CONTRIBUTIONS

FROM THE

PHYSIOLOGICAL LABORATORY

OF THE

MEDICO-CHIRURGICAL COLLEGE
OF PHILADELPHIA

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PART XX

OF

OTT'S CONTRIBUTIONS TO PHYSIOLOGY

1914

CONTENTS.

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THE EFFECT OF ANIMAL EXTRACTS AND IODINE UPON THE VOLUME OF THE THYROID GLAND.

By ISAAC OTT, M.D., AND JOHN C. SCOTT, M.D.

The volume of the thyroid was registered by a metal oncometer designed by Dr. Scott, attached to a modified piston recorder. The arterial tension in the carotid was also noted at the same time by a Huerthle manometer. The animals used were etherized dogs. A few received previous to the ether a small amount of morphine by the jugular. The thyroid was exposed and freed, the large blood-vessels being kept intact. Then the gland was encased in the oncometer, its blood-vessels running in through a small opening in the metal oncometer. This opening was made air-tight by means of cotton and vaselin. All the agents used were injected by the jugular in order to note the action upon the volume of the thyroid. A solution of infundibulin, 0.275 Cc., the active principle of the posterior part of the pituitary, had the most marked effect of all the glands in reducing the volume of the thyroid. This diminution at times was preceded by a momentary increase of the gland volume immediately after the injection. When the gland was diminishing the general blood-pressure was rising; the pulse-rate was slowed for a few seconds and then rose (Fig. 1).

The dried anterior glandular part of the pituitary was rubbed up with distilled water and part of the infusion injected. It increased the volume of the gland, an effect directly opposite to the action of the posterior nervous lobe. Whilst the thyroid was enlarging from the injection of the anterior part of the pituitary, the general arterial tension fell for a moment, and then rose above normal. The pulse-rate was temporarily slowed and then became normal (Fig. 2).

Hallion[1] has noted that an infusion of the whole pituitary reduced the volume of the thyroid. An infusion of the fresh ovaries of a pregnant cat rubbed up with normal saline augmented the volume of the thyroid, a fact previously noted by Hallion.[2] Whilst the thyroid was enlarging from the ovarian injection the blood-pressure rose slightly for about six seconds and then returned to normal. The pulse-rate was not changed (Fig. 3).

When fresh corpus luteum of the pig was rubbed up with normal saline solution and injected per jugular it increased the volume of the thyroid. When the thyroid was enlarging the general blood-pressure fell for a few seconds and then rose to a little above normal. The pulse rate was normal (Fig. 4).

[1] Delille, l'Hypophyse, p. 55; Paris, 1909.

[2] Hallion, Société de Biologie, July 6, 1907.

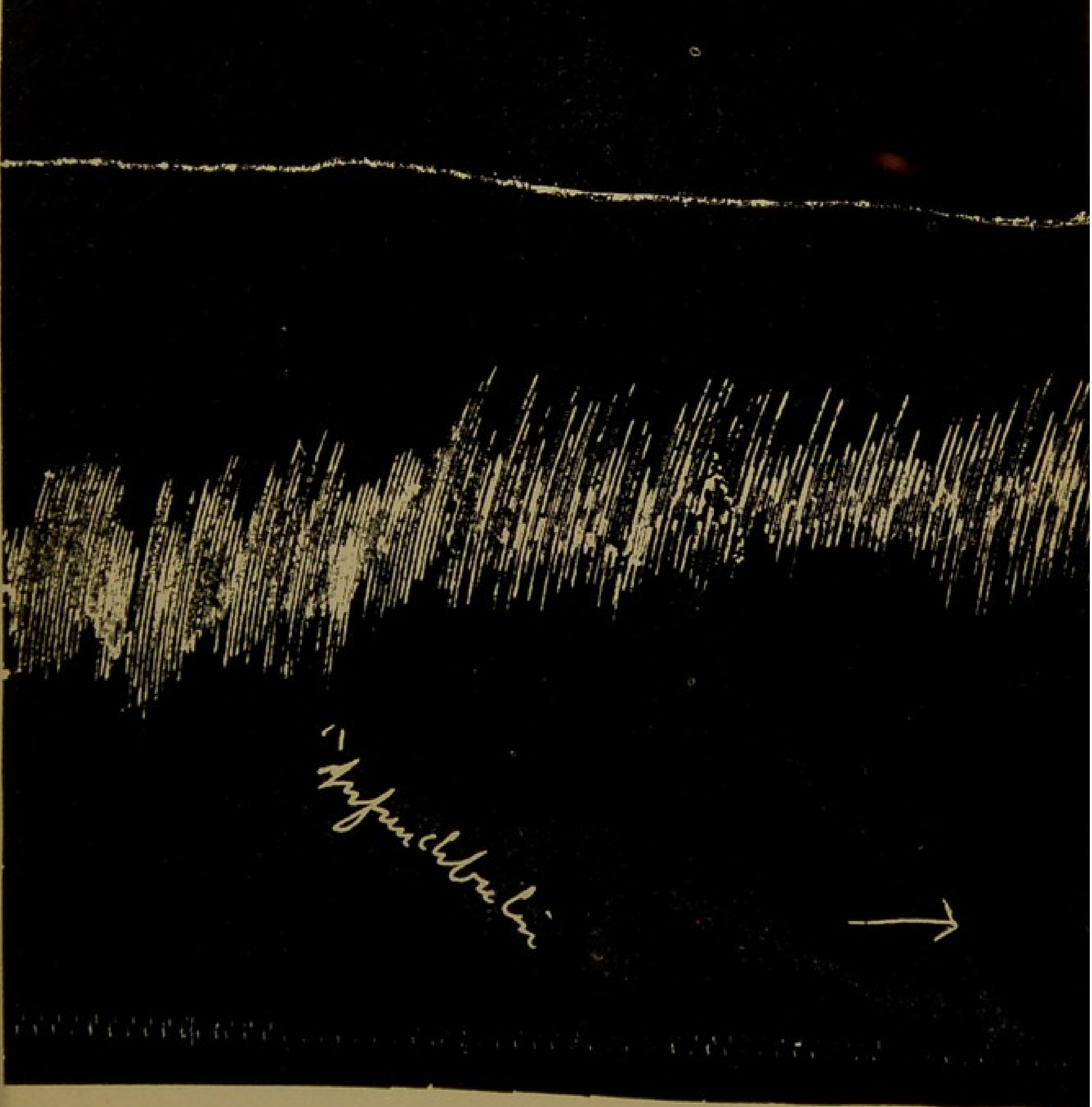

FIG. 1.—Effect of 0.275 Cc. of solution of infundibulin. Time markings every four seconds Uppermost line shows decreasing volume of thyroid ; the curves beneath are by Huerthle's manometer, registering heart beat and blood-pressure.

. 2.—Effect of infusion of anterior part of pituitary gland. Lowermost line, time markings every 4 seconds ; the second line above, the increase in the volume of the thyroid ; the topmost line, pulse curves and blood-pressure.

