

Healthy Life And Longevity

Thyroid Function in longevity



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- ❖ The past century has been marked by the **rapid growth of the oldest age groups (centenarians)** due to the overall increase of populations in almost all regions of the world as well as the concurrent decrease in leading causes of death.
- ❖ **Health organisations, medical knowledge and clinical practice** are among the contexts that **have most strongly felt the impact of this new patient's** arrival on the scene.
- ❖ **With age changes occur in all body systems**, including endocrine system **and changes in thyroid function are particularly important for its central role in metabolism, growth, immunity among others**, as well as its contribution to most common chronic age-related diseases.

Several clinical studies have been performed to investigate the role of thyroid function in aging and longevity obtaining contrasting results.

❖ **Hypothyroidism** is a frequent disease among the elderly. The most common symptoms of hypothyroidism in the old are:

1. Elevated cholesterol
2. A reduction of blood volume, systolic dysfunction, and slower heart rate, which may all contribute to heart failure.
3. Constipation due to infrequent bowel movements,
4. Joint and muscle pain
5. Balance problems in walking
6. Kidney dysfunction
7. memory loss and depression

❖ **Therefore, careful clinical and biochemical assessment is necessary**

❖ **We have published the first paper on this topic in J.Clin. Endocrinol Metab, 1993**

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Complex Alteration of Thyroid Function in Healthy Centenarians*

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- 41 healthy centenarians (100-110 yrs);**
- 33 healthy elderly (65-80 yrs)**
- 98 control subjects (20-64 yrs)**
- 52 patients with nonthyroidal illness (28-82 yrs)**

Thyroid function appeared **well preserved until 80 years in healthy subjects** while a **reduction of FT3 is observed in centenarians**, as consequence of reduced thyroid function and impairment of peripheral 5' deiodinase

Original Article

Heterogeneity of Thyroid Function and Impact of Peripheral Thyroxine Deiodination in Centenarians and Semi-Supercentenarians: Association With Functional Status and Mortality

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n. 672 subjects (age range 52-113 years)
including:

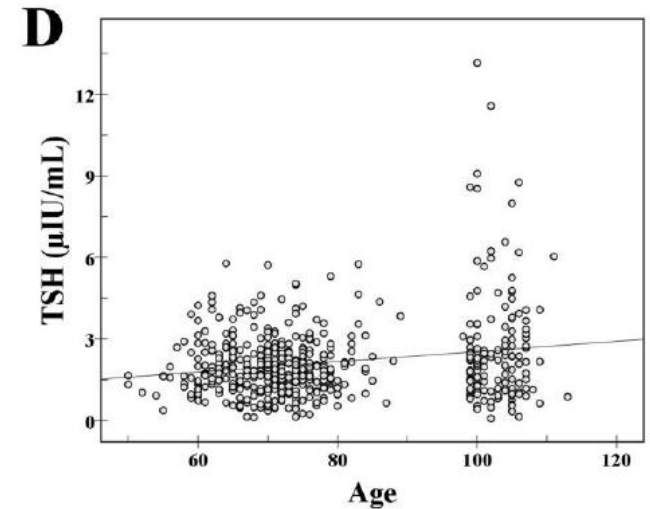
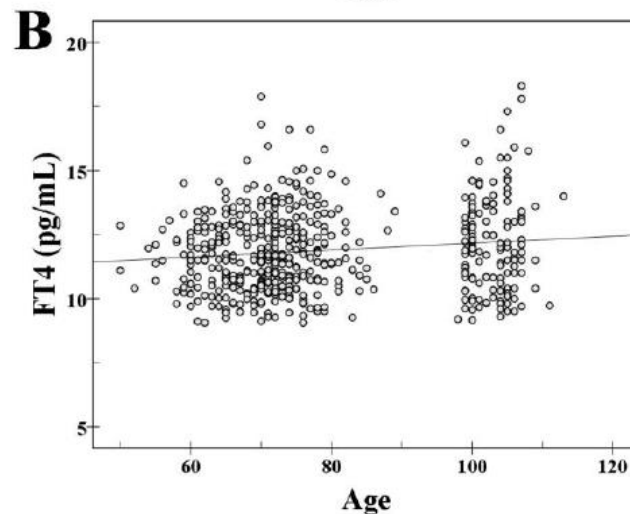
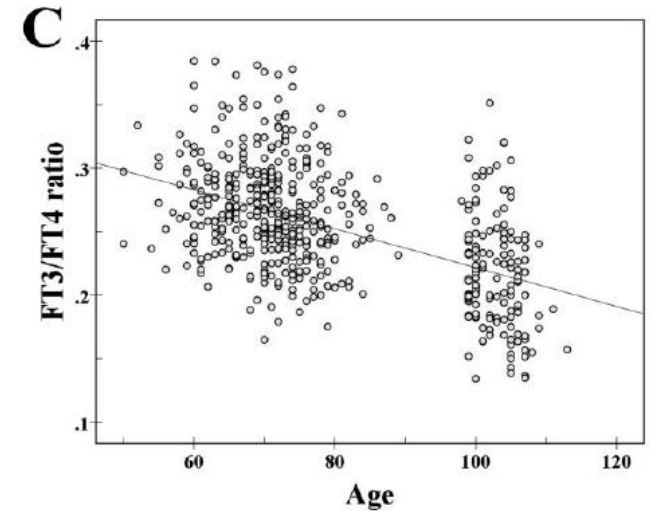
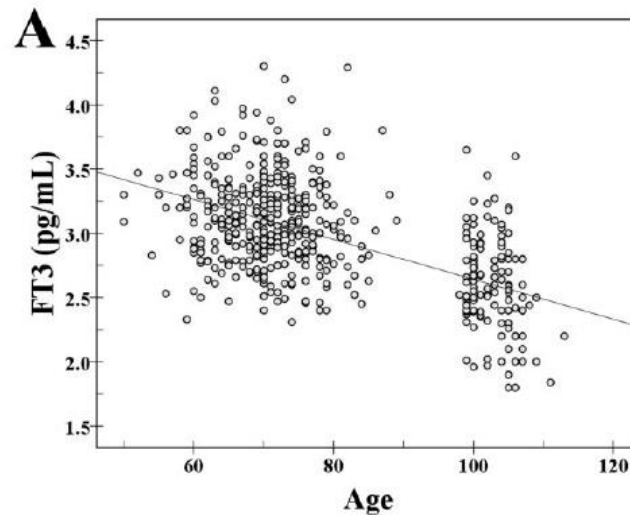
- n.144 100+

