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Studies on the Basal Metabolism in the Patients after the Operation of Cervical Carcinoma, Especially on the Effects of Autotransplantation of the Ovary and Castration

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Studies on the Basal Metabolism in the Patients after the Operation of Cervical Carcinoma, Especially on the Effects of Autotransplantation of the Ovary and Castration*

Susumu Higashi

Abstract

The evaluations of the basal metabolism before the operation, at the completion, and at the follow-up examinations, have been conducted on the patients with cervical carcinoma, all under the age of 50 years, and operated on in the Clinics of Obstetrics and Gynecology, Okayama University Medical School and the following results are obtained: 1. The basal metabolism of the patients with cervical carcinoma of either stage I or stage II as compared with that of the normal women is more accelerated; while the basal metabolism of the cervical carcinoma of stage II. is more augmented than that of the cervical carcinoma stage I. 2. The basal metabolism at the completion of operation is markedly lower than that before the operation. 3. In those who received the autotransplantation of the ovary concomitantly with operation, the basal metabolism once increases at the 4th month after the operative castration continues increasing up to the 8th month after the operation and after that it maintains a low stable state. 4. The basal metabolism of the basal metabolism, it has been recognized that the autotransplantation as compared with the castration exerts less influences on the somatic system and for a shorter period of time, and also the endocrine system of the former returns to the balanced condition earlier.

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STUDIES ON THE BASAL METABOLISM IN THE PATIENTS AFTER THE OPERATION OF CERVICAL CARCINOMA-ESPECIALLY ON THE EFFECTS OF AUTOTRANSPLAN TATION OF THE OVARY AND OF CASTRATION ON THE BASAL METABOLISM

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INTRODUCTION

In cancer of the uterus, it is believed that the pathological changes not only involve in the local conditions but also in the total organism, ultimately bringing about the alterations in the basal metabolism.

KAWABE¹⁷, TAKAYAMA⁴², ITO¹⁴ and KUMAGAI²³ have reported that the basal metabolism of the patients suffering from the uterine cancer has been found to be more active compared with that of the normal women. There are also many literatures concerning the alteration of the basal metabolism due to the treatment of uterine cancer such as reports by KAWA-BE¹⁷, UEDA⁴⁵, KATO¹⁶, TAKAYAMA⁴² and UNO⁴⁶; and more recently KUMAGAI²³ has made a comprehensive report on a considerable number of cases regarding the same subject.

On the operation of the patients with uterine cancer, especially that of the preclimacteric patients, with a view to facilitate a more adequate management of the ovary, the organ playing an important rôle in the female endocrine system, we in the clinics of the Okayama University Medical School employ deep x-ray radiation therapy after the operation of cervical carcinoma so that if the ovarian tissues are left behind, the ovarian tissues are damaged by x-ray or an cyst is occasionally formed which is sometimes erroneously by diagnozed as lymphatic metastasis. Furthermore, as the preventive measures against various lesions arising out of castration, the autotransplantation of the ovary by WAGNER's method has been instituted on the patients under 50 years old ever since 1938 under the direction of Prof. Yagi and as of December 1956 we have treated 946 cases with the same method.

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It seems reasonable to suppose that the bilateral extirpation of the ovaries gives rise to the dysfunction and hypertension of vegetative nerves in the endocrine system, resulting naturally in some alterations of the basal metabolism. Actually many reports on the alterations in the basal metabolism caused by castration have appeared since LOEWY and RICHTER²⁶ (1899). The literatures reporting from various aspects the beneficial effects of the transplantation of the ovary are likewise numerous since first reported by MORRIS³³ in 1896. On the other hand, the reports concerning the effects of transplantation of the ovary on the basal metabolism are indeed scarce, with exceptions of a few reports by TSUBARA⁴³, ZONDEK⁵¹ and HIGUCH1⁹; furthermore, no reports has as yet appeared on the autotransplantation of the ovary in the patient with cervical carcinoma on which the observations had been carried on for any considerable length of time.

In the present paper are presented a few interesting experiences which the author has encountered during his comparative observations on the basal metabolism of the preclimacteric patients either receiving autotransplantation of the ovary or castration, carried on continally from preoperative time to postoperative period.

CHAPTER 1.

The Basal Metabolism of the Patients with Cervical Carcinoma before Operation

As mentioned in the introduction, the majority of the available reports on the investigations evaluating the basal metabolism of the patients with uterine cancer state that the basal metabolism is accelerated in the patient as compared with that of the normal women. KUMAGAI²³, dividing the patients with cervical carcinoma according to the international classification, has reported in details the influences of operation of the basal metabolism, and confirms that the basal metabolism is likewise accelerated in the patients.

In the present series of experiments, for the purpose of evaluating the influences of autotransplantation of the ovary to be brought about later on the basal metabolism, the need for preoperative evaluation of the basal metabolism was apparent for the later comparison to be made, therefore, the preoperative evaluations have been carried out to meet this need.

I. MATERIAL OF STUDY

During the period from August 1955 to May 1956, of the patients admitted to the Clinics of Obstetrics and Gynecology of Okayama Un-

iversity Medical School, who had been microscopically verified to have the cervical carcinoma, and the ones who had been diagnosed as having the cervical carcinoma of stages I and II or and on whom abdominal extensive hysterectomy by the Okabayashi method had been performed 86 cases under the age of 50 years whose ovarian functions prior to operation had been adjudged to be normal were selected for the present study, excluding as best all those who had either some internal disorders or severe skin lesions, the causal factors of alteration in the basal metabolism.

As for the control, the normal, healthy group of the age range comparable to that of the patients, 31 cases of normal pregnant women of the age above 30 but below 50 years old, who were thought to be in perfectly healthy state were selected; and the evaluation of the basal metabolism has been carried out by the ROCK and HERTIG classification³⁸ during the periods of their intermenstruum.

II. METHOD

The KNIPPING apparatus, being capable of simultaneous evaluations of oxygen and carbon dioxide and simple and convenient in its manipulation, has been used. All the necessary precautionary measures before the study as well as the method of the evaluation were taken following those of KNIPPING's²⁰, and the actual evaluations were made at the Clinics of Obstetrics and Gynecology of Okayama University Medical School. Measurements were taken at the exact interval of 10 minutes, and the amounts of oxygen and carbon dioxide recorded on the kymograph were computed at 760 mm. Hg at 0°C; and from these values the respiratory quotient was obtained. Further, by computing the respiratory index, and obtaining the daily requirement of calories of each subject, the values so obtained were referred to HARRIS-BENEDICT's table and the percentage of the basal metabolism was determined. The amount of carbon dioxide produced by the reaction of the agents used was found to be 150 c.c. on the average according to the blind test.

As for the evaluation on the patients before the treatment, it was carried out the day after admission in order to avoid various influences of medications and treatment.