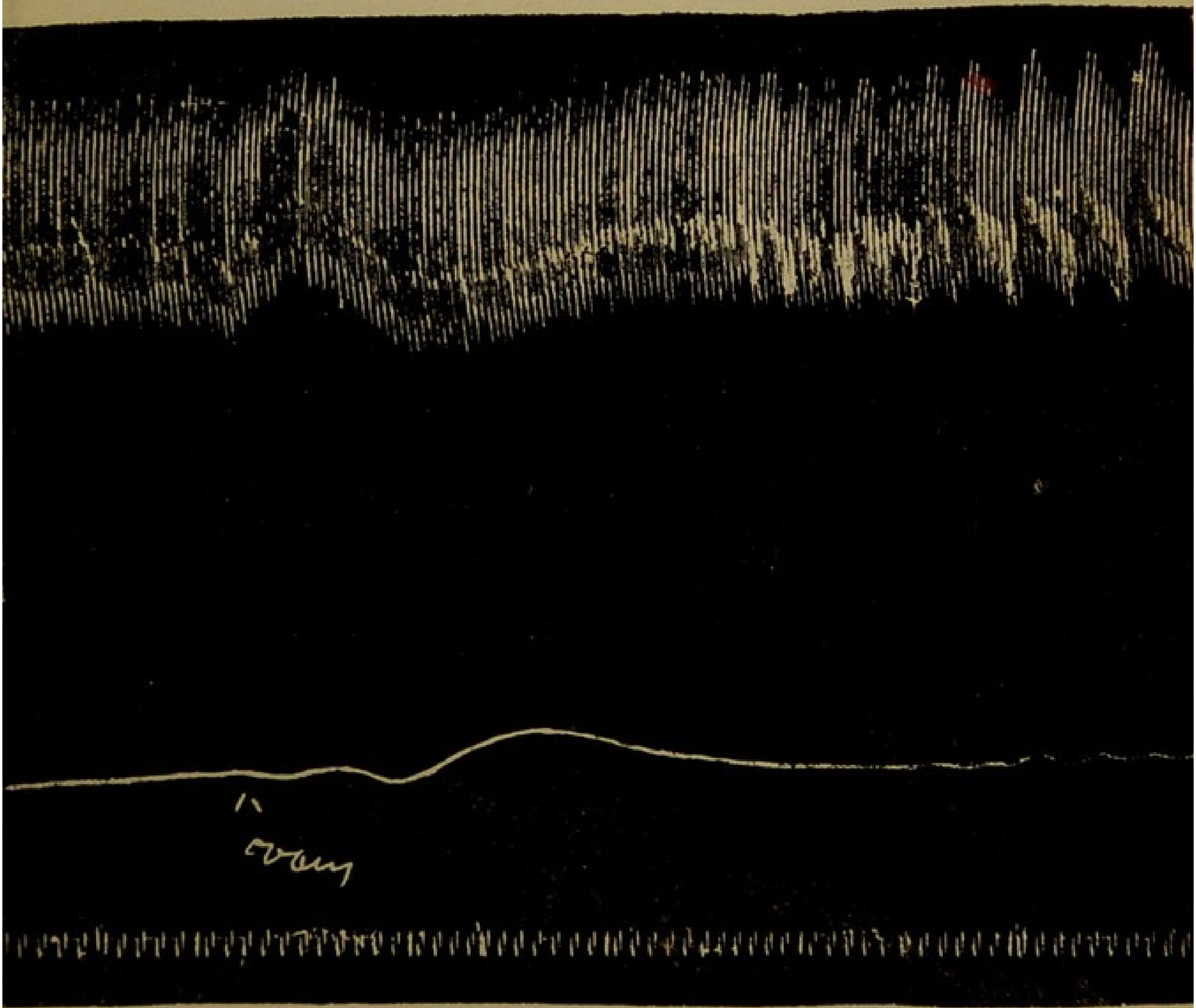

FIG. 3.—Effect of saline infusion of two ovaries of a pregnant cat upon volume of thyroid and the arterial tension ; the increase of volume of the thyroid lasted over a minute before the lever fell below the normal line.

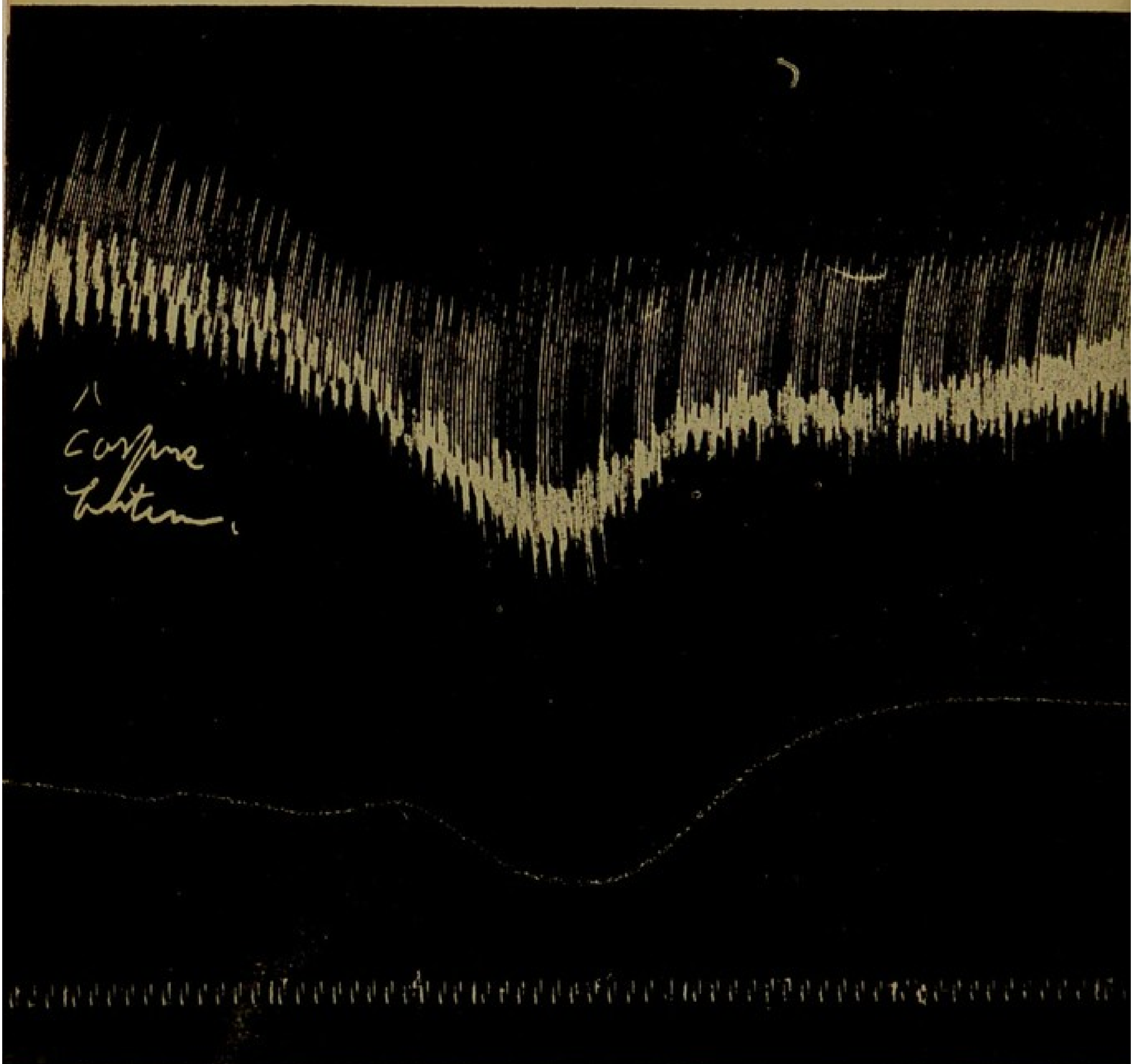

FIG. 4.—Effect of infusion of fresh corpus luteum of pig upon thyroid Lowest line, time markings every 4 seconds; next line, the increaseing volume of the thyroid; the topmost line, pulse and blood pressure.

Infusion of the thyroid augmented the size of the thyroid, whilst the general blood-pressure was lowered, which later became normal. The pulse-rate was not altered.

Infusion of thymus enlarged the gland, whilst the arterial tension was lowered for a couple of seconds, when it returned to normal. The pulse-rate was not changed.

Infusion of the mammary gland increased the size of the thyroid, whilst it lowered the general arterial tension for a few seconds, which then rose above normal. The pulse-rate was unchanged (Figs. 5 and 6).

Infusion of the parathyroid sometimes augmented and at other times decreased the volume of the gland. Whilst the parathyroids reduced blood-pressure for a few seconds, which then rose to normal, the pulse-rate was not changed.

Infusion of human placenta also increased the volume of the thyroid, whilst it lowered blood-pressure slightly for a few seconds, which then returned to normal; the pulse-rate was unchanged. Infusion of dried spleen and pancreas had but little effect upon the thyroid volume. Infusion of 0.0324 gramme of dried prostate, although not affecting the pulse-rate and momentarily lowering the blood-pressure, caused a fall in the volume of the gland, after the pulse and arterial tension became normal.

We[3] have shown that prostate has the most

[3] Proceedings of Society for Experimental Biology and Medicine, vol. 8, 1910.