- n. 70 105+

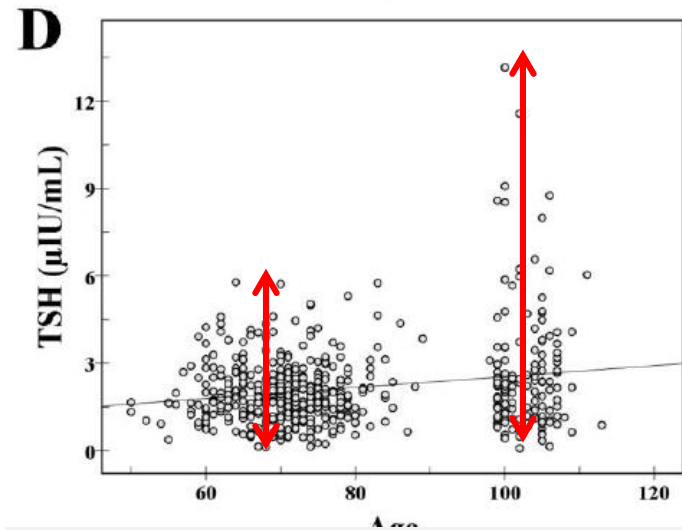
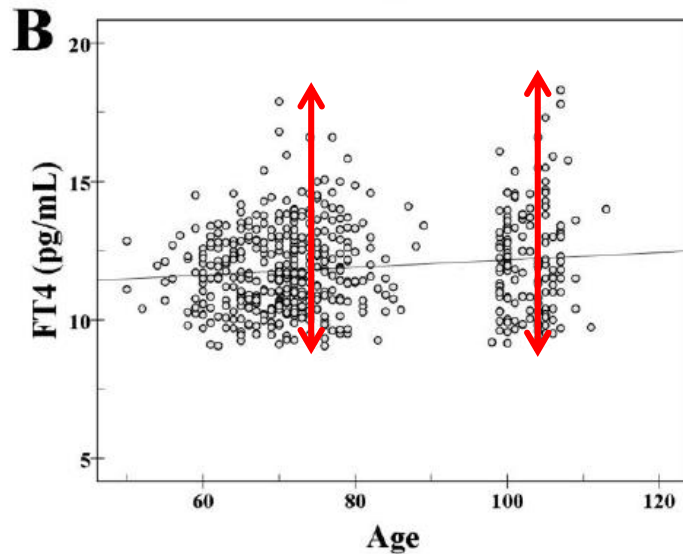
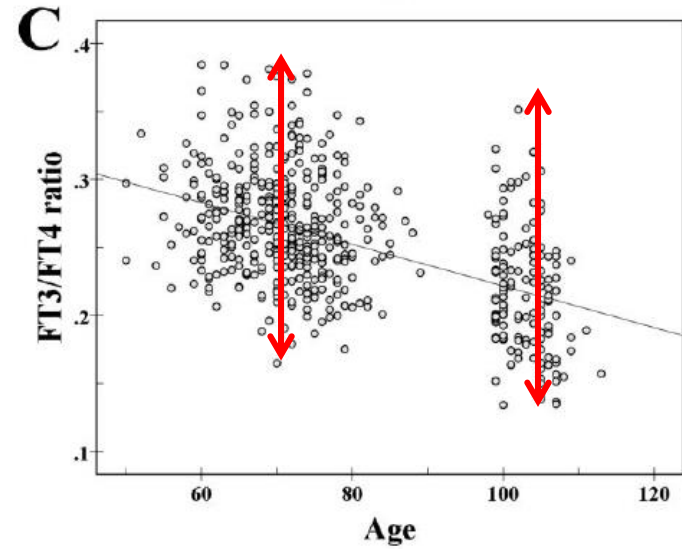
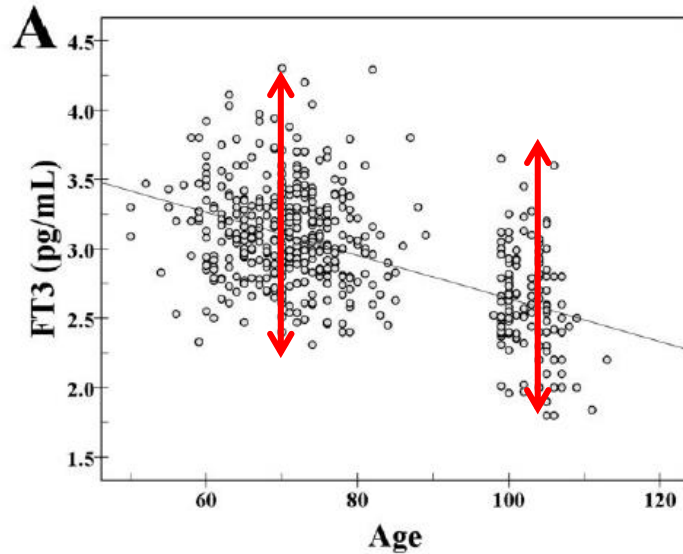
- n. 308 centenarian offspring

