

**Results of Operations for Graves' Disease with  
Reference to the Incidental Blood Conditions  
and Vascular System.**

By

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The haematological conditions found in Graves' (or Basedow's) disease have long been discussed by various medical experts but not yet definitely determined. Basedow himself believed, that this disease, which is called by his name in Germany, is one of the disturbances of the blood system, causing a diminution in the number of erythrocytes. Later, Leclave, Oppenheimer, Fr. Müller and Vorster etc. did not find any marked change of the blood at least in typical cases of this disease, and thought, it might be owing to some other complications, occurring at the same time when some haematological changes take place. On the other hand, Squira and Reynold (1886) insisted, that anaemia is one of principal symptoms of this disease. Their opinion was supported also by Mannheim (1894), Pössler and Krong (1895); the latter believed that there were some causal relations between anaemia and Morbus Basedowii. Moreover, Neisser (1899) reported a case accompanied by pernicious anaemia. Since Wunderlich (1856) noticed cases of a combination of this disease and chlorosis, many doctors, namely, Immermann, Beni-Barde, Teissier, Chvostek, Giudiceandrea, Hayen, v. Noorden, Kocher, Johnston, Klose and Lampé have observed cases of the same combination successively. In view of the fact, that greensickness and exophthalmic goitre seem to have some relation to the function of the germinal glands (especially

the ovary), such a combination need not be thought a mere accidental occurrence. Notwithstanding, from recent reports and our own experiences we must at present believe that the diminution of erythrocytes is not an essential feature of this disease. We shall return to this point later.

On the other hand, the findings of white cells have become a more interesting topic. Since Ciuffini (1906) noticed an abnormality of the proportional numbers of various kinds of white cells, his view has been accepted by Caro (1907), Kocher (1908), Jagic and Gordon (1908), Kurokawa (1909), Roth (1910), Inaoka (1910), Sudeck (1911), Baruch (1911) and Lampé (1912) etc. Above all, Th. Kocher, the famous surgeon in Bern, laid stress on the increase of lymphocytes at the expense of neutrophile polymorphonuclear leucocytes. He thought these findings important as a sign-post not only to the diagnosis, but to the indication and prognosis of the surgical treatment of this disease. His opinion has been supported by many followers, if arguments in opposition are not lacking. For example, Hanna etc. did not believe in the appearance of any regular changes of blood in *Morbus Basedowii*.

We have been engaged in the operative treatment of this disease for a year. For the sake of safety we selected only manifest cases, which could not be doubted by any clinicians, and most of them were treated once in the Internal Department of our University-Hospital as exophthalmic goitre.

We operated on ten cases, three of them "subtotally" (the term used by Bartlett), three by hemithyroid-isthmectomy, two by hemithyroidectomy, and two by ligation of unilateral arteria et vena thyroidea superior et inferior. Only one case of subtotal thyroidectomy died the day following the operation. The methods of operation were determined by the degree of size of struma; in other words, the very enlarged glands subtotally, the large ones by hemithyroid-isthmectomy, the middle sized ones by simple hemithyroidectomy, and the slightly enlarged ones by ligation. In every case the larger side of the enlarged gland, if it was possibly palpated, was extirpated or ligated. Generally, the results of operation were very satisfactory, the patients having been free more or less from subjective and objective complaints and grateful for the operation. One of the cases (the fourth case, S. M.) was treated for a long time with X-rays and medicines in the Medical Clinic, with no effect,

having finally become markedly cachectic. After subtotal thyroidectomy he has been recovering rather quickly, and he is able at present to work daily as hard as other healthy men. As symptomatic results of the operation should be mentioned; (1) disappearance of subjective complaints, for instance headache, insomnia, depression or excitement etc., (2) the decrease of vasomotoric disturbances, for example blushing, sweating etc., (3) disappearance or decrease of tachycardia and (4) of tremor, (5) of exophthalmus, finally (6) the decrease of blood pressure, and (7) the decrement of cardiac enlargement.

#### Number of the blood corpuscles.

It is well known, that the number of erythrocytes in men is about five millions in 1 c.mm., in the case of women about 4.5 millions and the variation of that number seems to occur to a relatively small extent in normal healthy human beings. On the other hand, the numerical conditions of white cells are more variable even in healthy persons. For example, Grawitz calculated the white cells at 5,000-10,000, Naegeli at 7-8,000, Curshmann 8,000-10,000, Arneth at 5,000-6,000, Lefas at 6,000-11,000, Tuffier at 4,000-10,000, Depage at 6,000-10,000. Judging by the reports of those famous haematologists, the minimum is 4,000, and the maximum 11,000 in health. In regard to the proportional mixture of different kinds of white cells, Naegeli counted 65-70% of the neutrophile polymorphonuclear leucocytes, 22-25% of the lymphocytes, 2-4% of the large mononuclear leucocytes and the transitional leucocytes, 0.5% of the mast cells. Grawitz, Ehrlich and Einhorn reckoned the neutrophile at 65-70%, the eosinophile and transitional at 10%, the large and small lymphocytes at 25%. Lefas calculated the neutrophile at 60-70%, the eosinophile at 1-3%, the small lymphocytes at 25-30%, the large lymphocytes at 4-6%, the mast cells at 0.05%, the transitional forms at 0-2%.

We shall now go on to the reviews of various reports, comparing them with the results of our own experience.

### I. Findings of Corpuscular Elements in the Blood in Graves' Disease.

#### (1) ERYTHROCYTES.

##### a. *Morphological changes in erythrocytes.*

Schur (1906) believes that in erythrocytes he found an appearance of minute bodies which are of various sizes, located always eccentrically, having a very distinct contour and showing special affinity to basic stains. He thought these bodies similar to blood platelets, from which, however, they can be discriminated by staining power. But such small intracellular corpuscles cannot be detected by others.

We too could not find these corpuscles in any of our cases. Generally it is unusual to find any morphological changes happening in the erythrocytes in this disease, at least in non-complicated cases.

