

BASAL METABOLISM AND BRONCHIAL ASTHMA

By

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The question what part is played by the thyroid gland in allergic diseases, is repeatedly met with in literature. The question is to be understood. With some bronchial asthma patients it occurs almost automatically to him who sees the thin, nervous patients. But also when the thyroid gland is not directly related to the arising of an allergic constitution or of allergic symptoms, we have to consider the question whether thyroid gland dysfunctions don't so frequently complicate an allergic affection that it is desirable to take them into account in the examination and in the therapy. Its importance is evident:

1. The nervous component which takes a very important part in many asthma patients, may arise from thyroid gland dysfunctions.
2. A quickened pulse may be a contra-indication for the use of adrenaline, as the patient—be it mostly for a short time— reacts on it unfavourably.
3. Potassium iodide therapy, sometimes continued for a very long time in asthma patients, may, besides its favourable effect, have an unfavourable effect on the general condition of the body, on account of its influence on the thyroid gland.
4. If a diet is prescribed on the ground of the skin tests made, the metabolic rate should be taken into account.

Dietary changes should not be made without at the same time considering general factors.

These four points keep their importance for the therapy, also when one is of opinion that the thyroid gland is not involved in effecting the allergic reaction. The question if in a number of cases the symptoms cannot be due to hypersensitiveness to the thyroid gland hormone (Hajos, Baer a. o.) may be considered to be out of the scope of this investigation.

The research into this matter is not yet finished, as conclusions are extremely difficult to draw.

Reading about the investigations made we come across various views. Text-books as a rule state, however, that the thyroid gland should be of little or no importance in the case of allergic diseases.

Képinow describes experiments in which anaphylactic shock was slowed down and allayed by administering a small dose of thyroid four days before the last injection, whereas a strong dose accelerated and intensified the shock. In animals from which the thyroid gland had been removed he could no longer evoke shock.

Nechkovitch could only partly affirm the latter statement. He found a toning down of the anaphylactic shock in animals from which the thyroid gland had been removed, but still there were indications of the local symptoms of the anaphylaxis.

Houssay and Cisneros describe experiments in dogs from which the thyroid gland had been extirpated. In these animals and their controls they tried to cause shock with horse-serum; in another series with peptone. Though in both groups an equally high titer of antibodies was found, no shock symptoms occurred in the animals without thyroid glands.

Garrelon and Santenoise also saw that they failed in evoking pepton-shock after eliminating the thyroid glands, which should be the consequence of the fact that the vagus tonus should issue via the thyroid gland.

Appelmans could not affirm these experiments in guinea-pigs.

Watman and Hasset found in guinea-pigs that thyroidectomy accelerated the development of gastric ulcers evoked by histamine; benadryl did not retard its arising. When thyroxine or thyroid gland powder were given in a high dose, a strongly increased sensitivity to acute histamine intoxication appeared. Thiouracil in various doses did not influence the development of the histamine gastric ulcer.

The relation between thyroid and suprarenal glands has also drawn the attention:

Roussel considers urticaria in the light of a disbalance between the thyroid and adrenal glands and declares it a possible cause of vasomotor instability. Thyroid secretion irritates the nervous fibre of the bloodvessels and causes vasodilatation; adrenal secretion gives vasoconstriction. Therefore Roussel desires determination of the metabolic rate as a guide to therapy.

Long and Miles state that they found an antagonistic functional activity between thyroid and adrenal cortex (A.C.T.H., Cortison). Thyroid should, according to them, increase the hypersensitivity whereas adrenal cortex hormones should decrease it.

Morrow Browns opposes this view. He ascertains that they co-operate, except for a thoroughly disturbed relation such as hyperthyroidism, in which case the adrenal is exhausted by thyroxine.

Garretson postulates that the thyroid first irritates the adrenal glands till they get worn out, in consequence of which vagotonia arises on account of decrease of sympathicotonia.

