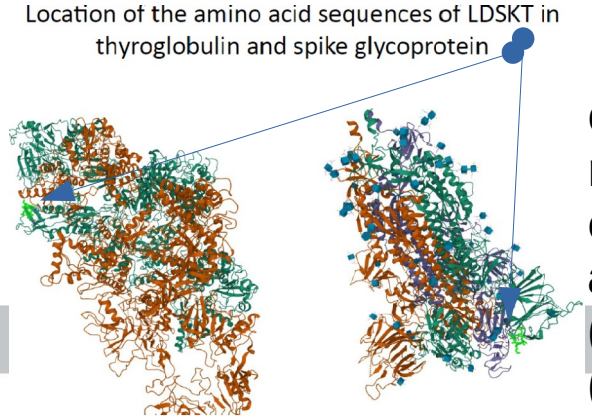
Stroev YI., Zinserling V.A., Churilov L.P., Yakovlev D.S. Health is the basis of human potential: problems and ways to solve them. 2021;16(1):378-388. eLIBRARY ID: 47669181, EDN: XOTDIB (in Russian)eLIBRARY ID: 47669181 EDN: XOTDIB

MOLECULAR MIMICRY BETWEEN KEY THYROID AUTOANTIGENS AND IMMUNODOMINANT PROTEIN OF SARS-CoV-2 MAY PROVOKE AUTOIMMUNITY

Thyroid autoantigens	Shared pentapeptides
Thyroglobulin (P01266)	FNFSQ, SAIGK, LDSKT
Thyrotropin receptor (P16473)	ICGDS, LLPLV
Thyroid peroxidase (P07202)	RAAEI







Our bioinformatic study with use of databases PDB and AlphaFold **revealed 6 pentapeptides common for thyroid autoantigens and SARS-CoV-2 (P0DTC2) spike glycoprotein (shown with grass-green).**

Conclusions

Ferritin in AIT tends to be low/low normal. Iron deficient anemia is associated with worse AIT.

Ferritin in AIT comorbid with COVID-19 significantly increases and requires long time for complete normalization.

In general, experienced COVID-19 did not aggravate the course of concomittant AIT, antithyroid autoantibodies level even tended to get lower for some time.

Thyroid is involved in COVID-19 with lymphocytic infiltration, at least in some cases. Antigen mimicry between key thyroid autoantigens exists, but its pathogenic role is unclear.


THANK YOU FOR ATTENTION!
Σας ευχαριστώ για την προσοχή σας!
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