*b. Number of erythrocytes.*

Although anaemia was thought previously a constant symptom in this disease, it was not verified by later observations. According to Th. Kocher, who examined 106 cases, the number of red corpuscles is usually about normal; in young female patients it can be exceptionally increased, sometimes to over 5 millions in one cubic millimeter. Caro, Jagic & Gordon, Baruch, Kurokawa and Inaoka reported the number as normal or slightly decreased. On the other hand, Oppenheimer, Fr. Müller, Scholz, Mackenzie and Humphry insisted that the number of erythrocytes and the content of haemoglobin are never decreased in so far as the cases are not complicated with other illness causing anaemia. Recent reports of Klose, Lampé and Liesegang agreed with the latter opinion. In our cases, the erythrocytes, as shown in Table IX, varied between 4.17 (fourth case) and 5.52 millions (fifth case) in 1 c.mm.; most of them were normal or slightly increased in number. Our fourth case was already in a cachectic condition, when he came under our treatment, and showed very typical symptoms of Morbus Basedowii. However, his erythrocytes were not much decreased in number, though he was looking pale.

*c. Haemoglobin content and staining power of erythrocytes.*

It was first noticed by Rosin (1904), that the erythrocytes of patients show an increased tendency to be stained by various blood stains, while their content of iron is usually diminished. We have investigated this quality carefully by examining various stains (Giemsa, Romanowsky, May-Grünwald, Leichman, Ehrlich's Triacid) and found, that Rosin is right in his view, for the red corpuscles of Basedow patients are more readily and more intensively stained than those of normal blood. We have also compared the red corpuscles of Basedow's disease with those of patients who were anaemic after long continued osteomyelitis or after the severe bleeding of haemorrhoids and found in those cases the staining capacity of erythrocytes to be weaker than normal. Further in regard to haemoglobin content those authorities who insist that there is a diminution in the number of erythrocytes in this disease, believe that it decreases in amount (Zappert, Vorster, Wysbaw, Ko-

cher). On the other hand, Ciuffini observed many cases of a diminution of haemoglobin content in spite of the increase of red corpuscles. Nicolas & Roth remarked a slight diminution of haemoglobin with the normal number of erythrocytes. Mackenzie, Humphry, Klose and Lampé did not believe in any change either of haemoglobin or of erythrocytes.

We examined the blood of each patient by Sahli's and Fleischl-Miescher's haemoglobinometer several times on different days (the so-called "digestion leucocytosis" being discarded), and found a minimum of 83%, a maximum of 95%, with an average of 87.4% (see Table IX). From the results of our examination we believe that the haemoglobin content of patients is usually normal, or possibly slightly increased, but only in early stages, especially in the case of young women with unimpaired nutrition.

## (2) WHITE CORPUSCLES.

Since Zappert (1893) made the first announcement on the subject, Miesowicz (1904), Ciuffini (1906) and Caro (1907) etc. laid stress on changes in the proportional mixture of white cells in this disease, which they regarded as pathognomonic. Above all, Caro believed it to be valuable for the differential diagnosis between toxic and non-toxic goitre; he thought that in the latter such a change of white cells never appears. In 1908, Kocher, Jagic and Gordon completed the foregoing theory by suggesting that the regular findings in Basedow's blood consist in the diminution of neutrophile polynuclear leucocytes and the increase of lymphocytes; in short, neutrophile leucocytopenia and hyperlymphocytosis (the so-called "Kocher's blood figures"). There have been many supporters of this theory, for example, Bühler, Roth, Van Lier, Carpi, Di Giovine, Kurloff, Stern, Kurokawa and Inaoka. We have examined fifteen cases of this disease, five of which have not yet been operated on. The findings of blood are as follows:—

### *a. Number of white cells.*

Regarding the number of white cells there are two different opinions; some believe that there is no difference from the normal (Caro, Bühler, Van Lier and Carpi), while the others found a slight or great decrease (Kocher, Roth, Kurloff). According to Kocher, the number of white corpuscles lies between 7,000 and 13,500 in 1 c.mm. In our cases the minimum was 8,200 and the



maximum 13,400 in 1 c.mm. So we do not regard this diminution as regular findings of Basedow's blood.

*b. Neutrophile polymorphonuclear leucocytes.*

Kocher and his co-workers found a marked decrease in neutrophile leucocytes in this disease; in serious cases coming down to 35%. Caro, Jagic & Gordon, Bühler, Roth, Baruch, Klose, Lampé and Liesegang numbered them at less than 40-50%. Most of our cases were normal or slightly decreased in percentage. Case No. 2 numbered 40%, while case No. 7 showed an exceptional high percentage (86.88%); the last case might have been due to a chronic inflammatory condition of tonsils.

TABLE I.

Number of cases	Name	Sex	Age	Number of white cells in 1 c.mm.	Neutrophile leucocytes		
					Percentage	Absolute number	
1	K. S.	W.	22	1,200	67.12	8,054.4	Before operation
2	T. M.	M.	29	8,300	40.06	3,324.9	"
3	S. G.	W.	26	13,400	61.4	8,227.6	"
4	S. M.	M.	33	8,250	59.6	4,917.0	"
5	H. O.	W.	27	11,800	72.16	8,514.8	"
6	K. A.	W.	32	12,000	68.67	8,240.4	"
7	T. T.	W.	14	10,000	86.88	8,688.0	"
8	M. K.	W.	31	13,200	57.90	7,642.8	"
9	T. K.	W.	44	8,000	41.14	3,292.0	"
10	I. O.	W.	19	9,400	69.68	6,549.9	"
11	T. M.	W.	36	9,400	50.07	4,706.5	"
12	K. A.	M.	49	11,500	65.27	7,506.6	"
13	B. T.	M.	46	10,000	47.07	4,407.0	"
14	K. N.	W.	26	9,400	55.58	5,224.5	"
15	K. S.	W.	16	8,000	56.75	4,540.0	"

*c. Eosinophile leucocytes.*

The percentage of eosinophile cells is reported by Kocher, Kurokawa and Inaoka not to vary in this disease. On the other hand, Kottmann believed that a slight increase of eosinophiles is a regular finding of Basedow's blood. In our cases the minimum was 0.23%, the maximum 12.98%. The maximal case might have

been caused by ankylostomiasis. A slight variation in the percentage of eosinophiles can also occur in normal blood.