III. RESULTS OF EXPERIMENTS

1. Values of normal healthy persons: In the determination of percentage of the basal metabolism in 31 cases of normal pregnant women of the age above 30 years, the maximum was 18.09 % and the minimum

3.00% (% will be omitted hereafter), the average of 10.24 and $u^2 = 26.57$; from these nominal average reliability limit becomes $12.13 \ge m \ge 8.35$ and dismissal limit, $20.92 \ge x_0 \ge -0.44$. However, the stochastic reliability has all been fixed at 95% (the same in the followings). Therefore, those above 20.93 and those below -0.45 have been determined to be positive values. Considering the age, the percentage of the basal metabolism above 40 years old was found to be 10.73 on the average, that under 40 years, 9.35; and no significant difference could be found stochastically between the two.

2. Patients with Cervical Carcinoma before the Treatment.

(1) By the international classification 85 cases with cervical carcinoma were divided according to their clinical stage; and the average values of the basal metabolism and positive percentages of respective groups were found to be as shown in Table 1.

(i) Significant difference can be seen between the values of the normal persons and both averages of the basal metabolism and positive percentages in the patients with either cervical carcinoma of stage I or of stage II, i.e. the values of the patients are significantly higher than those of the normal.

stage	nos. of cases	average value	positive nos. (%)	u ²
I	43	18.99 ± 2.57	16 (37.2%)	70.00
II	42	19.96 ± 2.65	19(45.2%)	72.07
normal	31	10.24 ± 1.89	0	26.57

Table 1. Comparison According to Clinical Stages

(ii) No significant difference between the average value of cervical carcinoma stage I and that of stage II can be seen but nevertheless that of the stage II shows a tendency of a greater acceleration than that of the stage I.

(2) Comparison according to the ages of the patients: The difference in values due to the age difference is not so significant among the normal mature women, but the results of the patients with cervical carcinoma are as shown in Table 2. Of the 85 patients, the oldest was 49 years and 11 months old while the youngest was 26 years and 4 months; and the average of the group was 41 years and 5 months.

In the patients with cervical carcinoma, no significant difference could be recognized either in their average value or in the positive percentage.

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age	cases	average	positive nos. (%)	u ²
under 39	29	18.77 ± 3.02	14 (48.3%)	63.00
over 40	56	19.83 ± 2.32	21 (37.5%)	75.13

Table 2. Comparison According to Age

(3) Comparison according to the parity of the patients: The maximum parity frequency was ten and the minimum was none (provided of course, all had been presumed to have had normal menstruation and normal ovarian functions). They are divided into four groups according to the number of times they became pregnant; group A, 0-1 time; group B, 2 to 3 times; group C, 4 to 5 times; and group D, 6 times or more. The results of their basal metabolism findings are shown in Table 3.

Frequencies	Cases	Average values	Positive nos. (%)	u ²
(A) 0—1	10	19.40 ± 4.91	3 (30.0%)	47.10
(B) 2—3	15	21.04 ± 4.94	7 (46.7%)	79.52
(C) 4—5	36	19.18 ± 3.27	16 (44.4%)	93.31
(D) 6 times or more	24	18.94 ± 2.89	9 (37.5%)	46.73

 Table 3.
 Comparison of the Basal Metabolism among the Patients According to their Frequencies of Pregnancy

(4) Comparison made according to the local findings of the patients: Local lesions of cervical carcinoma were divided into three findings; namely, erosion, cauliflower carcinoma (Blumenkohl), and volcano crater (Krater); and their comparative values are as shown in Table 4.

Table 4.Comparison of the Basal Metabolism According
to the Local Findings

local finding	cases	average	positive nos. (%)	u ²
Erosion	41	19.15 ± 2.76	17 (41.5%)	76.36
Cauliflower	35	19.05 ± 2.73	14 (40.0%)	63.15
Krater	9	22.56 ± 6.39	4 (44.4%)	69.09

No significant difference could be discernible between the respective values of average and positive percentage.

(5) Blood pressures and the basal metabolism : The blood pressures of the patients were divided into 4 groups of A (below 99), B (100-119),

C (120-139) and D (above 140); and the results of investigations on the relationship between the blood pressures and the basal metabolism at the time of admission are given in Table 5.

blood pressures	od pressures cases		positive nos. (%) u	
(A) below 99	2	14.91 ± 40.06	0	19.94
(B) 100 - 119	42	18.89 ± 2.45	16 (38.1%)	61.97
(C) 120 — 139	32	18.12 ± 2.87	12 (37.5%)	63.14
(D) over 140	9	27.98 ± 6.83	7 (77.8%)	79.12

Table 5. Relationship between the Blood Pressures and the Basal Metabolism

There is no significant difference other than the average values showing stochastically the relationships, (C) < (D) and (B) < (D), though there is a tendency that the higher the blood pressure the more accelerated the metabolism seems to be. As for the positive percentage, no marked difference could be seen either, however, nothing definitive can be said here since the number of cases both in (A) and (D) groups is not large enough.

(6) The erythrocyte counts and the basal metabolism : The relationships between the erythrocyte counts in 1c.mm. and the values of the basal metabolism are shown in Table 6.

erythrocyte counts (unit : million)	cases	average	positive nos. (%)	u ²
(A) under 2.50	3	19.93 ± 12.63	1 (33.3%)	25.86
(B) $2.51 - 3.00$	6	$\textbf{22.59} \pm \textbf{10.64}$	4 (66.7%)	102.47
(C) $3.01 - 3.50$	19	19.71 ± 3.44	8 (42.1%)	50.89
(D) $3.51 - 4.00$	32	18.47 ± 3.12	11 (34.4%)	74.54
(E) over 4.01	25	19.76 ± 3.80	11 (44.0%)	84.66

Table 6. Relationship between Erythrocyte Counts and the Basal Metabolism

No marked difference in respective averages and positive percentages can be noticed nor can any definite relationship be thought to exist between the erythrocyte counts and the basal metabolism.

(7) MANDELSTAMM's 6-degree test and the basal metabolism : The relationships between the types of the erythrocyte sedimentation, the

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rates of which had been classified by MANDELSTAMM's 6-degree test and their respective evaluations of the basal metabolism are shown in Table 7.

M type	cases	average	positive nos. (%)	u ²	
I	3	13.42 ± 14.76	0	35.36	
Π	7	$21.26 \pm 6.56 \qquad 4 (57.1\%)$		5 0. 3 9	
Ш	16	17.49 ± 5.00	6 (37.5%)	87.94	
IV	19	20.55 ± 4.06	10 (52.6%)	71.33	
V	21	19.69 ± 3.57	8 (38.1%)	61.59	
VI	19	20.15 ± 4.32	7 (36.8%)	80.50	

 Table 7. Relationship between the Mandelstamm Classification and the Basal Metabolism

Excepting the type I showing comparatively lower values, no significant difference in respective values, both in the averages and positive percentages, can be observed.