Heterogeneity of thyroid function in elderly, 100+ and 105+

In centenarians
and semi-
supercentenarians
higher level of
FT4 and lower
FT3/FT4 ratio are
associated with
impaired
functional status
and increased
mortality



Heterogeneity of thyroid function in elderly, 100+ and 105+

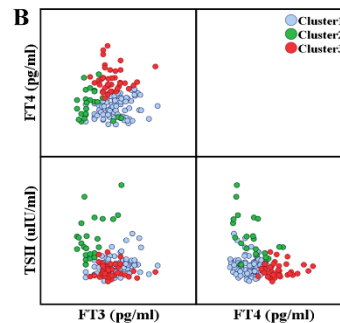


Heterogeneity of thyroid function in elderly, 100+ and 105+

Cluster analysis based on FT3, FT4 and TSH levels identified three clusters of CENT/105+

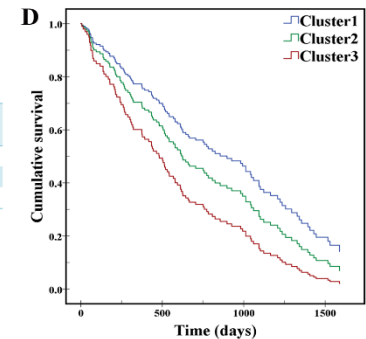
Cluster3, characterized by lower FT3 and TSH and higher FT4, shows the worst health status and the shortest survival.

	Cluster1	Cluster2	Cluster3	<i>p</i>		
	Reference	Lower FT3 and higher TSH	Lower FT3, higher FT4, lower TSH	1vs2	1vs3	2vs3
N	78	24	43			
Men:Women	21:57	7:17	7:36			
Age (yrs)	102.5 (2.9)	103.9 (3.2)	103.0 (3.2)	.039	.451	.194
FT3 (pg/mL)	2.7 (2.0-3.6)	2.0 (1.8-2.8)	2.5 (2.1-3.6)	<.001	.028	<.001
FT4 (pg/mL)	11.2 (9.2-13.4)	11.7 (9.5-15.2)	14.0 (12.2-18.3)	.352	<.001	<.001
TSH (μIU/mL)	2.2 (0.1-6.6)	5.0 (2.4-13.1)	1.4 (0.1-4.1)	<.001	.002	<.001
ADL score	3.5 (1.8)	2.9 (1.7)	2.6 (1.9)	.105	.002	.249
Handgrip strength (kg)	14.5 (5.8)	12.5 (6.4)	10.8 (5.1)	.178	.015	.544
Not performing Handgrip strength test, n (%)	12 (15.4)	8 (33.3)	20 (46.5)	.059	<.001	.296
SMMSE score ^a	19.6 (5.3)	20.9 (6.2)	18.4 (6.5)	.766	.041	.200
Unable to perform SMMSE, n (%)	18 (23.1)	5 (20.8)	18 (41.9)	.877	.033	.088
GDS score ^b	4.8 (3.4)	7.1 (4.9)	6.7 (4.0)	.402	.046	.927
Not answering to GDS, n (%)	19 (24.4)	11 (45.8)	18 (41.9)	.057	.048	.753
BMI (kg/m ²)	24.4 (17.7-34.7)	21.9 (20.1-26.6)	23.0 (13.3-30.4)	.134	.062	.131
C-Reactive Protein (mg/L)	3.4 (0.3-27.0)	5.0 (0.3-18.4)	3.9 (0.3-33.8)	.510	.059	.472
Glycaemia (mg/dL)	83 (62-269)	89 (64-221)	79 (41-142)	.580	.062	.131
Insulin (μIU/mL)	5.9 (0.2-72.9)	4.0 (1.4-32.6)	4.2 (1.3-14.8)	.067	.014	.951
HOMA-IR index	1.2 (0.1-2.3)	0.9 (0.2-8)	1.0 (0.2-3.3)	.200	.023	.690
Total cholesterol (mg/dL)	184 (117-301)	190 (122-284)	175 (103-322)	.941	.247	.590
HDL cholesterol (mg/dL)	47 (21-82)	48 (20-99)	47 (25-81)	.679	.490	.431
Triglycerides (mg/dL)	114 (55-535)	112 (62-209)	98 (56-220)	.974	.281	.484
Total protein ^d (g/dL)	6.8 (5.6-9.1)	6.7 (5.6-8.2)	6.7 (4.9-7.8)	.459	.082	.642
Estimated survival time (days)	932 (796-1068)	715 (525-905)	552 (409-694)	.098	.001	.256