*d. Small and large lymphocytes.*

TABLE II.

No.	Name	Small lymphocytes		Large lymphocytes		
		Percent	Absolute number	Percentage	Absolute number	
1	K. S.	23.35	2802.0	1.00	204.0	Before operation
2	T. M.	39.42	3271.8	4.17	346.1	"
3	S. G.	24.5	3283.0	3.00	402.0	"
4	S. M.	30.3	2499.7	3.20	264.0	"
5	H. O.	15.1	1781.8	2.09	246.6	"
6	K. A.	18.63	2235.6	1.47	176.4	"
7	T. T.	9.43	943.0	0.82	82.0	"
8	M. K.	24.64	3252.4	0.18	23.7	"
9	T. K.	41.15	3292.0	4.11	328.8	"
10	I. O.	21.94	2062.0	1.67	156.9	"
11	T. M.	33.05	3106.7	2.30	216.2	"
12	K. A.	16.39	1884.8	3.42	393.3	"
13	B. T.	37.02	3702.0	2.39	239.0	"
14	K. N.	34.70	3261.8	1.22	114.6	"
15	K. S.	30.82	2456.6	3.43	274.4	"

First Caro remarked that the percentage of lymphocytes in this disease sometimes rises to 50 percent or more, and the degree of this increase bears a close relation to the prognosis after operation. His opinion was supported by Kocher, Jagic & Gordon, Roth, Baruch, Van Lier and Kurloff, etc. Above all, Kurloff emphasized that hyperlymphocytosis is always distinctly manifest at least in typical cases of Basedow's disease, although it is not so or only slightly so in formes frustes. In our cases only one (case No. 9) showed a percentage of lymphocytes over 45%, another one (case No. 2) having over 40%. The rest of the cases did not show any special increase or decrease, even if they displayed undoubted symptoms of this disease. We cannot decide yet, whether the hyperlymphocytosis, which can be often found in this disease, is due to any other complications (for instance, some dis-

turbances of the thymus gland) or not. In any case, we do not believe yet that it is definitely pathognomonic. O. Naegeli has already noticed that a chronic disturbance of an organ, whether infectious or of a metabolic toxic character, can cause hyperlymphocytosis of the blood. Van Lier said, "Fälle von Morbus Basedowii, wo die Zahl der Lymphocyten steigt bis  $\pm 40\%$ , und die Zahl der polymorphokernigen Leucocyten herunter sinkt bis  $\pm 45\%$ , sind nicht zu operieren." He is right to a certain extent, if his proposition contains an exception; for example, one of our cases (case No. 9) with marked hyperlymphocytosis (over 45%) was operated on with satisfactory results.

*e. Basophile, large mononuclear and transitional leucocytes.*

Compared with the figures in the previous reports of other authorities, we found no increase in the percentage of basophile leucocytes in our cases. In regard to the large mononuclear and transitional cells, Caro saw a distinct increase in formes frustes, but only a slight increase in manifest cases; Jagic & Gordon, Roth, Van Lier and Kurloff observed a greater or less increase in percentage, Bühler and Carpie found no change. In our cases a moderate increase was observed. (See Table IX)

## II. Findings of Blood Viscosity and the Coagulation Period.

From an examination of the results of twelve cases Kottmann and Lidsky presumed that the blood in cases of exophthalmic goitre coagulated with more retardation than normal blood, and its viscosity generally increased. Kostlivy and Burton found the same results in their clinical and experimental experiences, if Pettavel, on the contrary, noticed the decrease of viscosity. In our cases we used Determann's viscosimeter for the examination of viscosity and Vierordt's capillary method and our own apparatus for the determination of coagulation time. According to Mayejima, the viscosity of normal men in Japan is 3.4-4.8, and of women 3.1-4.1. Compared with these figures our cases showed a slight increase, which Lidsky also observed. If the viscosity of blood should usually be proportional to the number of erythrocytes (Beck, Jacoby, Determann, Rotky and Kottmann), we have not found such a proportion in our cases, for in them increase of



viscosity was not accompanied by increase of erythrocytes. So the cause of the increased viscosity must have existed in the serum. Kaess remarked that in exophthalmic goitre the viscosity of the patients decreases in symphaticotonic cases, while it increases in vagotonic cases (for instance, as an effect of diarrhoea, or of hyperhidrosis). We cannot, however, confirm this, because occasionally we have not found any marked increase of viscosity in such cases of vagotonia as Kaess refers to. By the way, the increase of viscosity in simple goitre, if it occurs, seems to be always accompanied by an increase of erythrocytes; in other words, a real increase of viscosity in the serum, unconnected with the number of erythrocytes, has never been observed.

The velocity of coagulation is very variable even in normal blood, and this variation is due to the different methods of examination, to the differing quality of blood, to atmospheric temperature, and to conditions of bleeding etc. Vierordt gives the period of coagulation as 9 minutes, on an average, using his capillary method. According to Bordie and Bussel, the blood coagulates within 7–8 minutes in 20°C, while it needs only 3–4 minutes in 30°C.

We have also invariably examined the normal blood as a control at the time of testing the coagulation period of Basedow's blood, and comparison demonstrated that the normal blood coagulates completely in 4–5 minutes, whereas in the blood of Basedow's disease the coagulation takes 6–7 minutes, showing therefore marked retardation. By the way, in simple goitre we found no or at most very slight retardation only. Kottmann too noticed this retardation in exophthalmic goitre, but, on the contrary, a rapidity in myxoedema. Moreover, he held the velocity of coagulation to be an important factor in the differential diagnosis between hyperthyroidism and hypothyroidism.