Hajos stresses that in cases of bronchial asthma with indistinct aetiology, determination of the basal metabolic rate may indicate a displacement in the pluriglandular balance. Then the therapy aims at fighting a hypo- or hyperfunction. In his opinion thyroid-tablets will, in cases of hypothyroidism, give improvement of the anaphylactic status in the long run. They themselves do nothing in an attack. In thyrotoxicosis the tendency towards anaphylaxis should be greater than in myxoedema.

Croizat, Lagèze and Valin point out the great use of the iodine therapy in cases of asthma. They quote Lévi's theory that iodine should have its favourable influence as "Médication metathyroïdienne".

De Gennes and Mahoudeau point out the great difference in appreciation of the thyroid dysfunctions in former and present-day literature. Formerly they saw them as a main cause, whereas now we know that they are only reactions.

In a study on decreased basal metabolism de Langen indicates a synergy between thyroid hormones and adrenaline. Adrenaline intervenes quickly when higher demands are made upon metabolism. In the various seasons the quantity of adrenaline required to come to the same result, differs. In thyroidless animals 4 or 5 times as much adrenaline is necessary to get the same rise as in animals with thyroid glands. Thyroid hormone is suggested to sensitize the organism and the periphery, on account of which it reacts more easily to adrenaline. So thyroid hormone acts directly on metabolism and indirectly via the activity of adrenaline. Consequently there are patients with mere hypometabolism and others with hypothyroidism.

Adrenaline should work through the increase of the quantity of blood and the increased pressure of the blood flowing through an organ, by which the oxidation is activated. This stimulus should be effected in co-operation with the synergic histamine produced simultaneously.

He reports to have found several asthma patients among his cases of a low B.M.

Alexander states that in 22 cases of asthma studied by him the B. M. rate was decreased (with an average of —17.5 %). Occasionally the patient responded well to the thyroid therapy applied.

Novak, Zugsmith and Kahn found a lowered B.M. rate in many asthma patients.

Kern and Teller found in a total of 75 allergic patients: a normal B.M. rate in 71 %, an increased rate in 4 % and a lowered rate in 25 % of the cases. Thyroid therapy gave

no success. But they do assume that in asthma patients a higher percentage of enlarged thyroid glands or familiar thyrotoxicosis occurs. The lower B.M. rate is accounted for by a lowered thyroid activity as a consequence of the allergic status. They describe a patient with thyrotoxicosis in whom asthma appeared after being operated on. Though his B.M. rate became normal, and remained so, thyroid therapy gave only temporary improvement of his asthma.

Derbes and Engelhardt point out that, though the thyroid gland is no etiologic factor in asthma, in persons with restricted breath reserve dyspnea may occur in case of strongly increased B.M. rate.

Oehme and Paal studied in the Reid-Hunt reaction in asthma (positive in hyperthyroidism). Out of 17 cases, 12 appeared to be positive, while the test became strongly positive during attacks. They presume that the hormones stimulate the vegetative nervous system.

Selfridge believes that in case of disturbance of the chemical balance by the ductless glands, vegetative disturbances will occur with symptoms of vagotonia or sympathicotonia.

Janney presume that in hyperthyroidism there is increased susceptibility to infections; Wieder believes the opposite.

Widal and Abrami state that hypothyroidism as well as hyperthyroidism may afford an asthmatic picture. They see a relation between thyroid gland and vegetative nervous system. They describe some cases of asthmatics with Basedow's disease, in which irradiation of the thyroid gland also caused the asthma complaints to disappear.

In a number of patients with allergic diseases and of normal test persons Hermann determined their basal metabolic rates for a number of days; they were lying in a sickward as well as in an allergenproof chamber. During the time they were in the allergen-proof room, metabolism decreased in both groups; in the allergic patients, however, far more than in the controls. In the allergics he found even a decrease of 15 to 18 %.

Criep and Wechsler saw in 31 asthma patients a dysfunction of the thyroid gland in 35 % of the cases (26% increased, 9 % decreased). They see no causal relation though they infer that the thyroid gland may increase an existing predisposition.