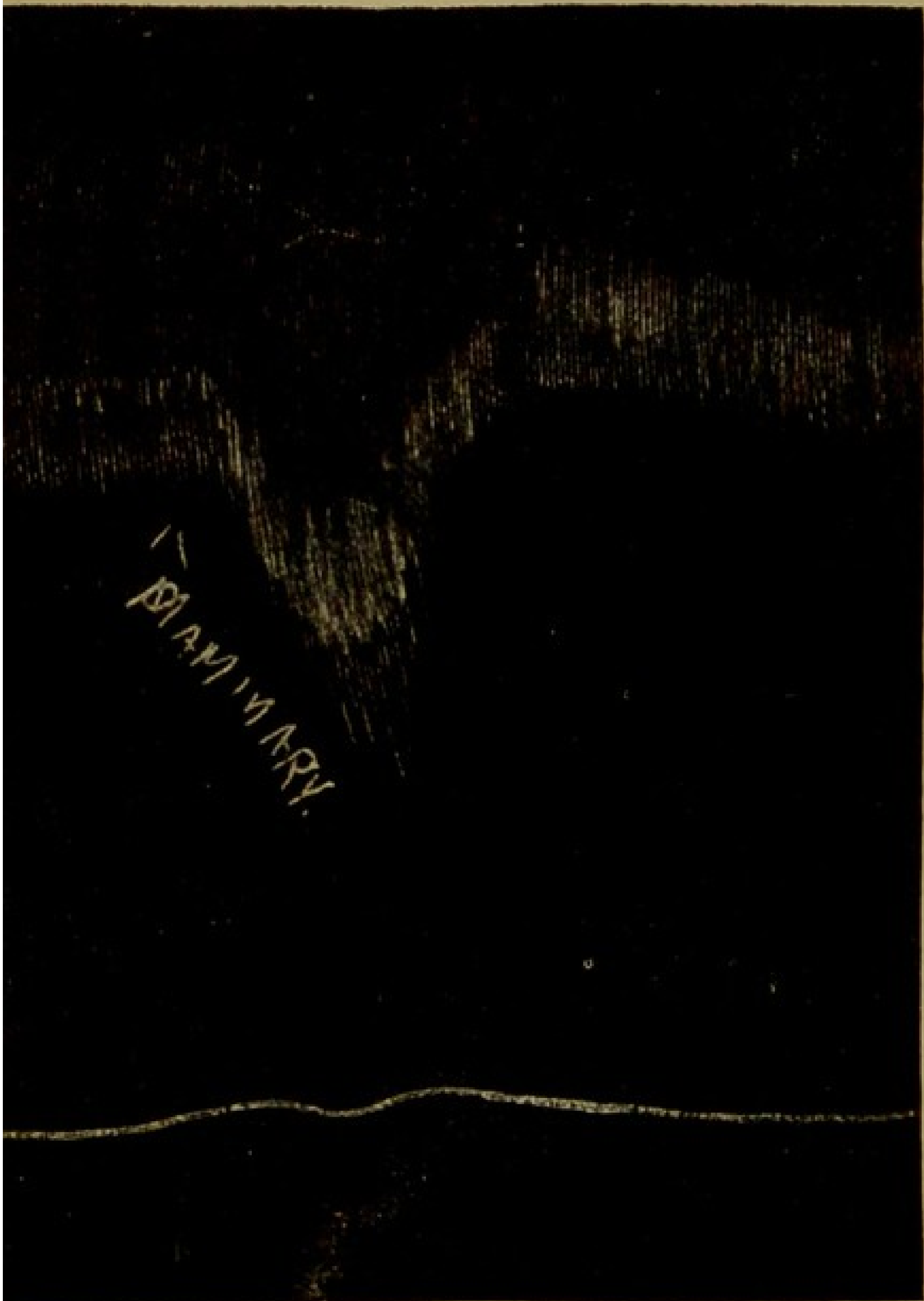

FIG. 5.—Effect of infusion of 0.2044 gramme mammary (in dried powder) upon volume of thyroid and the general blood-pressure in the dog.

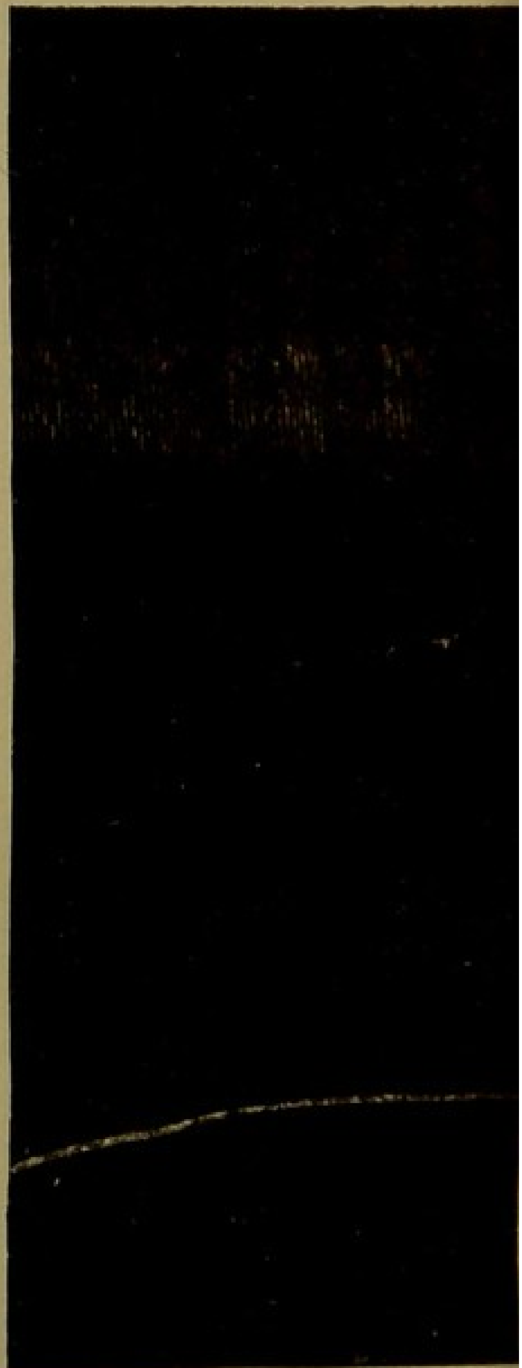

FIG. 6.—Shows rise 15 minutes after primary rise.

activity of all the glands with an internal secretion in augmenting the volume of erectile tissue in the male. Hallion[4] has recently confirmed it. Injection of solutions of iodine caused a slight increase in volume, whilst it reduced the blood-pressure for a few seconds, which then rose to normal. The rate of heart-beat was not altered. Infusions of dried orchitic extract, although diminishing momentarily the rate of the pulse and arterial tension, caused a slight decrease in the volume of the gland after the blood-pressure and pulse-rate returned to normal.

Infusion of the pineal gland caused a decrement in volume, whilst the blood pressure fell for a few seconds and then returned to normal. The rate of the heart-beat was unchanged. Adrenalin, after a momentary augmentation of the gland, diminished it. At the time of the volume-changes in the gland the blood-pressure was greatly increased and the pulse slowed temporarily.

Hence we can tabulate the results as follows:

Increase in volume of thyroid.	*Decrease.*	*No marked effect.*
Anterior part of pituitary.	Infundibulin.	Pancreas.
Iodine.	Prostate.	Spleen.
Placenta.	Pineal.	
Fresh ovary.	Orchitic extract.	
Fresh corpus luteum.	Adrenalin.	
Thyroid.		
Mammary.		
Thymus.		

The parathyroids increased and decreased the gland.

Thirty-six experiments were performed.

[4] Société de Biologie, 1, 1913.

These results should have some practical value in the treatment of exophthalmic goitre. We wish here to reduce this body, which resembles a great vascular sponge. Infundibulin and adrenalin are indicated. In myxedema we wish to increase the vascularity of the thyroid. Here we can use the anterior part of the pituitary or fresh corpus luteum, either singly or combined.

The great enlargement of the thyroid after the onset of menstruation can be explained by the activity of the formation of the corpora lutea.

(Reprinted from *The Alienist and Neurologist*, Vol. 34, No. 2, May, 1913.

ACTION OF TONSIL.

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Tonsils are composed of a spongelike connective tissue infiltrated with lymphoid cells, accumulated in nodular shape. These nodules are the germinating centers of the lymphoid cells. On the surface of the tonsil are tube-like crypts running inwards and lined with a stratified epithelium and whose walls are lined with lymphatic nodules. Lymphoid cells in large numbers are constantly passing through the stratified epithelium into the crypts to become free and to enter the mouth as the salivary corpuscles. Into the crypts mucous glands open. Delamere[1] states that excluding embryological differences there is only one difference between the tonsils and the lymphatic glands; in the latter the lymphatics traverse the gland whilst the lymphatics actually arise in the amygdalæ, which from this point of view are comparable to the spleen.