C

	Hazard ratio		
	B coefficient	Exp(B) (95% C.I.)	<i>p</i>
Cluster1	-	-	-
Cluster2	0.353	1.4 (0.8-2.4)	.204
Cluster3	0.709	2.0 (1.3-3.1)	.001



In conclusion:

- 1. FT3 and FT3/FT4 ratio decrease in age dependent manner, while FT4 and TSH increase.**
- 2. Higher FT4 and lower FT3/FT4 ratio in CENT/105+ are associated with an impaired functional status and an increased mortality.**
- 3. Cluster analysis indentified three clusters of CENT/105+ Cluster 3 characterized by lower FT3 and TSH and higher FT4 show the worst health and the shortest survival.**
- 4. Thus, the age-related changes of thyroid hormones extend to the most advanced age and CENT/105+ are highly heterogeneous regarding thyroid function. This heterogeneity is related to different health, functional and cognitive status, as well as with survival/mortality in CENT/105+.**

Thyroid fuction also seems to follow the remodelling theory of aging

THE “REMODELLING THEORY OF AGING”

(Franceschi et al., 1995; 2000)

Age-related changes of thyroid function, and particularly the **mild hypothyroidism** characteristic of centenarians, can be globally interpreted as the result of **lifelong accumulation of damages counteracted by continuous adaptive mechanisms.**

Clinically it is difficult to distinguish between the two!

This thyroid age-related changes have to be envisaged within the lifelong energy remodelling

(see the presentation of Prof. Salvioli on mitochondria in centenarians)

THE “REMODELLING THEORY OF AGING”

(Franceschi et al., 1995; 2000)

Heterogeneity dominates
also thyroid function in the
elderly and centenarians

The Aging Thyroid: A Reappraisal Within the Geroscience Integrated Perspective

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and Giovanni Vitale^{5,6†}

(*Endocrine Reviews* 40: 1250 – 1270, 2019)