(8) The rates of eythrocyte sedimentation and the basal metabolism: The relationships between the hourly rates of eythrocyte sedimentation and the values of the basal metabolism are shown in Table 8.

erythrocyte cases		average	positive nos. (%)	u ²
(A) under 20	48	19.41 ± 2.67	20 (41.7%)	84.64
(B) 21 - 40	20	19.49 ± 3.65	7 (35.0%)	60.94
(C) 41 - 60	7	19.13 ± 4.70	3 (42.9%)	25.84
(D) 61 — 80	6	23.17 ± 8.26	4 (66.7%)	61.98
(E) over 81	4	15.05 ± 11.79	1 (25.0%)	54.93

Table 8. Relationships between Erythrocyte Sedimentation and
the Basal Metabolism

Though there is no significant difference in the respective averages and positive percentages, in the case as (E) in which the rates of the hourly sedimentation are accelerated, the values tend to be lower than those of others; and it is of interest when this phenomenon is compared with a similar tendency in the type I of MANDELSTAMM's 6-degree test, which also gives lower values than the others.

(9) The KAUFMANN test and the basal metabolism : By performing

the KAUFMANN test which is really a test of the circulatory system, the relationships between the results of the test and the values of the respective basal metabolism have been compared as shown in Table 9.

Kaufmann value cases		average	positive nos. (%)	u ²
(A) under 79	4	21.46 ± 15.26	2 (50.0%)	91.97
(B ₁) 80 — 99	21	18.14 ± 3.73	8 (38.1%)	67.17
(B ₂) 100 - 119	33	19.63 ± 2.73	15 (45.5%)	59.48
(B ₃) 120 — 139	8	17.51 ± 8.40	2 (25.0%)	101.02
(C) over 140	19	21.06 ± 4.48	8 (42.1%)	86.51

Table 9. Relationships Between the Values of the KaufmannTest and Those of the Basal Metabolism

Though there is no striking difference in the averages and positive percentages among the groups (A), (B₁), (B₂), (B₃) and (C), the groups giving lower values in the KAUFMANN test such as (A) and (C) denote a tendency of acceleration in the basal metabolism compared with the B groups giving better results in the same test.

CHAPTER 2. THE BASAL METABOLISM OF THE PATIENTS WITH CERVICAL CARCINOMA AT THE TIME OF COMPLETION OF TREATMENT.

Up to the end of August 1956, of the patients visiting the clinics of Obstetrics and Gynecology of the Okayama University Medical School, diagnosed as having cervical carcinoma essentially of the stage I and the stage II, those patients under the age of 60 years were treated by OKA-BAYASHI's abdominal extensive hysterectomy; while those under 50 years old at that time, presumably having the normal menstruation cycle were treated as soon as feasible with unilateral and occasional, bilateral auto-transplantation of the ovary either into the rectus muscle or subfascially following WAGNER's method. After either of these operations those developing no especial complication were given 12 times of deep x-ray radiation treatment (300γ each) 21 days after the operation and the treatment was then terminated. During this treatment the site of the autotransplantation was covered by the lead plate so as to protect it from the danger of being irradiated directly by x-ray.

Concerning the influences of x-ray radiation on the basal metabolism, there are reports by UEDA⁴⁵, TAKAYAMA⁴², KATO¹⁵, UNO⁴⁶ and ITO¹⁴ avail-

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able. The author measured the basal metabolism on the completion of the operation on the patients with cervical carcinoma and made comparative studies of the values so obtained with those before the treatment.

I. MATERIAL AND METHOD

Of the patients mentioned in Chapter I, the study was carried on the 59 cases having no especial post-operative complication and improving excellently, excluding those who had recurrent attacks or whose post-operative conditions had not been so favorable after the dismissal from cilinics.

The method employed was the same as that in Chapter I and the measurements were taken on the morning after the completion of the treatment.

II. RESULTS OF STUDY.

(1) Comparison between the preoperative and the postoperative results : As for the values of the basal metabolism measured on the completion of treatment, the average is 14.47, (the amount = u^2) $u^2 = 94.50$, positive number and percentage are 22 (37.3%) respectively. When these values are compared to the respective values before treatment, namely, the average of 19.16, $u^2 = 77.57$, positive number and percentage, 26 (44.1%); they show comparative values as in Table 10.

period	cases	average	positive nos. (%)	u ²
before treatment	59	19.61	26 (44.1%)	77.57
on completion of treatment	59	14.47	22 (37.3%)	94.50

Table 10. Comparative Values before and after the Treatment

A marked difference can be seen between the preoperative and the postoperative averages [Pr { $|t| \ge 3.80$ } < 5% $\overline{Z} = 5.14$ u = 10.38 N = 59]. In other words, the values at the completion of treatment have markedly diminished from those before treatment. In the positive percentages of the two, no significant difference can be recognized. Those whose postoperative values of the basal metabolism decreased as compared to those before treatment numbered 42 cases out of the 59 treated (71.2%) and those whose values increased numbered 17 (28.8%).

(2) Comparison between the group receiving autotransplantation of the ovary and the castrated group: Thirty eight of the 59 cases received autotransplantation of the ovary at the time of operation while the so-

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called operative castration was performed on 21 cases.

(i) Comparison of average values : The average values of these respective cases compared to preoperative values of the basal metabolism are shown in Table 11.

Table 11.	Comparison	of	Averages	between	the Group	Persiving
Autotra	insplantation	of	the Ovar	y and th	e Castrated	Group

period	autotransplantation group	castrated group
preoperative	18.93 ± 2.94	20.84 ± 3.85
at the completion of treatment	13.24 ± 3.35	16.70 ± 3.81

In the transplantation group, those whose values decreased compared with the preoperative period numbered 28 (73.7%), while those who had shown an increase were 10 (26.3%); and the average was found to be 13.24 \pm 3.35. On the other hand, in the castrated group, those with a decrease were 14 (66.7%), while those with an increase 10 (33.3%); and their average was 16.70 \pm 3.81. A significant decrease in the average value at the completion of treatment is noted in the autotransplantation group [Pr { $|t| \ge 3.309$ } < 5% $\overline{Z} = 5.68$ u = 10.58 N = 38]. In the castrated group, however, no striking difference in the average at the time of completion of treatment as compared with that of pretreatment can be noted [Pr { $|t| \ge 1.85$ } > 5% $\overline{Z} = 4.15$ u = 10.28 N = 21], though the value has presumably had a tendency to decrease.

Moreover, values both before treatment and at the completion of treatment in the castrated group are higher as compared with the respecitive averages of the transplantation group, though the differences between the two groups are not so significant. Namely, the values at the completion of treatment compared to those before the treatment have tended to decrease in both the autotransplantation and the castrated groups, and the decreases in the values of the two more less paralleled with each other.

(ii) Comparison of positive percentage: Positive numbers and percentage of the basal metabolism both before and at the completion of treatment are compared in Table 12.