#### CONTENT OF BLOOD SUGAR.

The normal content of blood sugar seems not to be uniform. Liefmann & Stern, Reicher, Stein, Möckel and Frank observed it to be between 0.065–0.15%; Wacker, on the other hand, 0.14–0.18%. Tachau, Klose and Lampé regarded the average content as 0.078%. With respect to Graves' disease, Max Fleish saw in 40 cases spontaneous hyperglycaemia and in about 60% alimentary glycaemia. Dr Inaba has been engaged in the exami-

nation of glycaemia in our surgical laboratory and the results will be published later.

TABLE III.

*Velocity of the coagulation of blood in Graves' disease.*

Case	Coagulation periods			
	Before operation		After operation	
	Beginning	End	Beginning	End
1	5.2 mins.	6.5 mins.	3.2 mins.	4.1 mins.
2	5.5 "	7.0 "	+	
3	7.0 "	7.6 "	4.2 "	5.3 "
4	3.0 "	4.1 "	3.1 "	4.5 "
5	4.0 "	5.5 "	3.8 "	4.3 "
6	5.1 "	6.3 "	4.5 "	5.5 "
7	4.5 "	5.4 "	4.6 "	5.2 "
8	3.8 "	4.5 "	3.5 "	4.3 "
9	4.6 "	5.7 "	4.4 "	5.5 "
10	5.0 "	6.3 "	4.7 "	5.6 "
11	3.8 "	4.9 "	—	—
12	4.4 "	5.6 "	—	—
13	3.9 "	5.0 "	—	—
14	4.7 "	5.9 "	—	—
15	4.8 "	5.8 "	—	—

### III. The Results of Operation on the Blood.

As shown in Table IX, the changes of blood after operation for exophthalmic goitre consist principally in the altered percentages of two kinds of white cells; i.e. the increase of neutrophile polymorphonuclear leucocytes and the decrease of large and small lymphocytes. Kocher insisted that these changes of proportional relation of white cells to each other is a favorable sign in the operative treatment of Morbus Basedowii, and that, if they did not occur, the excision of the thyroid gland was not sufficient, and the remaining part of the gland should be once more resected. From our experience, however, such results of thyroidectomy on the blood seem to be only temporary,

and there is a gradual return again to the former percentages before operation, if observation after procedure is continued for a longer time than was taken by Kocher.

We usually found that after thyroidectomy the percentage of neutrophile leucocytes first increases for a short time, and decreases about 2 weeks later gradually to the number before operation, but sometimes shows a slightly increasing tendency again 3-4 weeks later. When examined six months or a year later, the figures of blood percentage are usually not very different from those before operation. Klose and Lampé found a much quicker deterioration of blood figures after thyroidectomy, pointing out that the increase in the absolute number of white cells and of percentage of neutrophile leucocytes at the expense of lymphocytes were observed only on the second and third day after operation, while they reverted quickly to the previous conditions on the fourth day; in short, there were no lasting results of procedure as far as blood percentage figures were concerned. We did not find such a quick reversal to previous conditions, but always a more gradual one. On the other hand, the changes of blood mentioned above are not peculiar to thyroidectomy in Basedow's disease, because we have found about the same changes after operations on other diseases in the neck, especially lymphadenitis colli tuberculosa. In the latter disease, the absolute number of white cells increases rapidly within twenty four hours after operation and their proportional number changes also, i.e., there is an increase of neutrophile leucocytes, a decrease of lymphocytes, the appearance or increase of eosinophile and a decrease of large mononuclear and transitional cells. All those changes are a temporary phenomenon and disappear in various periods of time lapse, on the average, one or three weeks after the operation. The degree and duration of these changes, moreover, can be referred to the conditions of nutrition of the patients, the quantity of bleeding, and the character of the wound (infected or non-infected) etc.

Baruch reported cases of patients, who became free from every clinical symptom of Graves' disease after operation, and had to be considered as entirely recovered, in spite of the hyperlymphocytosis still remaining at over 45%. At any rate, we believe at present, that the so-called Kocher's blood figures cannot be regarded as decisive for the determination of prognosis of operative treatment of Morbus Basedowii.

TABLE IV.

*Findings of the blood before and after the operation of lymphadenitis colli tuberculosa.*

	Before operation	After operation						
		1st day 10½ <sup>h</sup> .A.M.	2. " 10½ <sup>h</sup> .A.M.	3. " 11 <sup>h</sup> .A.M.	4. " 10½ <sup>h</sup> .A.M.	5. " 10½ <sup>h</sup> .A.M.	6. " 10½ <sup>h</sup> .A.M.	7. " 11 <sup>h</sup> .A.M.
Red corpuscles	4,160,000	4,020,000	3,800,000	3,700,000	3,750,000	3,520,000	3,800,000	4,400,000
White corp.	19,000	20,000	22,000	19,800	15,000	10,720	12,500	14,000
Neutrophile l.	70.9 %	80.91%	83.2 %	80.3 %	82.53%	80.15%	79.13%	73.1 %
Eosinophile l.	0	0	0	0.2 "	1.27 "	0.5 "	0.87 "	1.3 "
Small lymphocytes	26.81 "	17.82 "	10.2 "	13.1 "	13.33 "	13.3 "	14.5 "	19.5 "
Large lym.	0.89 "	0.57 "	0.31 "	0.81 "	0.64 "	1.43 "	1.63 "	1.61 "
Mast cells	0.86 "	1.18 "	1.39 "	1.89 "	0.64 "	1.07 "	0.87 "	0.82 "
Large mononuclear and transitionall.	5.04 "	4.02 "	4.9 "	3.9 "	1.59 "	3.0 "	4.0 "	4.07 "

TABLE V.