Endocrine Reviews
Endocrine Society

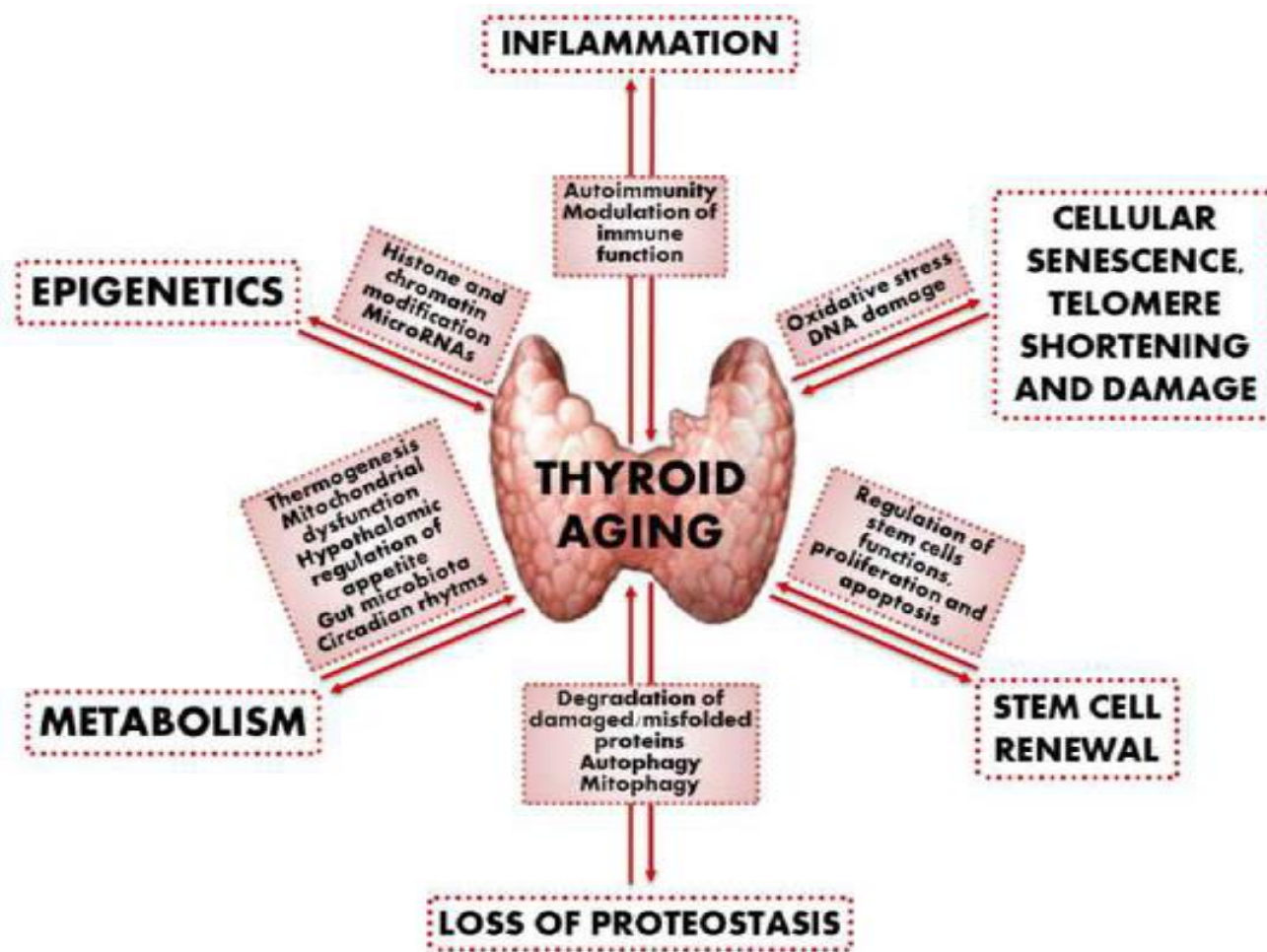
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THE AGING THYROID:

A REAPPRAISAL WITHIN THE GEROSCIENCE PERSPECTIVE



Franceschi et al., Endocrine Reviews, 2019

Thyroid aging within the Geroscience perspective

- Available data on the seven mechanistic pillars of geroscience are rather poor/scanty.
- Thus, the basic mechanisms of thyroid aging are still largely unknown (particularly in humans)