[1] The Lymphatics, page 84. 1904.

Functionally the tonsils are a means of defence against microbian invasion.

In our experiments the powdered dried tonsil of the calf was used. A few centigrams was rubbed up in a mortar with distilled water and filtered through paper. We also boiled the filtrate in some of our tests.

Circulation.

In the etherized cat both small and large doses always produced a fall of pressure (30 millimeters of mercury) and usually a decrease of heart beats, both lasting a short time, unless an infusion of 0.1296 gram was given when the depression of arterial tension may continue for several minutes with a slow and much stronger heart beat. A dose of infusion of 0.1296 gram can also produce immediately after the injection, a sudden arrest of the heart. After the temporary fall of pressure and of rate of pulse both are increased for a short time, when the effect passes off. This increase in rate of the beat of the heart may be 30 beats, and of pressure 12 millimeters of mercury. In the etherized rabbit the pulse may not decrease, but increase, after doses of an infusion of 0.0162 gram, but the pressure after a temporary fall becomes greater than previous to the injection. In larger doses of an infusion of 0.129 gram the pulse rate may fall, but the pressure augments considerably. The fall of the rate of the pulse was not due to any increased inhibitory action of the vagus, as it ensued after previous atropinization. We also tested the excitability of the vagus with Ludwig's shielded electrodes, but no increase of inhibitory power was noted. Hence we infer that the temporary decreased activity of the heart is due to an action of the tonsil on the muscular structure of the organ.

Renal Secretion.

The injection of an infusion of 0.1296 gram in divided doses is followed by a great increase in the secretion of the kidney for a short time, as the following experiment shows.

Cat, narcotized by 5 c.c. paraldehyde by the stomach, and afterwards the use of a small quantity of chloroform by inhalation.

Time P. M.	Drops of urine in 5 minutes.	
2.10	2	
2.15	6	
2.20	2	infusion of 0.012 gram per jugular.
2.25	5	
2.30	5	infusion of 0.0324 gram per jugular.
2.35	17	
2.40	16	
2.45	2	infusion of 0.0648 gram per jugular.
2.50	41	
2.55	66	
2.60	37	

Here there is an increase of over 30 times the original amount.

When an oncometer was used with Albrecht's piston recorder it was noted that the kidney was considerably enlarged, so much so in one instance that it loosened the lid of the oncometer. The increase in volume of the kidney is considerable and continues for some minutes. As to the cause of this great activity of the renal organ, it is difficult to be certain, for the kidney is enlarging when the general pressure is constant. We have shown that parathyroid, pineal and, with other observers, that infundibulin acts upon the kidney cell by a direct action. Now the vaso dilation of the kidney does not look like increased pressure in it, and the diuretic action keeps up after the rise in the general pressure has subsided. Hence we infer that the tonsil infusion acts directly upon the renal cells in promoting diuresis. It seems to be a stronger diuretic agent than either infundibulin, parathyroid or the pineal gland.[2] In fact it is the most powerful diuretic of all the internal secretions.

Intestinal Peristalsis.

We made use of the intestine of the etherized rabbit and the method of Magnus. We found it slightly increased the intestinal movements.

Uterine Contractions.

We used the uterus of the etherized cat in situ,

[2] (Ott) Internal secretions, page 24.

and a long, llght lever was attached to one of the uterine horis. The abdomen was filled with Ringer's solution heated to the temperature of the animal. The infusion of the tonsil was given per jugular. There was some increase in the activity of the contractions of the uterus.

Vesical Contraction.

In this case we attached the neck of the bladder by a cannula to a water manometer. The bladder was filled with normal saline solution of the temperature of the animal's body. The cat was etherized during the experiment. The tonsil increased the contractions of the bladder to a small extent.

Temperature.

The subcutaneous injection of an infusion of 0.1296 gram of tonsil in rabbit caused the temperature to fall 1.8°F. in an hour and a half. The animal was permitted to run about the laboratory.

Internal Secretion.

The fall of blood-pressure and the cardiac death after large doses of the tonsil per jugular are results obtained by other animal extracts, as pancreas and prostate. But these agents do not have any diuretic action. Hence we are led to the conclusion that the tonsils probably have an internal secretion.

secretin solution alone, then we believed the animal extract increased or decreased the secretion of the pancreatic juice. To determine if the same amount of secretin solution always produced about the same amount of pancreatic juice, we made the following experiments:

Experiment 18. Cat, etherized; effect of secretin solution on pancreatic secretion.

P. M.		Drops.
3.05	8 c. c. secretin solution injected per jugular	0
3.10	. . . .	7
3.15	. . . .	8
3.20	. . . .	2
3.25	8 c. c. secretin solution	4
3.30	. . . .	8
3.35	. . . .	1
3.40	8 c. c. secretin solution	5
3.45	. . . .	7

Experiment 17. Cat, etherized; effect of secretin on pancreatic secretion.

P. M.		Drops.
3.20	8 c. c. secretin	4
3.25	. . . .	6
3.30	. . . .	3
3.35	8 c. c. secretin	2
3.40	. . . .	6
3.45	. . . .	3
3.50	. . . .	2
3.55	8 c. c. secretin	8
4.00	. . . .	6
4.05	. . . .	3

As is seen (Exp. 18), 8 c. c. of secretin solution gives 8 drops as the highest in the first period, 8 drops as the highest in the second period, and 7 drops as the highest in the third period. As is seen, the results are fairly constant. Hence, an injection of the infusion of the animal extract in the second period leads to the conclusion as to an increase or decrease of pancreatic secretion. We tried 0.3 c. c. of adrenalin in solution and brought the secretion to a standstill, as had been pointed out by Drs. Pemberton and Sweet. Infundibulin (or pituitrin, or hypophysin of Fuehner) also produced the same results. Edmunds obtained the same results and attributed it to the anemia of the gland by vasoconstriction, but our experiments upon the volume of the pancreas show that adrenalin increases the gland volume, the vasoconstriction was only for three and a third minutes before the increase in volume, due to a vaso-dilation. We noted the same effects of adrenalin in studying the volume of the kidney and its increased secretion of urine. Infundibulin has at times a stage of vasoconstriction for about 3 minutes, and then increases the volume of the pancreas to a marked degree.

It is possible that the increase of volume after the use of adrenalin and infundibulin might be due to the added secretin, which also increases the volume, but when you come to examine their action on the spleen we find the same decrease of volume with a subsequent increase, just as we did with the pancreas.[2]

[2] American Medicine, April, 1914, p. 249.

Although there is a vasoconstriction by both adrenalin and infundibulin for about three minutes, after that we have a vasodilation. The vasoconstriction might account for the first five minutes of decrease of secretin. But for ten to twenty minutes afterward the secretion goes on decreasing, although at this time there is a vasodilation and an increase in the volume of the gland. In the case of the sweat glands, one of us has called out in the amputated leg of the cat a secretion by the irritation of the sciatic. And in the mammary gland we have an increase of the milk secretion with agents which produced a vasoconstriction, like infundibulin. Increased or decreased vascularity plays a minor part in the action of secreting glands. Hence, we believe with Sweet and Pemberton that there is a direct action of adrenalin and infundibulin upon the cells of the pancreas to diminish its secretion. The results of adrenalin are shown in the following experiment:

Experiment 19. Cat, etherized.

P. M.		Drops.
3.10	8 c. c. secretin solution	0
3.15	8 c. c. secretin solution	6
3.20		5
3.25	8 c. c. secretin solution	2
3.30	0.3 c. c. adrenalin solution	4
3.35		3
3.40		0

Experiment 2. Cat, etherized.

P. M.	Drops.	
3.10	0	
3.15	0	
3.20	0	2 c. c. secretin solution.
3.25	7	6 c. c. secretin solution.
3.30	4	0.3 c. c. adrenalin solution.
3.35	2	
3.40	3	
3.45	1	
3.50	0	
3.55	0	

As to pineal infusion, it increased the pancreatic secretion and increased the volume of the gland. We have the following experiments to prove it.

Experiment 12. Cat, etherized.