No significant change can be seen in the basal metabolism on the completion of treatment compared to that of before the treatment in both groups; at the same time there is no significant difference between the respective values of the transplantation and those of the castrated.

period	Group	cases	positive nos.	negative nos.	positive percentage
before treatment	autotr.	38	21	17	44.7%
	castrated	21	12	9	42.9%
at the completion	autotr.	38	24	14	36.8%
the oletion	castrated	21	13	8	38.1%

Table 12.	Comparison of Positive Numbers and Percentages be	oth
	Before and on the Completion of Treatment	

CHAPTER 3. THE BASAL METABOLISM AT THE FOLLOW. UP EXAMINATIONS OF THE CASES AFTER THE TREATMENT OF CERVICAL CARCINOMA.

All the patients receiving the treatment of cervical carcinoma either by operation or radiation at our clinics are examined at a fixed interval for the period of five years after leaving the clinics, and their conditions are constantly watched by doctor. Moreover, they are advised as a matter of routine to receive physical examination every other month for the first one year after their discharge from the clinics.

In an attempt mainly to determine what influences the autotransplantation of the ovary or the operative castration would be brought upon the basal metabolism at the time of operation, the author made comparative studies continuously on the basal mtabolism before and immediately after the treatment, and at the periodic follow-up examinations, of the same individuals.

I. MATERIAL.

The evaluations of the basal metabolism were carried on the patients mentioned in Chapter I, who had received a given treatment and were visiting our clinics for the follow-up examinations.

Those who had been examined for the period of 4 months after the operation numbered 58 cases, those for the 6-month period 45 cases, those for 8 months numbered 43, those for 10 months were 38, those for 12 months 31 cases, and those who had been albe to be checked for one year and three months numbered 14. Periodic examination over one year after the operation is made once in every three months, therefore, for the examination over one year after the operation, a unit of the examining period is set at one year and three months. Those whose postoperative condi-

tions were not favorable and recurrent cases are, of course, not included in the present study.

II. METHOD.

The method as described in Chapter I was used. Subjects were requested as much as possible to visit the clinic one day before examination and hospitalized for a day and evaluated on the following morning. Those who had not been hospitalized did not partake breakfast, nor any tea or water, and came by available conveyances; and immediately upon their arrival at the clinic they were made to lie down quietly for at least one hour and then the evaluations of the basal metabolism were done only when the patient was perfectly in normal condition with regular respiration and pulsations.

III. THE RESULTS OF EXPERIMENT.

The results of the basal metabolism at various periods examined are listed in Tables 13 and 14 and in Figure 1, respectively.

(1) Up to 4 months after the operation (at the first examination, 58 cases). Of the 58 cases, 38 were autotransplantation group, while 20 were castrated cases.

(i) Autotransplantation group (38 cases). Twenty six cases (68.4%) show an increase in the basal metabolism compared to that on the completion of operation, 12 cases (31.6%) show a decrease in the same period; and their average is 18.76 \pm 3.46, positive number and percentage are 12 (31.6%).

When these values are compared to those before the treatment, the average values are approximately the same in either stage and no significant difference can be recognized between the two; while on the other hand, when these values are compared to those on the completion of operation, a marked increase [Pr { $|t| \ge 3.46$ } <5% $\overline{Z} = 5.52$ u = 9.82 N = 38] can be observed. As for the positive percentage, there is hardly any difference between that before treatment and that on the completion of treatment.

(ii) Castrated group (20cases). Thirteen cases (65.0%) show an increase in the basal metabolism since the completion of operation, while 7 cases (35.0%) show a decrease; and their average value is 22.54 ± 6.14 , positive numbers and percentage are 10 (50.0%). When these values are compared to those before the treatment, the average value is about the same or a little higher in some but there is really no marked difference; while

when compared to those on the completion of operation, there is a significant increase $[\Pr \{|t| \ge 2.094\} < 5\% \ \overline{Z} = 6.125 \ u = 13.08 \ N = 20]$. Between the positive percentages of both before and on the completion of operation there is no significant difference.

(iii) Comparison between the autotransplantation group and castrated group. Although castrated group shows continually higher value since the preoperative period compared to those of the autotransplantation group, even in this instance no significant difference is discernible. Namely, the two groups present parallel changes both at the preoperative stage and on the completion of operation. Even in the positive percentages, no significant difference exists between the two groups.

(2) Five to six months after the operation (45cases). Thirty cases had autotransplantation of the ovary at the time of operation, and the castrated cases numbered 15.

(i) Autotransplantation group (30 cases). Six cases (20.0 %) show an increase in the basal metabolism as compared to the cases examined up to 4 months after the operation, while 24 cases (80.0 %) show a decrease; and in comparison to the preoperative values, 10 cases (33.3 %) show an increase while 20 cases (66.7 %) a decrease. Their average is 13.29 \pm 3.71, and the positive numbers and percentage are 10 (33.3 %). The average value compared to that up to 4 months after the operation shows a marked decrease [Pr { $|t| \ge 4.061$ } < 5 % $\overline{Z} = 5.85$ u = 7.89 N = 30]; while the positive percentage in comparison with that of 4 months after the operation show no significant difference.

(ii) Castrated group (15 cases). Eight cases (53.3 %) show an increase in the basal metabolism as compared to that up to 4 months after the operation, while 7 cases (46.7%) show a decrease. When compared to the preoperative values, those showing an increase number 7 cases (46.7%) and those a decrease 8 cases (53.3%); and their average value is 21.29 \pm 5.34, and the positive numbers and percentage are 7 (46.7%).

When the average is compared with that up to 4 months after the operation, there is a slight tendency of decreasing but actually no significant difference; and when compared to the pretreatment values, there is no significant difference either. Namely, those whose values rose to or over the level up to 4 months after the operation still show a high value even 5-6 months after the operation.

The positive percentage differs not to any marked degree compared to either that before the operation or that up to 4 months afterwards.

(iii) Comparison between the two groups. The respective values of the basal metabolism of the two group are about the same throughout the

periods ranging from preoperative to 4 months after operation; and the changes in the basal metabolism, moving more or less parallel to each other have become rather pronounced 5-6 months after the operation $[\Pr \{ |t| \ge 2.57 \} < 5 \% F_s = 1.058 \ \omega^2 = 96.85 \ t_s = 2.57];$ and moreover, the castrated group clearly presents an accelerated state. Positive percentages of the two groups indicate no significant difference.

renous of Measurement									
	period	before opera- tion	pletion	tion up	tion 5-	tion 7-	after opera- tion 9- 10th mo.		after operation 13—15th
trans.	cases G. U. average	38 18.93 ±2.94	38 13.24	38 18.76	30 13.29	27 13.86	25 10.25	20 13.45	mo. 9 10.41 ±7.17
castra- ted	cases G. U. average	21 20.84 ±3.85	21 16.70 ±3.81	20 22.54 ±6.14	15 21.29 ±5.34	16 20.53 ±6.10	13 12.98 ±3.38	11 13.69 ±5.22	5 11.86 ±4.11

Table 13. Number of Cases and Average Values at Various Periods of Measur

(3) Seven-eight months after the operation (43 cases). Those who received autotransplantation of the ovary at the time of operation number 27 cases, and the castrated cases 16.