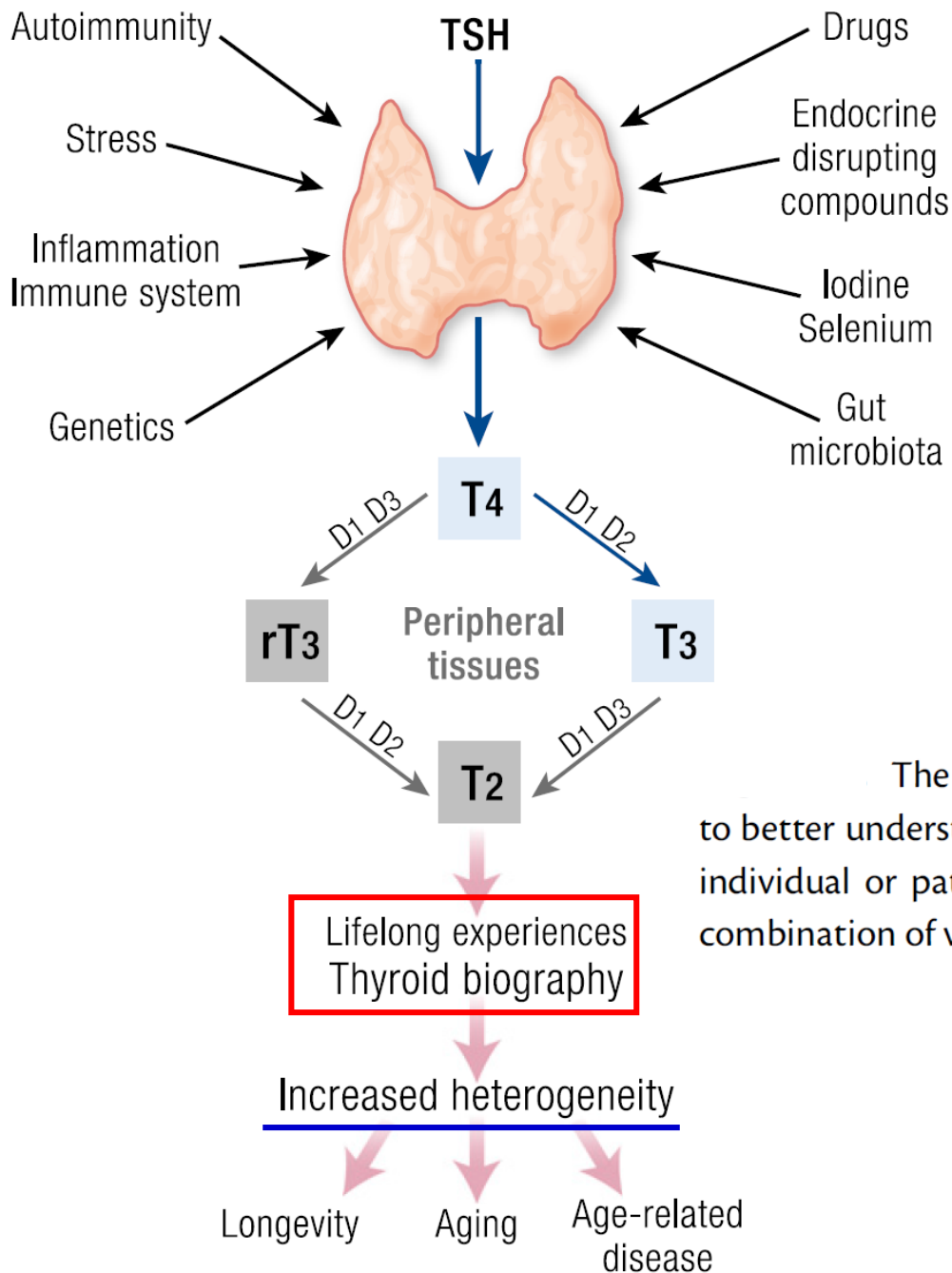


Immunobiography and the Heterogeneity of Immune Responses in the Elderly: A Focus on Inflammaging and Trained Immunity

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Aging/Inflammaging beyond chronological age