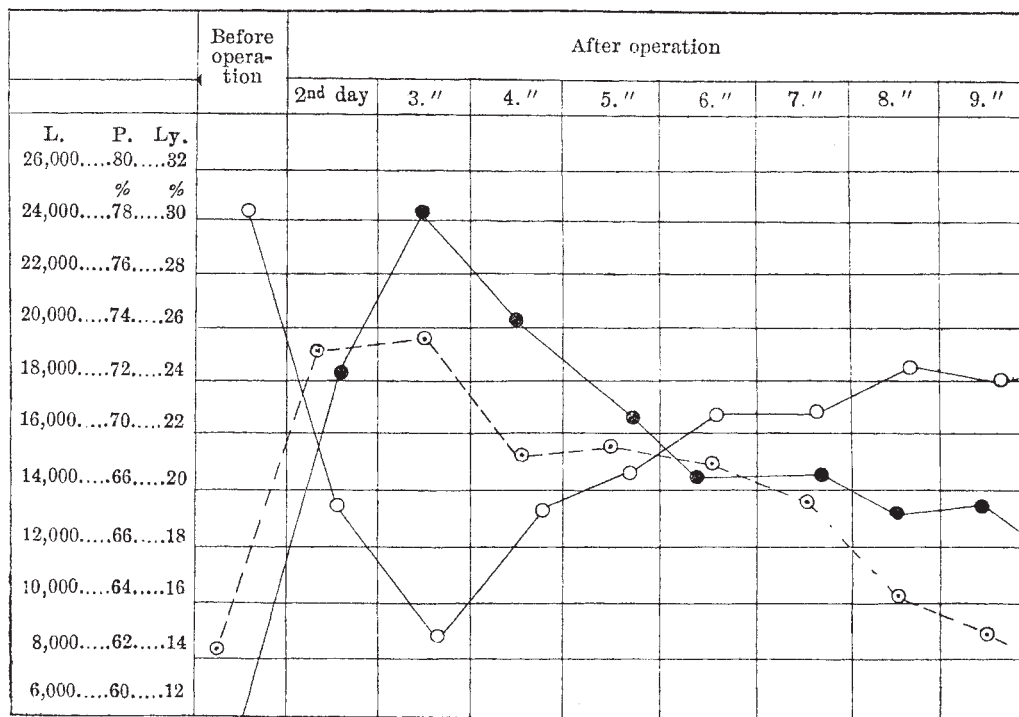
*Findings of the blood before and after the operation of Graves' disease.*

	Before operation	After operation						
		2nd day 10½ <sup>h</sup> .A.M.	3. " 11 <sup>h</sup> .A.M.	4. " 10½ <sup>h</sup> .A.M.	5. " 11 <sup>h</sup> .A.M.	6. " 10½ <sup>h</sup> .A.M.	7. " 10½ <sup>h</sup> .A.M.	8. " 10½ <sup>h</sup> .A.M.
Red corpuscles	4,170,000	4,010,000	3,700,000	3,758,000	3,670,000	3,805,000	3,975,000	4,200,000
White corp.	8,250	19,000	19,500	15,600	15,700	15,000	13,600	10,000
Neutrophile l.	59.6%	73.2%	78.4%	74.2%	71.4%	68.6%	68.5%	67.47%
Eosinophile l.	1.9 "	1.5 "	1.3 "	1.2 "	1.7 "	1.5 "	1.2 "	1.33 "
Small lymphocytes	30.3 "	19.3 "	14.6 "	18.8 "	20.6 "	23.3 "	23.4 "	25.0 "
Large lym.	3.2 "	1.4 "	1.1 "	1.2 "	1.5 "	1.8 "	2.1 "	2.2 "
Mast cells	2.5 "	2.3 "	2.6 "	2.1 "	2.3 "	2.7 "	2.5 "	3.76 "
Large mononuclear and transitionall.	2.5 "	2.3 "	2.0 "	2.5 "	2.5 "	2.1 "	2.3 "	2.2 "

TABLE VI.

*Changes of white blood corpuscles before and after the operation in Graves' disease.*

*(Sekiguchi and Ohara)*



- ⊙ Absolute number of white blood corpuscles.
- Percentage of polymorphonuclear leucocytes.
- Percentage of lymphocytes.

#### IV. Observations of Circulatory System.

##### a. Pulse.

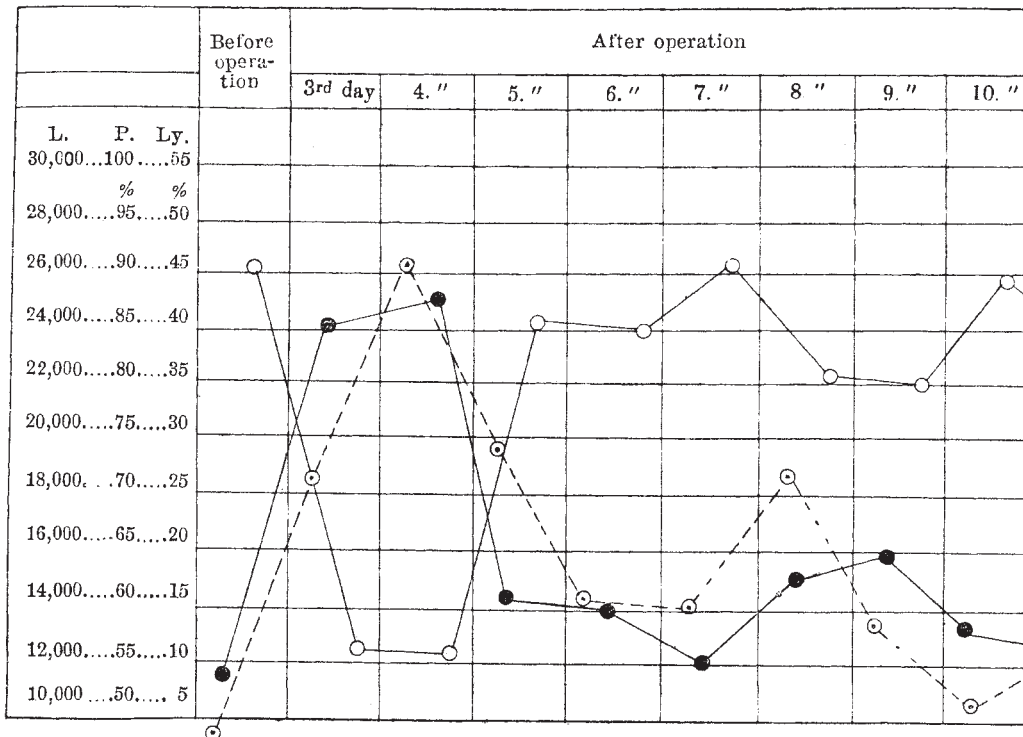
In almost all cases of Graves' disease tachycardia is one of the symptoms, which are almost invariable. Leischner and Marburg called a pulsation of over 100 beats a minute tachycardia, Klose, on the other hand, determined its minimum at 90 per minute. Our cases showed a number of pulses between 105 and 135, some of them 150 per minute, when excited. Having used Jacquet's sphygmometer, we found in our cases pulsus rhythmicus et equalis, magnus et durus. Baruch noticed pulsus arhythmicus in circa 13% of this disease which we hope to treat operatively hereafter, though we have not had a case yet. Taking the recorded venous pulsa-