(i) Autotransplantation group (27 cases). Of the 27 cases, 16(59.3%)show an increase in the basal metabolism, and 10 (37.0 %) a decrease, while one (3.7 %) shows no change, as compared to those up to 5-6 months after the operation. When compared to that before the treatment, those who show an increase number 9 (33.3 %), those who had a decrease 18 (66.7 %); while the average is 13.86 \pm 3.64, and the positive number and percentage are 7 (25.9%). The average as compared to that up to 5 -6 months after the operation, is more or less the same and no significant difference can be found; while when this is compared to the average before the operation, clearly there is a significant difference [Pr $\{|t| \ge$ 2.66} < 5 % \overline{Z} = 5.07 u = 9.90 N = 27]. Positive percentage compared to those of the preoperative and 5-6 months after operation, there is no significant difference.

(ii) Castrated group (16cases). As compared to the 5-6th month examination, 7cases(46.7%) showan increase while 8(53.3%) a decrease (one case is excluded from this comparison as she did not visit for examination at that time though she received regular follow-up examinations continuously ever since then). When compared to the preoperative values 6 cases (37.5 %) show an increase while 10 (62.5 %) a decrease. The average value is 20.53 \pm 6.10, the positive numbers are 7 (43.8 %); and then this average in compared to that of 5-6 months after operation there is no marked

difference between the two though there is a slight tendency of decrease $[\Pr \{ |t| \ge 0.886 \} > 5 \% \ \overline{Z} = 1.485 \ u = 6.49 \ N = 15]$. When the average is compared to that before operation, no significant difference can be seen either. Namely, though there was a slight tendency of decrease after 4 months, they maintained still a high value. As for the positive percentage when compared to either that before or to that 5-6 months after operation, no marked difference can be seen in either case.

(iii) Comparison between the two groups. Even at this stage similar to the comparison at the 5–6 month period, the average values of the two groups differ significantly [Pr { $|t| \ge 2.097$ } < 5% F_s = 1.55 $\omega^2 = 101.77$ t_s = 2.097]. In other words, the autotransplantation group as compared with the castrated group shows a markedly lower basal metabolism. In the positive percentage, however, no marked difference can be observed between the two groups.

(4) Nine to ten months after the operation (38 cases). These 38 cases are consisted of 25 cases receiving the autotransplantation at the operation and 13 cases the castration.

(i) Autotransplantation group (25 cases). At this examination the basal metabolism compared to that of 7-8 month period, 9 cases (37.5%) show an increase while 15 cases (62.5%) a decrease. Those whose basal metabolism was higher than the pretreatment level number 5 cases (20.0%) while 20 cases (80.0%) show a marked decrease. The average value is 10.25 ± 3.22 , and the positive numbers are 5 (20.0%).

The average value compared with the pretreatment average stochastically shows a significant difference $[\Pr \{|t| \ge 3.386\} < 5\% \quad \overline{Z} = 8.50$ $u = 12.55 \quad N = 25]$: though this average does not differ significantly when compared with that at 7—8 month period. That is to say the values since the 5—6 month examination are more or less the same though there have been slight fluctuations. Similarly in the positive percentage no significant difference can be recognized as compared with that before the operation ($x_s^2 = 4.06$). Namely, even in the percentage abnormal values clearly has declined since the preoperation period; and no marked change can be seen between this percentage and that at the 7—8 month period (Fig. 1).

(ii) Castrated group (13 cases). Comparing with that of the 7-8 month period, in this group there are 2 cases (15.4 %) showing an increase in the basal metabolism, while 11 cases (84.6 %) show a decrease. On the other hand, comparing to the preoperative value, one case (7.7 %) shows an increase and 12 cases (92.3 %) a decrease; and this group like the autotransplantation group likewise shows a definite dimunition.



Fig. 1. Fluctuation Curves of Averages at Various Measurement Time.

Their average value is found to be 12.98 ± 3.38 , while not one case has given positive value. When the average is compared with that of 7— 8 month examination, there is a significant difference between the two $[\Pr \{|t| \ge 2.646\} < 5\%$ $\overline{Z} = 6.18$ u = 8.42 N = 13]. Namely, the basal metabolism which has shown high values between the periods from the 4th month to the 7—8th examination definitely gives lower values by the 9—10th examination. When the value at this stage is compared with the preoperative value, a significant difference can be recognized $[\Pr \{|t| \ge 5.072\} < 5\%$ $\overline{Z} = 8.82$ u = 6.27 N = 13]. As for the comparison of the positive percentage with both that before the operation and that of the 7—8th month period there can be seen a lowering tendency with a distinct difference (X²_s = 5.54 and X²_s = 5.23).

(iii) Comparison between the autotransplantation group and the castrated group. Average values of the basal metabolism in the castrated group are higher both at the 5—6th month examination and at the 7— 8th month examination with a marked difference compared to the respective averages of the autotransplantation group; and even at the 9—10th month examination it has been still higher than that of the autotransplantation group, whereas at this latter examination stochastically the difference of the values between the two groups tends to disappear again.

Moreover, no significant difference in the positive percentages can be seen between the two groups.

(5) Eleven to twelve months after the operation (31 cases). Of the 31 cases with whom the periodical examinations have bee successfully carried out from the preoperative period without interruption to the 11 - 12th month examination, 20 cases are the ones with the autotransplantation of the ovary and 11 with the castration.

(i) Autotransplantation group (20 cases). As compared to the 9— 10th month examination, 14 cases (70.0 %) show an increase in the basal metabolism while 6 cases (30.0 %) a decrease; and on comparing with that before the operation, 5 cases (25.0 %) show an increase, and 15 cases (75.0 %) a decrease. The average value of this group at the 11—12th month examination is 13.45 ± 3.57 , and the positive numbers, 5(25.0 %). And when compared to the respective values of the 9—10th month examination, the rates of either an increase or a decrease and the average have had an increasing tendency though stochastically no marked difference has been found between the values of this stage and those at the 9—10th month examination.

As for the positive percentages both before and after the operation, compared to the respective percentages at the 9-10th examination, no change can be recognized.

(ii) Castrated group (11 cases). Six cases (54.5 %) of the castrated group show an increase since the 9—10th period while 5 cases (45.5 %) a decrease. When compared to that before the operation, 2 cases (18.2 %) show an increase and 9 cases (81.8 %) a decrease; and the average is 13.69 \pm 5.22, and positive numbers, 3 (27.3 %).

When the average is compared with that at the 9-10th month examination, though there is a slight tendency on the rise, no marked change can be seen since that time. Comparing to that before the operation, it differs markedly [Pr { $|t| \ge 2.76$ } < 5% \overline{Z} = 7.94 u = 9.54 N = 11], showing lower values. As for the average values looking from the rates of an increase or a decrease, it is seen that they are lower than the values before the treatment but they do not differ materially from those at the 9-10th month period. However, in the positive percentages at this stage as compared to both before the operation and at the 9-10th month no change can be recognized.