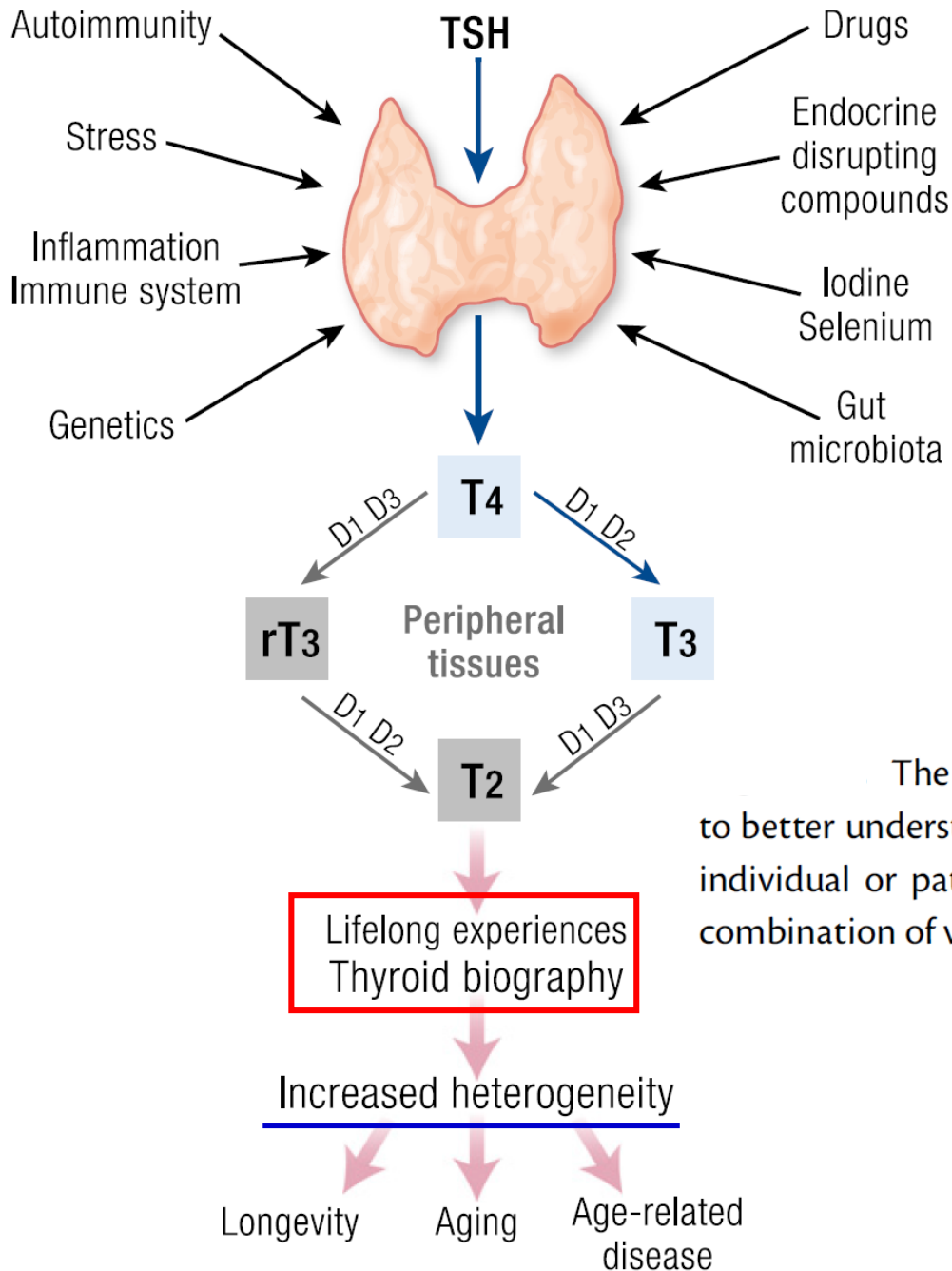


A lack of knowledge on major variables that impact on thyroid aging

The new concept of “thyroid biography” is proposed to better understand the heterogeneity of thyroid aging in each individual or patient as a consequence of the unique combination of variables impinging lifelong on thyroid function.

**Franceschi et al.,
Endocrine Reviews 2019**

**Franceschi et al.,
Endocrine Reviews 2019**



In this perspective a lifelong collection of data on thyroid function could help clinicians in making decisions regarding TH treatment of the elderly and the oldest old, at present a controversial issue

The new concept of “thyroid biography” is proposed to better understand the heterogeneity of thyroid aging in each individual or patient as a consequence of the unique combination of variables impinging lifelong on thyroid function.



**Thanks
for
your
attention**