TABLE VII.

*Changes of white blood corpuscles before and after the operation in Graves' disease.*

*(Klose and Lampé)*



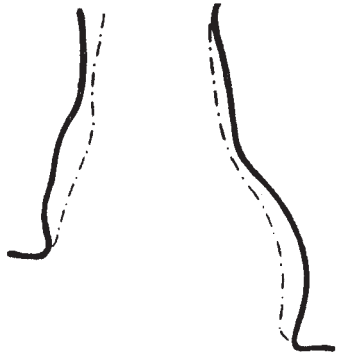
tion, we found that the ascending legs of the pulse curve showed usually no variation, whereas the descending legs often revealed distinct elevation of catacrotic waves. We examined also the analysis of venous pulsation and discovered the distance between auricular waves and carotic peaks, i.e. the conduction of auriculoventricular impulses lies in many cases under 0.2 second, in other words, there is no special check to the conduction of impulse.

*b. Heart.*

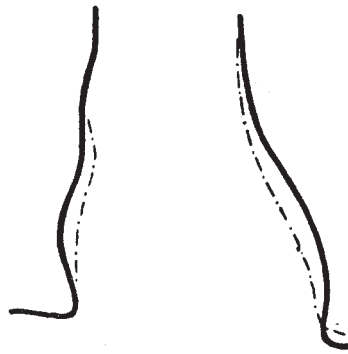
With reference to the heart, in this disease not only are functional disturbances such as tachycardia observed, but sometimes also organic changes such as hypertrophia and dilatation. Kocher found only four cases of normal volume of heart among 80 cases examined, while the others showed an enlargement of relative, as well as absolute, cardiac dulness. According to Schulze, Eppinger, Klose, Murry, Riedel and others, such a cardiac dilatation

*Orthocardiograms of the heart in Graves' disease before and operation.*

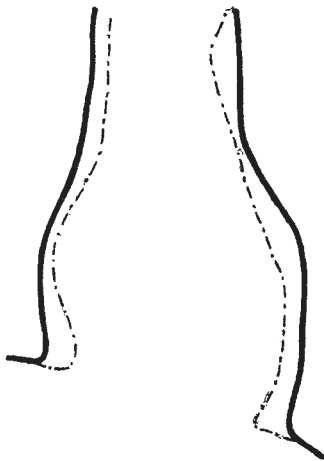
Thick lines=the cardiac border before the operation.  
Dotted lines=the cardiac border after the operation.



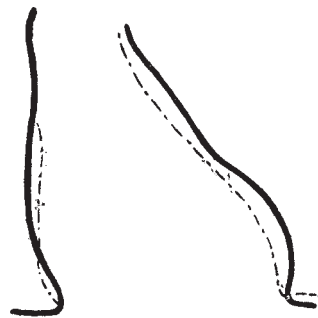
Case No. 1.  
K. S. (w) 22 years old, examined  
4 weeks after the operation.



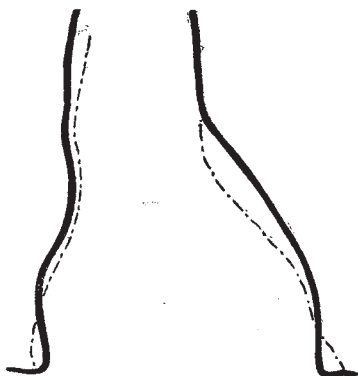
Case No. 3.  
S. G. (w) 26 years old, examined  
11 months after the operation.



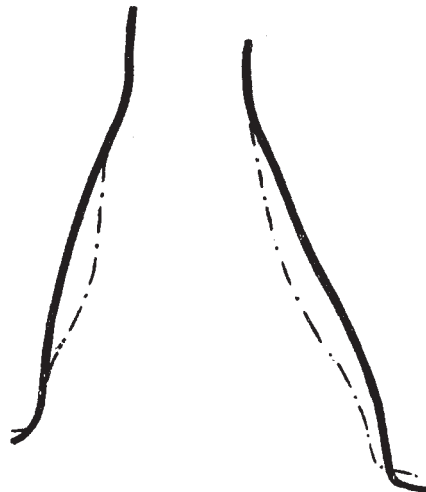
Case No. 4.  
S. M. (m) 33 years old, examined  
11 months after the operation.



Case No. 7.  
T. T. (w) 14 years old, examined  
5 weeks after the operation.



Case No. 8.  
M. K. (w) 31 years old, examined  
5 weeks after the operation.