(iii) Comparison between the two groups. During the whole periodic examinations, this is the period where the average value difference between the autotransplantation and the castrated groups is least; hence naturally no marked difference is recognizable at this period. Moreover,

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period	group	cases	negative nos.	positive nos.	positive percentage
up to 4th mo.	(+)	38	26	12	31.6%
up to 4th mo.	(-)	20	10	10	50.0%
56th mo.	(+)	30	20	10	33.3%
5-oth mo.	(-)	15	8	7	46.7%
7-8th mo.	(+)	27	20	7	25.9%
78th mo.	(-)	16	9	7	43.8%
9-10th mo.	(+)	25	20	5	20.0%
5-10th mo.	(-)	13	13	0	0%
11-12th mo.	(+)	20	15	5	25.0%
11-12th mo.	(-)	11	8	3	27.3%
later than	(+)	9	7	2	22.2%
12th mo.	(-)	5	5	0	0%

Table 14. Positive Percentage at the Various Periods of Measurement.

no striking difference in the positive percentage between the two groups can likewise be seen.

(6) Thirteenth to 15th month examination (14 cases). Those on whom it has been possible of making periodical examinations successively from the preoperative period to the 13 - 15th month number 14 cases; and of the 14 cases, 9 cases are the autotransplanted ones and 5 cases are the castrated. Though the number of cases is small, the results are as follows:

(i) Autotransplantation group (9 cases). In comparison with the values at the 11-12th month examination, 5 cases (55.6 %) show an increase while 4 cases (44.4 %) a decrease. And on comparing to the pre-operative values, there is none that shows an increase while all the 9 cases show a decrease. The average value is 10.41 ± 7.17 and the positive numbers, 2 (22.2 %). It is clear that the average, when compared with that of the 11-12th month examination, shows a decrease but no significant difference, whereas compared to the preoperative average it is decreased with a significant difference [Pr { $|t| \ge 5.16$ } < 5% $\overline{Z} = 11.52$ u = 6.69 N = 9]. Namely, they are lower than those of the 11-12th month examination and even from the average and the rates of an increase or a decrease, it can be seen that respective values of the two are more or less the same.

In the positive percentages compared with those of preoperative and of the 11 - 12th month values, no striking difference is discernible.

(ii) Castrated group (5 cases). Compared to the values at the 11 -

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12th month examination, there is none showing an increase but 4(80.0%) show a decrease, while one (20.0%) is unchanged; and when compared with preoperative values, not one shows an increase though all have presented diminished values.

The average value is 11.86 ± 4.11 , but there is none showing positive value. In comparison with the 11 - 12th month average there is a tendency of decrease but without any significant difference; while in comparing with the preoperative values, a decrease with a significant difference [Pr { $|t| \ge 4.34$ } < 5 % $\overline{Z} = 12.01$ u = 5.91 N = 5] can be observed.

On account of small number of cases no significant difference can be recognized when compared with the positive percentages of the 11-12th month examination.

(iii) Comparison of the two groups. Even at this examination (13 - 15th month), though the castrated group shows a comparatively higher average than the transplantation group, there is really no significant difference between the two groups. In other words, these two groups seem to show, similar to the period between the preoperative and up to 4th month, rather parallel changes between the periods, the 11 - 12th month and the 13 - 15th month. Even in the positive percentages no material difference can be recognizable between the two.

SUMMARY AND DISCUSSION

Concerning the basal metabolism of the patient with uterine cancer, KAWABE¹⁷ states that those who show an abnormal augmentation of the basal metabolism amount to 64.3 % of all the uterine cancer patients he has dealt with and the basal metabolism of the postclimacterium is markedly more abnormal than that of preclimacterium; and he further re ports that the majority of the patients show the abnormal augmentation of the basal metabolims in consonant with the rate of the cancer growth. TAKAYAMA⁴², dividing the patients into the operable and the inoperable groups, mentions that both groups show an increase of the basal metabolism and adds that the basal metabolism of the former is more accelerated than that of the latter. ITO¹⁴ likewise states that the basal metabolism of the patients with cervical carcinoma is generally augmented while he claims that the augmentation in inoprable cases is greater and moreover the change of the basal metabolism does not necessarily parallel with the rate of cancer progress. UÉDA45 on the contrary has pointed out that the basal metabolism decreases with the rate of cancer growth. KUMAGAI²³

states that the basal metabolism of the patients with cervical carcinoma according to the international classification is clearly augmented as compared with that of the normal women and that it is accelerated in proportion to the rate of the cancer growth. In the present studies likewise it has been found that the basal metabolism in the patients with operable cervical carcinoma according to the international classification is clearly more augmented than that of the normal women, and that in clinics the metabolism at the stage II, though not so significantly, rather tends to increase more than that of the stage I.

SAITO³⁹ and KUMAGAI²³ mention that in the climacteric women the basal metabolism increases itself, and it increases more after the fortieth year but it again decreases after the fiftieth year. In the author's experience, the basal metabolism of over 40 year-old patient compared with that under 40 years shows a lower value though not quite significantly. This seems to be due to the fact that all the subjects were of preclimacteric age being under fifty years. Furthermore, even in the cases similar to those observed by KUMAGAI²³ the basal metabolism of the patient with high blood pressures has been found to have a tendency of augmentation. In addition, the relationships between the basal metabolism and the frequencies of pregnancy, local findings, erythrocyte counts, blood sedimentation as well as MANDELSTAMM's and KAUFMANN's tests have been investigated but no special relationship can be found.

Of the literature reporting what alterations the operative therapy would bring upon the basal metabolism of the patient with cervical carcinoma, there are reports by KAWABE¹⁷ and KUMAGAI²³. According to the reports, KAWABE¹⁷ states that the basal metabolism returns to the preoperational level by the second week after operation, while KUMAGAI²³ reports that on the tenth day after operation the average value already drops below the preoperational level and that the values at the completion of operation likewise are lower than the peroperational. Again there are many reports on the radiation therapy, especially on the influences of Röentogen ray upon the basal metabolism; HIRAMATSU¹¹, NAGAUCHI³⁶, MAEDA²⁸, ITO¹⁴ and JUNGENBERG¹⁵ claim that with a small amount of xray radiation the basal metabolism is augmented while with a larger amount it is decreased. KATO¹⁸ and ITO¹⁴, however, state that the basal metabolism of patients with cervical carcinoma is decreased by x-ray radiation and it keeps on decreasing without ever rising again. In the present studies, the results on the completion of the treatment have presented a significant decrease compared with the pretreatment values. This seems, as mentioned by KAWABE¹⁷ and KUMAGAI²³, to be due to the recovery of

systemic conditions after the removal of malignant tumor as well as to the effects of deep x-ray radiation. Effects of the autotransplantation of the ovary or of the castration, performed concomitantly with operation, have not yet appeared at the completion of treatment.