Simpson, Sonnenschein, Criep, McElroy, Unger and Barnes saw a normal B.M. in asthma patients. In 500 asthma-cases Witts saw myxoedema in 0.6 %, and hyperthyroidism in 0.2 %. Hill saw in 38 cases of cretinism 1 case of asthma, in 72 cases of myxoedema 3 asthmatics, in 150 cases of thyrotoxicosis no asthma.

Van Niekerk found in 98 patients: normal B.M. in 51 cases, decreased in 13, increased in 4 cases and in the remaining patients fluctuating rates.

Topper and Mulier found in children with bronchial asthma: normal B.M. in 74 % of the cases, negative in 26 %; they consider this decrease as a consequence of asthma, because the tissues were difficient in thyroxine because of the paroxysms.

Tuft states that asthma is rather often complicated by dysfunction of one of the ductless glands, e.g. hyperthyroidism, but that improvement of this defect does not nearly always bring about improvement of the asthma.

Vaughan and Black saw in asthma more lowered than increased basal metabolic rates, though both were observed. Though endocrine disturbances, according to them, occur disconnected with allergic disturbances, they point out that allergic treatment sometimes does not take effect before the endocrine disturbance has also been mastered.

My own research comprises a number of 420 patients with bronchial asthma. No difference was made between the intrinsic and extrinsic form, or clearly nervous asthma. A large majority, however, belonged to the mixed type, in which an endogenous as well as an exogenous and a nervous factor were present. Most patients were metabolized polyclinically, all of which at the Diaconessenhuis at Utrecht, where always the same nurse and the same apparatus (Knipping)

were used. All the patients got the instruction to keep quiet the day before (because of the economic conditions the consumption of meat, beans and peas, eggs and similar albumens has already been highly restricted in the Netherlands); to go to bed early on the previous evening, no medicine and to come to the metabolic department in the morning without having breakfasted or having done any work. There they were given some more hours of rest, after which the basal metabolic rate was determined.

Frequently I was able to check the results clinically, in which cases I could certify that there were no discrepancies.

The cases were not only restricted to Utrecht, but also came from quite different parts of the Netherlands. Thus local deviations (Utrecht is notorious for frequent occurrence of goitre) could be expelled.

B.M. rates between -10 and $+20$ were appreciated as normal, higher rates as hypermetabolism, lower ones as hypometabolism.

Out of 420 cases I found:

27 cases of hypometabolism (6.3 %).

114 cases of hypermetabolism (26.7 %).

So in 67 % of the cases the B.M. rate was within the limits agreed upon as normal.

The division was:

Hypo- metabolism	Number of cases	Normal B.M. rate	Number of cases	Hyper- metabolism	Number of cases
-30 to -20	2	-10 to -0	57	$+20$ to $+25$	51
-20 to -10	25	normal	12	$+26$ to $+30$	32
		0 to $+10$	122	$+31$ to $+40$	22
		$+10$ to $+19$	95	$+40$ to $+50$	6
				$+50$ to $+60$	1
				$+60$ to $+70$	2

In a great number of hyperthyroidism cases we could suffice with the normal dietary and rest prescriptions, in the others the advice of the specialist for internal medicine was taken. It is not to be wondered at that especially in the cases of highly increased metabolism, the therapy brought

on considerable improvement together with the patients' feeling better and their improving response to the asthma therapy.

The age of the patient plays a prominent part:

420 patients:			
Age	Number	Hypo- metabolism	Hyper- metabolism
4-10 years	15	2	5
10-20 years	105	9	17
20-30 years	98	6	22
30-40 years	81	4	28
40-50 years	64	3	18
50-60 years	49	2	19
60-70 years	7	1	4
70-80 years	1	0	1

Exactly at the earlier ages it was important to find hypo-metabolism. These were often slow children, sluggish at school, among friends and at home. They were difficult to stimulate to any activity. Administration of a thyreoid dose together with control of their metabolic rates did not directly result in improvement of their asthma. But the children showed a generally improved condition, became more vivacious, appeared to be more capable. In the long run this resulted again in decrease of their asthma attacks.