Case No. 10.  
I. O. (w) 19 years old, examined  
5 weeks after the operation.

was observed in 40 to 50% of cases of this disease, which we recognized in our cases even in more increased percentages. We photographed the heart with X-rays (orthodiagraphy) shining through dorso-ventrally. The maximal diameters, compared before and after the operation, showed a difference of between 0.5 and 2 cm., though there was none or only a slight difference in case of simple ligation of blood vessels. It should be remembered, that chronic nephritis and beriberi were strictly excluded by scrupulous examination from our cases. It has been reported by others, that cardiac dilatation in this disease is manifested more in the left heart. For instance, Baruch noticed its dilatation in 63% cases on the left, 29% on both sides, only 8% on the right. On the contrary, Fr. Müller said, that the right heart is distinctly more frequently affected than the left. In our cases we found rather more dilatation of the left heart and if both sides of the heart were affected, the enlargement of the left side seemed to be more distinct than the right. In autopsy, Eppinger, Krug, Baruch and Klose found modification of the muscle fibres, the residuum of old myocarditis or arteriosclerotic changes of endocardium. Whether such changes of heart are due to the direct influence of thyroid toxine on the cardiac muscles or nerves, no definitive conclusion can be drawn yet.

TABLE VIII.

*Changes of the maximal diameters of the heart before and after the operation in Graves' disease.  
(By orthocardiography)*

Cases	Name	Sex	Before operation cm.	After operation cm.	Difference cm.	Methods of operation
1	K. S.	♀	10.0	8.0	2.0	Hemithyroidectomy
3	S. G.	♀	9.7	8.2	1.5	Hemithyroid-isthmectomy
4	S. M.	♂	9.5	8.5	1.0	Subtotal extirpation
7	T. T.	♀	9.0	8.5	0.5	Ligation of the vessels
8	M. K.	♀	9.7	9.7	0	Ligation of the vessels
10	I. O.	♀	9.5	8.5	1.0	Hemithyroid-isthmectomy

*c. Blood pressure.*

There is not much variation of blood pressure in normal human

beings. Its maximal (systolic) pressure is reported by Klemperer as 110–125 mm. Hg, by Nishimura as 100–130 mm. Hg. According to Shibayama of the Medical Department of our University, systolic pressure lies in 105–122 mm. Hg at 15–30 years of age, and in 85–99 mm. Hg in children under 15 years old. At any rate, the blood pressure of the masculine sex is usually higher than that of the female. Tycos remarked that the pulse amplitude must be considered abnormal, when it is under 25 mm. Hg or over 50 mm. Hg.

In regard to the blood pressure of Graves' disease, the reports of observers do not coincide. Spiethoff found the normal rate of pressure in cases in which the disease was not much advanced. Gärtner investigated as many as 89 cases and observed 30 cases under 100 mm. Hg (also subnormal), 25 cases between 100–120 mm. Hg, 23 cases between 125–130 mm. Hg, 10 cases between 130–150 mm. Hg, and only one case of 160 mm. Hg. According to Klose and Lampé, most of the patients showed about normal pressure, and only an increase in exceptional cases. As is well known, the blood pressure is influenced by various factors, for example, by the variation in the apparatus used for measuring, by atmospheric pressure, by psychical excitement, by physical movement, by nutrition conditions and by medicines taken etc. We have taken those factors into considerations, and repeated the measurements several times, using Tycos' and by Riva-Rocci's sphygmomanometers. We determined not only the systolic but also the diastolic pressure, so measuring the pulse amplitude by their difference (see Table IX). Summarising the results, we found usually the systolic pressure in 104–140 mm. Hg and the diastolic pressure in 36–85 mm. Hg. Although the pressure in a systolic or diastolic phasis may possibly be within normal limits, the pulse amplitude is sometimes distinctly increased. Therefore, the measurement of the latter must not be neglected, even if the systolic pressure seems to be normal. At any rate, we found in our investigations that the blood pressure usually decreases continuously after thyroidectomy, systolic pressure for example, decreasing from 140 to 120 mm. Hg and diastolic pressure from 74 to 66 mm. Hg.

*d. Cardiac sounds.*

In this disease, it is known by clinicians that a musical timbre can be sometimes auscultated at the heart-apex or pulmonary valves. We also recognized this very often in our cases. Baruch ascribed

such timbre or murmurs to the relative insufficiency of heart in consequence of its dilatation.

### Conclusions.

1. In Graves' disease the percentage of neutrophile polymorphonuclear leucocytes increases after thyroidectomy, while that of the lymphocytes decreases in number.

2. But those changes can continue only for the time being and there is a gradual return to about the same conditions before procedure.

3. Further, such a change of percentage of white cells, is not a typical finding after thyroidectomy in Graves' disease, because we have found nearly the same phenomenon after other operations on the neck (for instance, that of Lymphadenitis colli t.b.c.).

4. The ligation on blood vessels on one side seems to have less influence on the blood figure percentage than thyroidectomy.

5. The results of operation on the blood directly afterwards, however, cannot be differentiated by the grades of the latter (sub-total excision, hemithyroid-isthmectomy, hemithyroidectomy); in other words, we cannot find exactly any gradual difference in the blood figures after operation, though the methods of the latter differ.

6. The most striking feature after operation is the distinct decrease of cardiac enlargement in orthocardiography, which is not so manifest after simple ligation of the thyroid vessels unilaterally.

7. Recuperation of impaired nutrition is almost unmistakably observed after operation. Furthermore, the decrease or disappearance of subjective or objective symptoms (tachycardia, tremor, exophthalmus, hyperhidrosis etc.) has been usually observed after operation, on which point we shall publish in detail a further report of our investigations later.

8. The decrease of blood pressure is another favorable sign after operation, which usually appears more markedly after the excision of glands than on the ligation of vessels.

9. The coagulation period of blood seems to be changed after operation (especially after thyroidectomy), the commencement of coagulation being accelerated. But the time needed for the completion of coagulation has been very differently recorded after operation, and we cannot yet draw any certain conclusions.



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TABLE IX.

Changes of the blood in Graves' disease before and after the operation.