P. M.		Drops.
3.10	8 c. c. secretin solution	0
3.15		10
3.20		13
3.25	8 c. c. secretin plus .06 gram pineal	7
3.30		18
3.35		16
3.40		10
3.45		9
3.50	8 c. c. secretin	15
3.55		15
4.00		10

Experiment 13. Cat, etherized.

P. M.		Drops.
3.20	8 c. c. secretin solution plus .06 gram pineal	8
3.25		13

P.M.		Drops
3.30		9
3.35	8 c. c. secretin solution plus .06 gram pineal	8
3.40		16
3.45		11
3.50	8 c. c. secretin solution	12
3.55		10

As to the infusion of the parathyroid, we also found an increased secretion and the greatest increase in the volume of the pancreas.

Experiment 16. Cat, etherized.

P. M.		Drops.
3.00	8 c. c. secretin solution	0
3.05		12
3.10		8
3.15		5
3.20	8 c. c. secretin solution plus .06 gram parathyroid	19
3.25		12
3.30		7
3.35	8 c. c. secretin solution	14
3.40		8

Experiment 22. Cat, etherized.

P. M.		Drops.
2.59		0
3.00	8 c. c. secretin solution	17
3.05		12
3.10		8
3.15	8 c. c. secretin solution plus .06 gram parathyroid	24
3.20		14
3.25		9
3.30	8 c. c. secretin	16
3.35		10
3.40		5

As to the infusion of the mammary gland, it increased the pancreatic secretion and also increased the volume of the gland.

Experiment 25. Cat, etherized.

P. M.		Drops.
2.55		0
3.00	8 c. c. secretin solution	15
3.05		10
3.10		6
3.15	8 c. c. secretin solution plus .06 gram mammary gland	20
3.20		16
3.25		8
3.30	8 c. c. secretin solution	20
3.35		14
3.45		7

Experiment 26. Cat, etherized.

P. M.		Drops.
3.19		0
3.20	8 c. c. secretin solution	16
3.25		21
3.30		19
3.35		14
3.40	8 c. c. secretin solution plus .06 gram mammary	23
3.45		22
3.50		23
3.55		17
4.00	8 c. c. secretin solution	20
4.05		21
4.10		17
4.15		15

Experiment 28.

P. M.		Drops.
2.45		0
2.50	8 c. c. secretin solution	17

P.M.		Drops
2.55		20
3.00		9
3.05		5
3.10	8 c. c. secretin solution plus .03 gram mammary	24
3.15		23
3.20		17
3.25		8
3.30	8 c. c. secretin solution	15
3.35		12
3.40		8
3.45		4

Appended is a resumé of the effect of some of the animal extracts upon the pancreatic secretion and the volume of this gland.

Animal Extracts	Pancreatic Volume[3]	Pancreatic Secretion
Parathyroid	increases	increases
Secretin	increases	increases
Mammary	increases	increases
Infundibulin	decreases for 3 minutes, then increases	decreases (Sweet & Pemberton)
Adrenalin	decreases for 3 1-3 minutes, then increases	decreases (Sweet & Pemberton)
Pineal	increases	increases

This resumé shows that all the extracts used increased the volume of the pancreas and also increased the pancreatic secretion except adrenalin and infundibulin. Twenty eight experiments were performed.

[3] See Therapeutic Gazette, 1914.

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ACTION OF CORPUS LUTEUM UPON THE MAMMARY GLANDS

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All workers agree as to the presence of a hormone increasing the size of the mammary glands — for Lane-Claypon and Starling it is in the foetus, for Foà, Biedel and Koenigstein it is also in the foetus; Bouchacourt, Lederer and Prizbram and Basch, it is in the placenta; Ancel, Bouin, O'Donoghue and others, it is in the corpora lutea.

Ott and Scott[1] were the first to show that injections of an extract of corpora lutea and certain other extracts increase the secretion of milk to a marked degree.

Mammary gland enlargement and the quantity of milk secreted should stand in direct relation. But in virgin animals the breasts do not contain milk, and the effect of the internal secretions upon their mammary hypertrophy is yet to be determined.

[1] Ott and Scott. Soc. Exp. Biology and Medicine. Feb., 1902.

Foges[2] found that the uterus was not a factor in the pubertal growth of the mammary glands. Aschner and Grigoriu[3] found that the effect of injecting placental extract into virgin guinea pigs was followed by a development of the mammae and succeeded by milk secretion.

Fellner[4] found that extracts of corpus luteum and placenta, when injected, caused hypertrophy with production of milk in the mammary glands.

Solovjev[5] presents a preliminary report on the effect of ovarian extract on the mammary glands of guinea pigs and gives the following conclusions:

(1) Ovarian extract is toxic to pregnant and nursing guinea pigs, but has no effect on others.

(2) Extracts of corpora lutea have no effect on either pregnant nor non-pregnant guinea pigs.

(3) Subcutaneous injection of ovarian extract causes secretion of colostrum in females that have borne young once or oftener. In multipara the mammary glands are enlarged.

(4) Injection of the extract of corpora lutea has no such effect.

(5) Injection of ovarian extract and the extract of the corpora lutea into nursing animals and animals that have ceased to nurse does not pro-

[2] Foges. Centralblatt f. Physiologie. Vol. 19; 1905.

[3] Aschner and Grigoriu. Archiv. f. Gynakol. Vol. 94; 1911.

[4] Fellner. Archiv. f. Gynakol. Vol. 100; 1913.

[5] Roussy Vratch. April 7, 1912.

duce any increase in the secretion of milk, nor does it prolong the period of lactation.

At puberty the mammary glands enlarge more or less permanently. In menstruation the mammary glands also increase in size.

Hammond and Marshall[6] have shown that hypertrophy of the mammary glands ensues on about the nineteenth day of coition in pseudo-pregnant rabbits by a definite secretion of milk. This mammary hypertrophy can ensue in rabbits from which the uterus has been removed while still immature. The development of the corpora lutea of pseudo-pregnancy is further correlated with uterine hypertrophy and hyperaemia followed by extravasation of blood.

The uterine changes are comparable to those which occur in true pregnancy and afford confirmation of the view that the corpora lutea are a necessary factor in causing and maintaining the raised nutrition of the uterus during the first part of the period of gestation.

Our experiments were made upon virgin rabbits. The corpora lutea of the cow was rubbed up with sterilized water and injected every three days for a month hypodermically. The rabbits were of the same size. Care was taken that no sepsis ensued from the injections.

[6] Hammond and Marshall. Proceedings of the Royal Society. B. Vol. 87, p. 422.

Dr. Scott makes the following report of an examination of the mammary glands.

Macroscopically:

The glands were more than twice as large as those of the control animal and contained milk, which in the control did not exist. The glandular tissue was a deeper grayish color, that of the control was pale and less vascular.

Microscopically:

The injected glands showed a markedly increased number of parenchymatous cells with a lessened amount of connective tissue. The cells were larger and had a deeper staining and more granular protoplasm than the control glandular cells. The nuclei were correspondingly larger.

THERMOTAXIC FIBERS IN VAGI AND SYMPATHETIC.