The part taken by any infectious factor, was ascertained by determination of the blood sedimentation rate:

Basal Metabolic Rate	Blood Sedimentation Rate:	
	normal	increased
below 10	13	14
within normal limits	184	95
more than 20	62	52

In some cases treatment of the infectious process effected a decrease of the metabolic rate. Especially in the cases just a little above +20. Presumably, however, the rest prescribed at the same time was in general more important

than the medicinal and vaccinal therapy. The appearance of an infectious process (with increased B. S. rate) as a new complication, however, never caused an increased B.M.

Other co-symptoms were looked for. Symptoms like tremors a.o. were only found in very high B.M. rates. Enlarged thyroid glands occurred in decreased, normal as well as in increased basal metabolisms.

The pulse frequency was also registered: see page 335.

From this it may be seen that in rather a great number of cases the pulse is over 100 during the test (the patient having had ample time for rest previously). We may say indeed that especially these patients after administration of adrenaline, complain of an unpleasant feeling of palpitations and such like.

BLOODPRESSURE

in 420 patients: decreased: 55.66 %.
increased: 9.06 %.
normal: 35.27 %.

in patients with hypometabolism:
decreased: 76.47 %.
increased: 5.29 %.
normal: 18.24 %.

in patients with normal B.M. rate:
decreased: 53.67 %.
increased: 7.07 %.
normal: 39.25 %.

in patients with hypermetabolism:
decreased: 56.62 %.
increased: 14.45 %.
normal: 28.91 %.

We may conclude from this that especially decreased metabolism is often attended with decreased tension, whereas in increased metabolism increased bloodpressure occurs in rather more cases.

Whereas the tension in normal cases undergoes little or

no change during the treatment, we do see in treating metabolism that hypotension in hypometabolism, and hypertension in hypermetabolism rather tend to the normal.

In only 11 cases a tension was found in which the diastolic pressure sank to 0, but of those 11 the basal metabolic rate was normal in 8 cases.

Finally we looked for a relation to the eosinophilia of the blood (as evidence of a distinct, purely allergic factor).

Eosinophilia		Decreased B. M.	Normal B. M.	Increased B. M.
below	5	35.29 %	43.83 %	32.66 %
above	4	35.29 %	35.63 %	40.70 %
above	10	29.41 %	20.54 %	26.63 %

From this it appears, as is repeatedly presumed in literature, that the allergic condition is often complicated by a dysfunction of the thyroid gland. In decreased as well as in increased basal metabolism the frequency of bronchial asthma cases with an increased eosinophilic cell content of the blood is higher than in cases with normal metabolic rates.

The numbers are not so high, it is true, that we can attach absolute value to them, on the other hand they are high enough to be a definite indication.

As our conclusion we may say that the thyroid gland shows a normal function in most of the asthma cases, but that the percentage in which a dysfunction has been found is so high, that we must assume that in the allergic status the thyroid gland is often involved in the process. Treatment of these deviations never gave direct improvement of the bronchial asthma, though it did give indirect improvement, because the patient began to feel better generally, became less nervous, often slept better, became thicker, in consequence of which he could better resist colds and such, and little by little began to have fewer attacks. Avoidance of adrenaline in case of hyperthyroidism, giving up the continuous use of potassium iodide and giving a proper diet are

therapeutic measures which brought considerable improvement to some patients. It seems unlikely to assume that the thyroid gland exerts an influence in the arising of bronchial asthma, but they are likely to be both a consequence of one and the same allergic constitution and may influence each other unfavourably.

Thyroid gland treatment should, with this in view, never be counted by itself as a treatment of bronchial asthma, but be considered as an essential expedient, side by side to the specific therapy applied.

SUMMARY

In 420 patients an investigation after the occurrence of thyroid gland dysfunctions is reported. In 26 % increased metabolic rates were found, in 6 % decreased. The therapy applied gave improvement of the general condition and decreased the influence of the nervous factor.

Patients with increased blood eosinophilia give the impression of having a tendency towards thyroid gland dysfunction.

In case of continued potassium iodide therapy, prolonged diet and adrenaline injections, determination of the basal metabolic rate is most useful.

Besides a summary of literature is given, in which various views are placed side by side.

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