Cases	Name	Sex	Age	Opera- tion	Blood pressure (Tyco's)			Vis- cosity (Deter- mann)	Hæmo- globin % (Sahli)	Number of ery- throcytes in 1 c.mm.	Number of white cells in 1 c.mm.	Propor- tion of red and white cells	Neutrophile polymorpho- nuclear i.		Eosinophile i.		Basophile i.		Small lymphocytes		Large lymphocytes		Large mono- nuclear and transitional		Remarks
					S. P.	D. P.	Pulse ampl.						%	Absol. No.	%	Absol. No.	%	Absol. No.	%	Absol. No.	%	Absol. No.	%	Absol. No.	
1	K. S.	W	22	{ before after	110 97	62 64	48 33	58 50	4,716,000 4,650,000	12,000 9,000	388:1 537:1	67:13 60:69	2:02 3:26	242:4 263:4	1:10 0:94	133:0 84:6	23:35 29:50	2,802:0 2,685:0	1:70 2:35	204:0 911:5	4:71 3:26	565:2 288:4	{ Hemithyroidectomy dextra, ex- amined 2 months post operat.		
2	T. M.	M	29	{ before after	126 126	60 60	66 66	65	5,240,000	8,300	631:1	40:06	12:98	1,077:34	0:49	40:67	39:42	3,271:8	4:17	346:1	2:88	219:04	{ Subtotal extirpation, exitus 18h. p. o.		
3	S. G.	W	26	{ before after	145 114	65 66	80 48	5:6 4:5	4,896,000 4,624,000	13,400 10,000	364:1 462:1	61:4 54:62	6:7 12:3	897:7 123:0	3:20 0:47	428:8 47:0	24:5 26:0	3,233:0 2,600:0	5:0 1:66	402:0 165:0	1:20 4:96	100:8 496:0	{ Hemithyroid-isthmectomy, exami- ned 1 year p. o.		
4	S. M.	M	33	{ before after	128 126	65 64	63 62	5:2 4:0	4,170,000 4,248,000	8,650 9,200	505:1 461:1	59:6 48:83	1:9 10:5	156:75 966:0	2:50 0:61	208:2 56:12	30:3 26:51	2,497:7 2,438:7	3:20 3:91	264:0 359:9	2:5 9:54	208:3 677:7	{ Subtotal extirpation, examined 1 year p. o.		
5	H. O.	W	27	{ before after	125 120	65 60	60 60	5:8 5:0	4,960,000 5,624,000	11,800 10,000	420:1 552:1	72:16 68:83	5:8 12:98	664:4 1,238:0	1:37 0:97	161:66 97:0	15:10 13:53	1,751:3 1,353:0	2:09 1:35	246:6 135:0	3:48 2:94	410:6 294:0	{ Subtotal extirpation, examined 1 month p. o.		
6	K. A.	W	32	{ before after	115 110	66 64	49 46	4:5 3:5	4,740,000 4,600,000	12,000 9,000	395:1 510:1	68:87 70:27	5:39 5:27	646:8 474:3	3:43 1:33	411:6 146:7	18:63 18:75	2,235:6 1,687:5	1:47 0:95	176:4 31:5	2:41 3:53	289:2 317:7	{ Hemithyroid-isthmectomy, exami- ned 2 months p. o.		
7	T. T.	W	14	{ before after	104 97	65 66	39 31	5:0 3:8	4,800,000 4,250,000	10,000 12,000	480:1 354:1	86:88 71:81	0:41 0:23	41:0 27:6	1:23 2:06	123:0 247:2	9:43 19:49	943:0 2,338:3	0:82 2:29	32:0 274:5	1:23 4:12	123:0 494:4	{ Ligation of A. et V. thyroid. sup. et inf., examined 2 m. p. o.		
8	M. K.	W	31	{ before after	120 112	64 62	56 50	5:9 5:2	4,528,000 4,860,000	13,200 8,200	343:1 605:1	57:90 56:90	10:11 10:7	1,234:5 377:4	3:68 1:93	485:7 158:2	24:64 24:82	3,252:4 1,035:2	0:18 1:30	23:7 106:6	3:49 5:25	460:6 430:5	{ Ligation of A. et V. thyroid. sup. et inf., examined 2 m. p. o.		
9	T. K.	W	44	{ before after	158 126	62 87	96 39	4:8 3:9	4,264,000 4,720,000	8,000 12,000	533:1 350:1	41:14 58:50	4:7 4:19	376:0 502:8	2:32 0:79	225:6 94:8	41:15 30:88	3,292:0 3,705:6	4:11 2:09	323:8 94:8	6:08 3:15	486:4 380:0	{ Hemithyroidectomy, examined 4 weeks p. o.		
10	I. O.	W	19	{ before after	108 104	72 74	36 30	5:6 4:1	5,552,000 4,800,000	9,400 10,400	598:1 462:1	69:68 67:83	1:34 2:5	125:06 260:0	0:85 0:23	79:9 28:99	21:94 23:46	2,082:0 1,439:8	1:67 1:37	156:9 142:4	4:52 5:01	424:3 521:04	{ Hemithyroid-isthmectomy, exami- ned 5 weeks p. o.		
11	T. M.	W	36	no	128	72	56	5:2	5,046,000	9,400	586:1	50:07	7:73	726:6	1:65	155:1	33:05	3,106:7	2:30	216:2	5:20	488:8	Medical and X-rays treatment.		
12	K. A.	M	49	no	140	55	85	5:6	5,500,000	11,500	482:1	65:27	9:13	1,049:9	2:37	272:2	16:39	1,884:8	3:42	393:3	3:42	395:3	"		
13	B. T.	M	46	no	139	70	69	5:5	5,200,000	10,000	520:1	47:07	6:94	694:0	1:52	152:0	37:02	3,702:0	2:39	239:0	5:06	506:0	"		
14	K. N.	W	26	no	120	64	56	6:2	5,248,800	9,400	568:1	55:58	3:64	342:1	2:43	228:4	34:70	3,261:8	1:22	114:6	2:43	228:4	"		
15	K. S.	W	16	no	105	65	40	5:1	4,650,000	8,000	381:1	56:75	3:43	274:4	2:0	160:0	30:82	2,465:6	3:43	274:4	3:57	285:6	"		