BY

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AND

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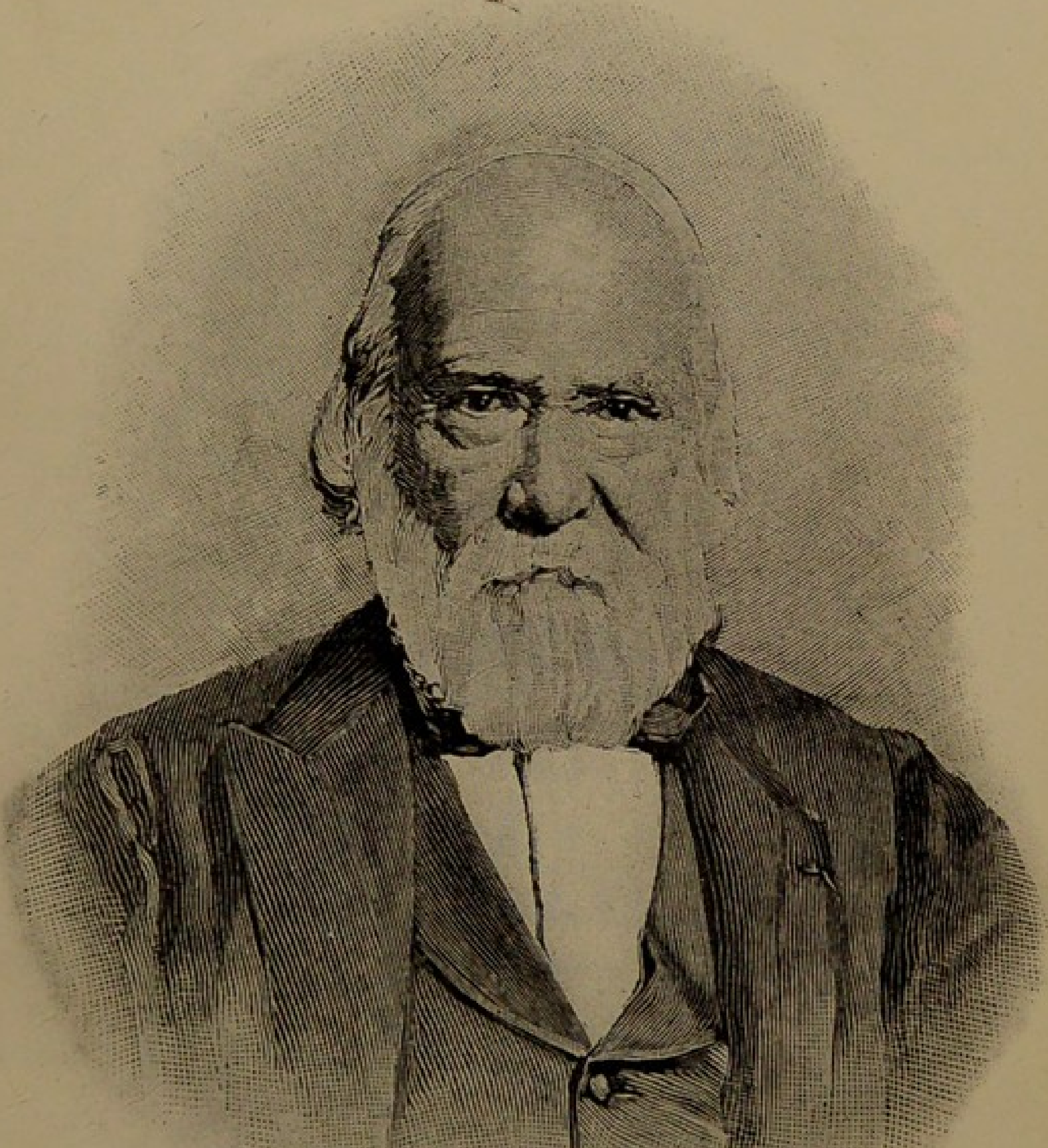
One[1] of us was the first to demonstrate that the tuber cinereum was a thermogenic center, and whose irritation causes the greatest rise of temperature. A transverse section in the corpus striatum produced a rise to 111½° F.—a rise of 6¾° F, which one[2] of us was the first to publish.

Isenschmid and Schnitzler[3] after a series of experiments arrived at the conclusion that the regulation of temperature was mainly in the tuber cinereum, and that the corpus striatum plays a subordinate part, for an animal without the corpora striata and cerebral hemispheres can regulate its temperature just as he normally does. They state that thermo-regulation stands and falls with the tuber cinereum.

[1] Ott. Journal of Nervous and Mental Diseases. July, 1893.

[2] Ott. Journal of Nervous and Mental Diseases. Vol. XI, No. 2, page 141. April, 1884.

[3] Isenschmid u. Schnitzler. Archiv. f. Exp. Path. u. Pharmakol. Band 76. Heft 3 and 4. p. 202.



C. E. BROWN-SEQUARD

1817-1894

[Reprinted from THE MEDICAL BULLETIN, 1896.]

DR. BROWN-SEQUARD.*

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Philadelphia.

The faculty of the college have selected me to give the introductory address at the opening of this semester of the school. Had I been consulted I could have given them much better advice as to their choice. But as there was no way to retreat I presume some subject must be inflicted upon you.

In the selection of a subject this evening I have been governed by a desire to give a more extended notice of the life of a man who occupied a prominent position in America, England and France. I feel that he has not quite received the amount of recognition in this country that his merits deserve, and while I may add but little to it, yet I shall attempt it, however feeble it may be. Besides, he was a friend of mine whom I highly esteemed. I refer to Brown-Sequard, a name you have doubtless heard. He was a Creole, born in 1817, in the Isle of Mauritius, a dependency of France. He was a posthumous child. His father was a Philadelphian and a sea

* An introductory address to the students of the Medico-Chirurgical College of Philadelphia, October 1, 1896.

captain by the name of Brown. His mother was a Creole lady by the name of Sequard. His father died on a voyage to the East Indies.

In his early life he styled himself Edward Brown-Sequard. After the '50s he signed himself Charles Edward Brown-Sequard. The data of the early years of his life are wanting. After the death of his father his mother made a living sufficient to bring up her child. At the age of 15 he became a clerk in a store. While a clerk he began to write pieces for the theatre, romances and poetry. At the age of 20 he persuaded his mother to embark for France.

He arrived in Paris in 1838. He had a letter of recommendation to Charles Nodier, to whom he wished to present a romance, which Nodier read, but advised him to leave romance alone. This good advice was like similar advice given to Bernard, who came to Paris with a five-act tragedy.

Brown-Sequard's life, while in itself a romance, was turned toward the consuming passion of his life—that of medicine. At that period (1838) the illustrious Magendie was in the zenith of his fame, although quite aged. In the second year of medical study he began to manifest a great passion for physiology, and worked with his preceptor, Martin-Magron, repeating his master's experiments. Then his mother died, whom he adored, and for a long time he was incapable of doing anything, and commenced the wandering life which was so extraordinary in a person occupied with physiology. After traveling considerably he embarked for his native country, and afterward returned to Paris, where he obtained his degree of medicine in 1846 at the age of 29.

In 1849 he was assistant physician to a cholera hospital. At the age of 35 he left France, having been concerned in some machinations antagonistic to the government. Arriving in New York he gave French lessons and a course in physiology. He was elected Professor of Physiology at Richmond, 1854-55.

By the kindness of Dr. W. B. McCaw, late Dean of the Medical College of Virginia, I have obtained some information about his life in Richmond. His letter reads as follows:

"I was very intimate with him, and worked with him in many of his vivisections. He was the most expert operator on the living subject I ever saw, and his dogs, rabbits and guinea pigs were cauterized and handled in the most artistic way. He was mostly engaged with a comparison between the drug, opium and the new bromides, chloral and that class of remedies. By trephining the skulls of guinea pigs he studied the effects of opium and narcotics on the dura mater. Alternating with chloral and bromides he proved that the opiate always engorged the membranes of the brain, while chloral bleached the dura mater.

"Ever since that time the profession has recognized the fact and acted upon it, as in the sudden convulsions of children and the uremic convulsions of Bright's disease.

"The enthusiastic nature of Brown-Sequard shows us his whole life and bearing. Simple-minded and guileless, he was truth itself as far as he saw it. His most affectionate nature made dear friends wherever he was."

He left Richmond because he had no time for original work. The news that he had been awarded a prize at Paris caused him to decide to return to France. Next we hear of him in charge of a cholera hospital in his birthplace. While here he was awarded a gold medal for his devotion and services during the epidemic. In 1855 he was a teacher of physiology in New York and a practicing physician.

In the same year he returned to Paris, and, in common with Charles Robin, he furnished a private laboratory, where he passed nearly two years. He had some students, as Rosenthal, of Vienna; Westphal and Czermack. In 1857 and 1858 he was giving lectures at the Royal College of Physicians, where his fascinating manner, breadth and depth of knowledge of the nervous system made a powerful impression on English minds, influencing them to a more extensive study of the nervous system.

Owing to the high esteem in which his lectures were held he was asked to repeat them at Edinburgh, Glasgow and Dublin. From his great reception he established himself in London as a neurologist, having refused a chair at Glasgow on account of the bad climate. In 1861, at the age of 44 years, he gave the Goulstonian lectures. When the Hospital for Epilepsy and Paralysis in London, in 1861, was established, Brown-Sequard was made a visiting physician, and here it was that he instituted his bromide treatment of epilepsy, which still remains our sheet anchor, notwithstanding many substitutes, additions and alterations.

While in London he had a large practice and made money, but he could not sacrifice what he loved better than his life, the search of truth in the direction of physiology.