The basal metabolism at the follow-up examinations seems, as already stated by KUMAGAI²³, to receive hardly any influence of tumor. As for the report concerning the basal metabolism at these examination periods, there is only a report by KUMAGAI²³ as far as the author has been able to collect. According to this report it is stated that in the cases operated upon there is no appreciable difference in the basal metabolism (2 months after discharge or about three months after operation) examination as compared with that at the completion of treatment and that at the fourth month examination, rising higher than the level at the completion of treatment, returns to the same level before the treatment, and that at the 6th examination it has decreased markedly and returns to the level at the completion of therapy. It further states that in the cases on whom autotransplantation of the ovary has been performed the values at each followup examination are almost balanced, while in those on whom the transplantation has not been performed, alterations are, in contrast, marked, and that the basal metabolism at the 4th month examination is markedly accelerated as compared with either that at the second month or at the 6th month. Although the subjects studied by the present author differ from the cases observed by KUMAGA1²³ and also there are differences of time elements in the results of the two, yet the progress curves more or less coincide with each other. Namely, in the author's cases, the basal metabolism of those who received the autotransplantation shows a decrease at the completion of therapy and rising again at the 4th month after the operation reaches almost to the pretreatment level; and at the 5-6th month examination, decreasing clearly, it presents practically the same values as those at the completion of therapy; and thereafter it gives almost balanced values though there are some slight fluctuations (Table 1).

Ever since 1896 when MORRIS³³ first reported on the autotranspalntation of the ovary, many reports on the auto- or homoiotransplantation have appeared. As for the literature on the autotransplantation of the ovary, there are relatively many reports by such investigators as MAUC-LAIRE³¹, NATTRAS³⁴, SIPPEL⁴⁰, TUFFIER⁴⁴, EMILIO⁶, GUNTER K. F. SCHU-LTZE⁴¹, UNTERBERGER⁴⁷, BICKENBACH³, MANSFELD³⁰, KUHN²², ONO³⁵ and YAGI⁵⁰, while the reports mentioning the application of the autotransplantation to patients with cervical carcinoma are not so many; there are

only such reports as by SIPPEL⁴⁰, MANSFELD³⁰, MANDELSTRAMM²⁹, TU-MANOFF, ONO³⁵, HIRAISHI and YOKOO¹⁰, YAGI⁵⁰ and LEWIN²⁴.

As regards the methods of the transplantation, various methods can be enumerated, and moreover, the criteria for the determination of efficacy of the transplantation have been sought until recently by the existence or non-existence of castration symptoms, the conditions of onset of menstruations or by histological examinations, but today there are those like BUXTON and WONG⁴, MORIYA³² and HOZAKI¹³, who are pursuing the functions of transplantation of the ovary by studying the excretory conditions of estrogen, examining vaginal smears and the basal body temperature. However, studies on the effects of ovarian transplantation on the basal metabolism of the patient are only a few in number such as those of TSUBRA⁴³, ZONDEK⁵¹, LIEBESNY²⁵ and HIGUCHI⁹.

TSUBRA⁴³ notes effects of the transplantation from the augmentation however slight of the basal metabolism in experimental rabbits after the ovarian transplantation, and ZONDEK⁵¹ reports of 15 per cent augmentation of the basal metabolism occurring on the 6th week after intra-femoral muscle transplantation of the ovary performed on a forty-year old, castrated woman. LIEBESNY²⁵ likewise mentions of an acceleration of the basal metabolism after the transplantation, while HIGUCHI⁹ states that after a homoiotransplantation he noticed an unmistakable augmentation on the third month after the transplantation, and it was still high at the 8-9th month and at the 15th month examinations and it began to decrease on the 19th month. It is, however, unfortunate that none of these results can be compared directly with the author's experimental results inasmuch as the number of cases reported are relatively small and none of these observations have been carried out at any fixed intervals nor are they autotransplantation cases performed on the patients with cervical carcinoma; yet the fact that the basal metabolism does augment in a relatively short time after the transplantation in both theirs and author's coincides with each other.

On the other hand, since LOEWY u. RICHTER²⁶ reported his experimental results concerning the effects of the castration on the basal metabolism, many reports on the same subject have appeared so far. FELIX GÁL⁷ notes that he has observed a decrease of the basal metabolism in the majority of human beings given operational castration, while L. ZUNTZ⁵² claims that though he sees no decrease in a short time after the operation, he has noticed as much as 20 per cent decrease 3 months later. COLLET and SMITH⁵ state the basal metabolism after 3—5 years' lapse of time has been found to have decreased to 20 per cent. WINTZ⁴⁹ likewise mentions

that after operational castration on the 27 persons of the age range of 30 to 35 years by the KNIPPING apparatus he found an average decrease of 18 per cent 6-24 months after the castration. In addition KRAUL u. HAL-TER²¹, KLAFTEN¹⁹, PLAUT and TIMM³¹ and HIGUCHI⁹ have also noticed a decrease in the basal metabolism after the castration. Contrary to these, KING and PATTERSON¹⁶, LOFFLER²⁷, HORNUNG¹² and HEYN⁸ claim that the castration exerts hardly any influence upon the basal metabolism.

AKIYAMA's² report is the only one that tells of observations carried on for a long period of time on the fluctuations of the basal metabolism after castration; and according to this report the cases whose basal metabolism shows an increase along with the lapse of time after the castration usually begins to decrease gradually.

Viewing the castrated cases in the present studies, the basal metabolism decreases at the completion of treatment and it rises to the pretreatment level or above on the fourth month after the operation, and thereafter it keeps on increasing up to the 7-8th month and by the 9-10th month it begins to decrease markedly reaching to the level lower than that at the completion of treatment. After that it seems to show a low value continuously though with slight fluctuations. In other words, this fact agrees well with the observations reported by various investigators, 'that the basal metabolism which has continuously been on the increase, will in a long run decrease finally.'

From these results, it is clear that the basal metabolism of the castrated group up to the 9-10th month after the operation fluctuates and augments more markedly than that of the autotransplantation group. The fact that dysfunction of the vegetative nerves are brought about when the functions of the ovary are abolished by the castration has already been noted by ADLER³, VAGLIO⁴⁸, SAITO⁵⁹ and KUMAGAI²³. However, when these vegetative nerves are in a highly tensive state where they react markedly even to a slight intrinsic or extrinsic stimulus, the majority of the cases show an augmentation in the functions of adrenals and thyroid gland, being important links in the endocrinal system, brought about by the cessation of steroid hormone secretion of the ovary after the castration. Under such circumstances it can be thought that the basal metabolism of the patients as compared with that of the normal persons would show a markedly greater acceleration.

In those who show augmentation of the basal metabolism on the 4th month after the transplantation, the ovary so transplanted being unable to function fully is actually in the state of castration and hence show an augmentation by reasons mentioned just previously but the

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transplanted ovary at the 5-6th month later seems to be functioning properly and the endocrine system also appears to be in a stable state.