So he quit this life and accepted a chair at Harvard. His marriage to the niece of Daniel Webster also had weight in the determination to go to Harvard.

By the kindness of Professor Bowditch I have had the pleasure of reading his introductory address, which was delivered on November 7, 1866. He closes it with the following remarks to future investigators: "If you are seriously willing to work you can dispense with any special teaching, and what is still more important, I am sure that you must succeed. If you have the will you will soon find that scientific and practical facts abound." Have the will, he repeats, and you will soon help science, to which, I might add, that you will also do much for your own personal success. His assistant, Dr. Thomas Dwight,* speaks of him as being extremely kind, and seemed to take an interest in his progress. He thought that young men were much attached to him by his kindness and impressed by his brilliancy and enthusiasm. In Boston he seemed to be satisfied, and Agassiz was his friend.

But he lost his wife, and this, like the death of his mother, sent him wandering about the suburbs of Paris and London, but always working at something in physiology.

But neither grief nor loss of position could quench the spirit for experimentation. Soon he went to work and found that sections of the sciatic nerve were followed by epileptic attacks; and he also discovered new facts about the spinal cord. In 1868 he founded the Archives of Physiology with Charcot and Vulpian, and he was nominated to the Chair of Experimental Pathology in the Faculty of Medicine. While holding

* Personal letter.

his chair he made numerous discoveries: The hereditary transmission of nervous lesions, the centre of respiration, spinal epilepsy; that injuries of the nerve centres could cause hemorrhages and edema of the viscera.

During the siege of Paris he visited the United States and collected sums of money to forward to his unfortunate countrymen. Having married another American lady he gave up his chair in Paris, and in 1872 took up his residence in New York, where he proposed to practice part of his time and devote part to his researches. Here he established the Archives of Scientific and Practical Medicine. It was at this time, after some studies abroad, that I called upon Browne-Sequard to take a course with him in neuro-physiology.

But I found him unwilling on account of want of time, stating that his assistant, Dr. E. Dupuy, had just left him. He treated me cordially and gave me quite a discourse upon his researches. In 1875 he returned to London, but soon left for Paris. In 1874 he made experiments upon the thermic irritations of the cortex, lectured upon amaurosis and hemianesthesia. He gave three lectures at the Royal College of Physicians to demonstrate that the same lesion of the brain's cortex is able to produce different symptoms and in different parts of the body. He did not believe in what is called the localization theory: "that each part of the brain is connected with a certain movement or sensation, and not with any other."

He believed that inhibition and dynamogeny would explain these phenomena, and while localization is established yet inhibition and dynamogeny will still come more to the front as time rolls by. It was not that he had made a mistake and tried to uphold it rather than admit in his later years his error that he hammered away with experiments to establish the inhibitory-dynamogenic theory against that of localization.

He found it a heavy task, as he admits in a letter to Dr. J. Ogle in 1879. He was then 62 and wrote as follows: "My lecturing and some patients take all my time. I have a very much harder fight for the doctrines relating to the brain than I had at the time I first became acquainted with you for the doctrines relating to the spinal cord. If I did not love truth much more than comfort, ease and quietness I would give up the painful, heavy task I have given myself. So long, however, as I have breath or power and mind and body I shall continue the efforts begun in London in 1861 in my Goulstonian lectures."

This letter shows that he had the fibrous mental and physical power which makes a man. So great was his enthusiasm for the carrying on of physiological investigation that he often made himself very sick in his studies upon digestion when he swallowed pieces of sponges attached to a thread for withdrawal so as to obtain gastric juice.

At another time he had drawn from his arm about a half a pound of blood, to be injected into the arm of a decapitated criminal in order to study the effect of arterial and venous blood upon the tissues. When a man will undergo such injuries we know that he is terribly in earnest in his work.

And I say to you that if you wish to succeed well you also must be terribly in earnest. For nearly fifty years he sacrificed everything for his love of science. He did not make researches for renown or the sensation of being celebrated, for he was simplicity itself in all things. In 1876 he married a lady of Geneva, Switzerland. At this place he was offered the Chair of Physiology, now held by another old giant, Schiff. But the death of Magendie's successor, Bernard, left that chair for Brown-Sequard, which he accepted and held for sixteen years up to the day of his death.

Private Life.

Was there ever a man who loved to move from place to place more than our illustrious friend? He crossed the Atlantic over sixty-six times. In private life he seemed to be taken up

During the first ten years of his medical life he published sixty-six articles; in his second decennial, thirty-five; in the third, sixty-eight, and in his fourth decennial, two hundred and sixty-six. I shall now take up his most important discoveries.

He established in an unassailible manner, contrary to the classic opinion, that conducting fibres of sensation of feeling decussate in the spinal cord, so that a transverse section of one-half of the spinal cord is followed by paralysis of motion on the side of section or loss of sensation on the opposite side. This enables surgeons to diagnosticate the existence of certain one-sided lesions of the spinal cord. He also discovered the relation existing between the tissues and the blood, that the energy and histological properties of the tissues of a recently-amputated limb could be restored by the injection of defibrinated blood and oxygen. He was the first physiologist to find out that blood vessels contracted under the action of electricity upon certain nerves. There is no doubt of his discovery of the vaso-constrictors and their mode of action upon the blood vessels and the temperature of the corresponding parts. He also found out that epilepsy could be experimentally produced and could be inherited. In the late years of his life he tried to establish that the inhibitory action of certain lesions on irritation of certain parts of the nervous system had an action upon the activity of certain other parts of the nervous system seated at a distance from the site of original injury.

In 1858 he published some researches made with Professor Francis Gurney Smith, of this city, that starch could be changed into sugar in the stomach even when it contained a very acid gastric juice. In 1856 he showed that the extirpation of the adrenals soon caused death. He also was among the first to suggest the injecting of glandular tissue and the theory of internal secretion. These are a few of his important discoveries.

Glandular physiology, in its widespread ramifications, applied to other ductless glands of the body, has revolutionized many parts of physiology and pathology. It is only in its infancy. Its maze of metabolic changes hold many facts to be discovered. The secretion of the ductless gland opens up new avenues of investigation, which will enrich the science of physiology and the practical application of these facts in therapeutics. We have a silent and hitherto unsuspected secretion going on which plays a most important and unknown part in our economy.

Very potent remedies are the ductless glands, where but a few thousandths of a grain of a gland, like the pituitary, greatly elevates arterial tension. Several of these animal extracts, as I have shown, are thermogenic agents; others are not. Some, like the thyroid, greatly depress the rate of the heart.

When we see the cures produced by the thyroid powder, or one of its active principles—iodothyrine—in myxedema, cretinism, obesity, and in my own experience of a cure of sclerema; when we see the changes of acromegaly arrested by the pituitary; Addison's disease improved by the adrenals, we cannot help seeing their power. We see in the action of these extracts the simple external manifestations of the great forces at play in the nutrition of the economy. When Brown-Sequard was laughed at in regard to his orchitic extract—yes, even reviled—all his friends knew he was right, but his quackish imitators for the greed of gain exaggerated its qualities, so that the reaction necessarily fell upon the originator. But his researches and facts about it live, while his revilers are numbered among the great unknown. Dr. Pregl, by a series of most elaborate researches, has shown that the orchitic extract increases one's neuro-muscular power. It is stated that he spent nearly 1,000 francs in the gratuitous distribution of the orchitic extract.

He loved science for itself, and as president of the Biological Society of Paris he sincerely rejoiced in every new fact received before it as though he had been the author himself.

From 1846 to 1894, for forty-eight years, his original genius gave him no rest but to quench it by research, whether in Richmond, Philadelphia, New York, Boston, London or Paris. At all times and at all places he worked away without any external driving power, without any pecuniary reward, rather with much pecuniary loss.

I say without these things he worked for all he was capable of at any spare moment that he had at what he loved more than position, power or money; that is the science of physiology. Laboremus was the watchword of Septimus Severus; laboremus was the ensign on his high standard until the day of his death. In judging from what I personally observed he suffered but little from ill health; he was of sturdy frame, good color in his cheeks, with brown eyes with a great sheen in them, behind which rested a powerful mind. I say it was with his great physical power that he was enabled to let his mind carry on the numerous researches.

He was not a man of one idea which, when exhausted, closed his career; but in whatever direction he worked he threw a bright and illuminating effulgence through the gifts of intellect, personal fascination and magnetism.