In those whose values of the basal metabolism approach close to those of normal person since the 9-10th month after the castration, giving more or less stable values, other various organs of the endocrine system seem to be functioning quite harmoniously despite the castration of the ovary.

From these observations on the changes of the basal metabolism, it can be deduced that the transplantation of the ovary as compared with the castration exerts for a shorter period of time relatively less influences on the endocrine system and consequently on the somatic system.

The relatively small number of cases who have be possible of examining periodically over one year after the operation precludes drawing any definite conclusions concerning the fluctuations of the basal metabolism at the periods later than one year, hence a great deal can be expected from the further study on this subject.

CONCLUSION

The evaluations of the basal metabolism before the operation, at the completion, and at the follow-up examinations, have been conducted on the patients with cervical carcinoma, all under the age of 50 years, and operated on in the Clinics of Obstetrics and Gynecology, Okayama University Medical School and the following results are obtained :

1. The basal metabolism of the patients with cervical carcinoma of either stage I or stage II as compared with that of the normal women is more accelerated; while the basal metabolism of the cervical carcinoma of stage II. is more augmented than that of the cervical carcinoma stage I.

2. The basal metabolism at the completion of operation is markedly lower than that before the operation.

3. In those who received the autotransplantation of the ovary concomitantly with operation, the basal metabolism once increases at the 4th month after the operation and after that it maintains a low stable state.

4. The basal metabolism of those who received the operative castration continues increasing up to the 8th month after the operation and thereafter it returns to a rather balanced state.

5. From the aspects of the fluctuations of the basal metabolism, it has been recognized that the autotransplantation as compared with the castration exerts less influences on the somatic system and for a shorter period of time, and also the endocrine system of the former returns to the balanced condition earlier. 216

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REFERENCES

- 1. ADLER, L. : Arch. Obst. & Gynec., 58, 51, 1953.
- 2. AKIYAMA, Y.: Sanfu Kiyo, Vol. 26, No. 8, p. 49, 1943.
- 3. BICKENBACH, W. : Zschr. f. G. u. G., 103, 146, 1932.
- 4. BUXTON, C.L. & WONG, S.H.: Am. J. Obst. & Gyn., 60, 401, 1950.
- 5. COLLETT, M.E. & SMITH, J.T.: Am. J. Obst. & Gyn., 34, 639, 1937.
- 6. EMILIO, F.: Kl. Wschr., 5, 1926.
- 7. FELIX, G.: Str. Therap., 41, 559, 1931.
- 8. HEYN, A.: Arch. f. Gyn., 129, 1927.
- 9. HIGUCHI, T.: Keio-Igaku, Vol. 14, No. 11, p. 1667, 1934.
- 10. HIRAISHI, K. & YOKOO, K. : San to Fu, Vol. 16, No. 9, p. 13, 1949.
- 11. HIRAMATSU, S. : Juzen-kaishi, Vol. 40, No. 11, p. 4593, 1935.
- 12. HORNUNG, R. : Zbl. f. Gyn., 51, 1927.
- 13. HOZAKI, T.: The Jap. J. of Obst. & Gyn.
- 14. ITO, M.: Jap. Roent. J., Vol. 17, p. 115, 1929.
- 15. JUNGENBERG, A.: Str. Therap., 34, 288, 1929.
- 16. KATOH, K. : Jissen-Igaku, Vol. 17, p. 1, 1934.
- 17. KAWABE, S.: Jap. Gyn. J. Vol. 41, No. 1, 2, 3, p. 10, 1946.
- 18. KING & PATTERSON. : J. Am. Med. Assoc., 91, 1928.
- 19. KLAFTEN, E. : Arch. f. Gyn., 129, 1927.
- 20. KNIPPING, H.W.: Kl. Gasstoffwechsel Technik, 1928.
- 21. KRAUL, L. u. HALTER, G. : Zschr. f. G. u. G., 87, 1924.
- 22. KUHN, C.L.: Am. J. Obst. & Gyn., Vol. 45, 704, 1943.
- 23. KUMAGAI, N.: The Jap. J. of Obst. & Gyn., Vol. 3, No. 2, 1957.
- 24. LEWIN, E.: Zbl. f. Gyn., 77, 5, S. 167, 1955.
- 25. LIEBESNY, P. : Kl. Wschr., 28, 1925, 2, 4, 1927, W. Kl. Wschr. 45, 1922.
- 26. LOEWY u. RICHTER, A. : Arch. f. Anat. u. Physiol., 174, 1899.
- 27. LÖFFLER, .: Zschr., Kl., Med., 87, 1916.
- 28. MAEDA, Y.: Juzen-Kaishi, Vol. 42, No. 2, p. 328, 1940.
- 29. MANDELSTAMM, A.: Zbl. f. Gyn., 50, 1925.
- 30. MANSFELD, O.P.: Zbl. f. Gyn., 10, 1925, Arch. f. Gyn., 117, 1922.
- 31. MAUCLAIRE, .: Zbl. f. Gyn., 37, 1920.
- 32. MORIYA, M. : Hokkaido Gyn. J., Vol. 1, No. 2, p. 14, 1940.
- 33. MORRIS, .: Zbl. f. Gyn., S. 221, 1902, Med. Record, V. 69.
- 34. NATTRAS, J.H.: Zbl. f. Gyn., 7, 1924.
- 35. ONO, S. : Jap. Gyn. J., Vol. 25, No. 11, p. 1100, 1930.
- 36. NAGAUCHI, U. : Hokkaido-Ishi, Vol. 11, No. 10, p. 2205, 1933.
- 37. PLAUT, R. u. TIMM, H.A.: Kl. Wschr., 37, 1924.
- 38. ROCK, J. & HERTIG, A.T. : Am. J. Obst. & Gyn., Vol. 47, 149, 1944.
- 39. SAITO, H.: Jap. Gyn. J., Vol. 6, No. 3, p. 241, 1954.
- 40. SIPPEL, P. : Arch. f. Gyn., 68, 1923.
- 41. GÜNTER, K.F. SCHULTZE : Zbl. f. Gyn., 1, 1928.

42. TAKAYAMA, H. : Tokyo-Igaku, No. 2887, p. 1713, 1934.

43. TSUBRA, .: Biochem. Zschr., 143, 1923.

44. TUFFIER, M.T.: Surg. Gyn. & Obst., 20, 30, 1915.

45. UEDA, T. : Kinki Gyn. J., Vol. 15, p. 646, 1932.

46. UNO, T.: Tokyo-Igaku, No. 2922, p. 755, 1935.

47. UNTERBERGER, F. : Arch. f. Gyn., 110, 172, 1919.

48. VAGLIO, .: Arch. f. Gyn., 95, 349, 1912.

49. WINTZ, H. : Zbl. f. Gyn., 14, 1926.

50. YAGI, H.: Operation, Vol. 5, No. 6, 1951.

51. ZONDEK, B. : Kl. Wschr., 42, 2001, 1925.

52. ZUNTZ, L.: Arch. f. Gyn., 96, 188, 1912.