He will remain unforgotten by his numerous friends, scholars and admirers. And while I am making the attempt in this short sketch to give a picture of this great personality I feel how difficult a task I have undertaken in regard to the position of a peculiar person like Brown-Sequard. We must remember that physiology, compared with the other sciences, is comparatively young, and it is only in the last seventy-five years that it has been cultivated.

All sides of phenomena interested Brown-Sequard. He understood that many problems of the nervous system could be solved by the cultivation of neighboring subjects in anatomy, physics and chemistry, although he did hardly any microscopic work. Although in 1847 Ludwig, Helmholtz, Du Bois-Reymond, Hering and Bruecke were cultivating the physical origin of all phenomena, we see Brown-Sequard influenced by the same spirit, a spirit, by the way, cultivated by Magendie, and who subjected everything to what he called the experimental method, that is, physical and chemical tests in contradistinction to the vitalistic ideas of Bichat.

I say that these ideas of Magendie were propagated when Germany was still plunged in the shadows of philosophy. It was under the influence of these teachings that the mind of Brown-Sequard was moulded in the direction of the experimental method which he continued to use all his life. In his last years he discovered as many new facts as at any other period of his life.

As to his honors, he was a member of many learned societies. He succeeded Vulpian in the section of medicine in the Academy. He was a laureate of the Institute, with the biennial prize of 1885. In 1886 he obtained the Baly medal of the Royal College of Physicians, and in 1881 was made an LL. D. by the University of Cambridge. Death as before removed his estimable wife, who, for eighteen years, was most devoted to him. This great grief and the burden of seventy-seven years were too much for him to bear, and he succumbed to an attack of apoplexy.

If we compare Brown-Sequard with Ludwig or Bernard, we find that he did not have as great originality of discovery in him or the many-sided ability to attack new problems. But we can say of Brown-Sequard what Burdon-Sanderson has said of Ludwig: "There were not a few of them who, for the first time in their lives, came into personal relation with a man who was utterly free from selfish aim and vain ambition; who was scrupulously conscientious in all that he said and did; who was what he seemed and seemed what he was, and who had no other aim than the advancement of science, and that advancement saw no other end than the increase of human happiness."

And now a few words to our students. In the name of the faculty I extend to all a most hearty welcome to this most active and progressive college, a college young in years, vigorous in growth, expansive in its future and annually putting forth a fruitage of good and well-educated young men.

As to the arrangement of the college you will find some changes the walls have undergone—a transformation—a new coat—a sort of ecdysis.

The laboratories of pathology, chemistry and experimental therapeutics have been transferred to Eighteenth street to meet the increased size of our classes. The histological laboratory has been enlarged, both for the purposes of histology and for an important factor in our school—free recitations. A children's department of the hospital has been opened up on Eighteenth street.

You will have a new teacher of pathology, Professor Joseph McFarland, who comes to us from the University of Pennsylvania, succeeding a graduate of the school, Professor Sangree, who has gone to Vanderbilt University, Tennessee.

You will find here teachers thoroughly in earnest to instruct you in the art and science of medicine, for we all know that life is short and medical art is long, and especially long, to be covered in three years. But by great industry and patience you will master the foundation and details of the practice of your future life.

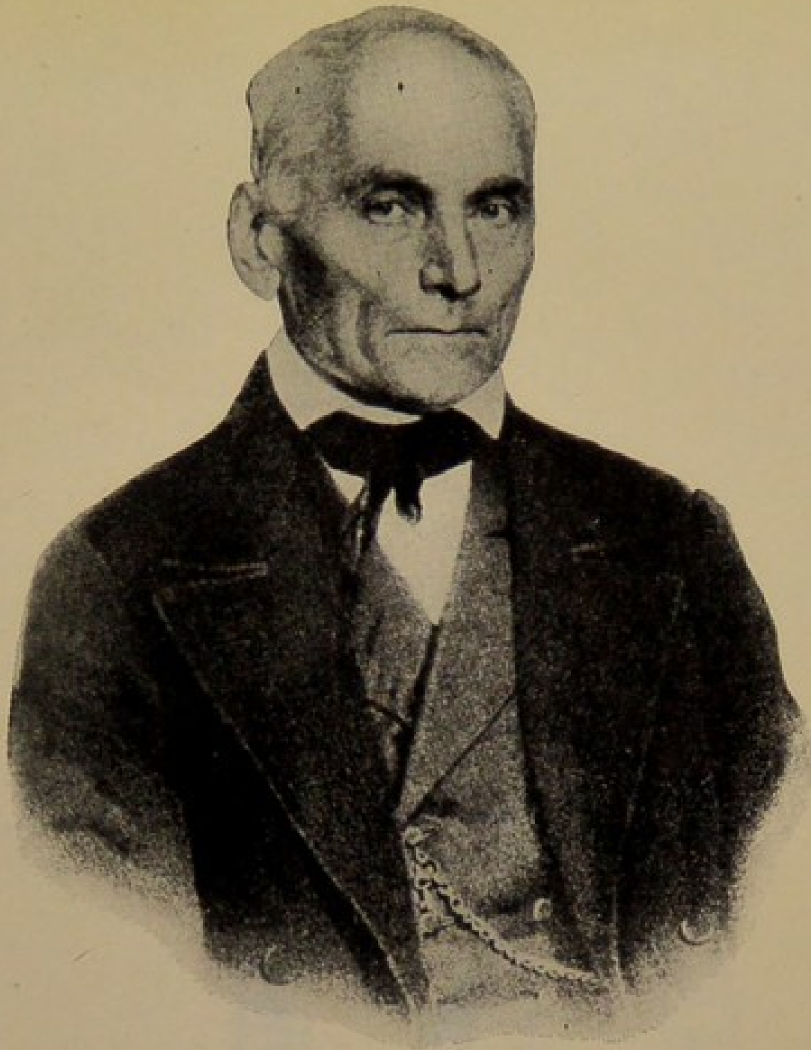
Remember, as to your studies that it is to do or die as regards your success in the future.

The recent success of our students in the acquirement of hospital positions shows that the students and the teachers of the college are doing good work.

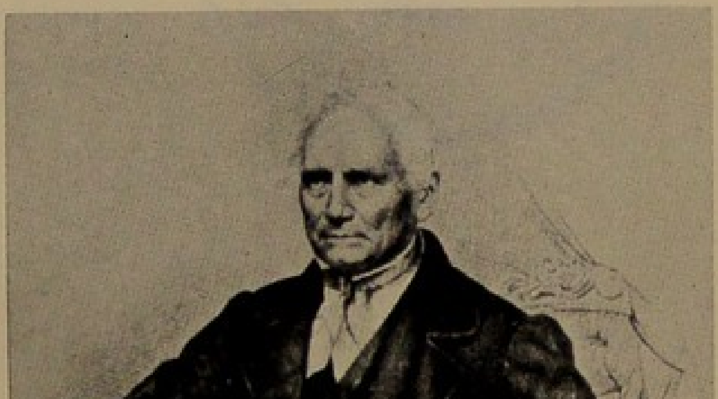
Eighteen hospital positions have been obtained by the members of our last graduating class of 54. That is, one-third of the class have become resident physicians, and many of them only by a hard competitive examination. The Medico-Chirurgical College expects every man to do his duty. Do not forget that you have undertaken a heavy task, which your teachers will need to lighten.

I have just laid before you the life of a great man who worked under disadvantages much greater than I expect you to; but he reached the pinnacle of greatness, although only a sea captain's son. Humble in origin, humble all his life, as became the great man that he was, yet he acquired all the earthly honor that a medical man could aspire to.

Papers consulted: Notice sur les Travaux scientifiques. Du Docteur C. E. Brown-Sequard. Archives de Physiologie, 1894. London Lancet, 1894. Société de Biologie, 1894.



PURKINJE (Locy)



JOHANN EVANGELISTA PURKINJE (Garrison)
Professor of Physiology at Breslau, 1823–1850.
After 1850 Professor of Physiology at Prague.
Died 1869.

PURKINJE—THE PHYSIOLOGIST.

Ladies and Gentlemen:

In the rolling along of years it has fallen by rotation upon me to deliver the introductory address this evening. For your pleasure I wish it had been laid upon someone more able to extend the welcome greetings on this occasion—an occasion which is of the highest importance to the Honorable Board of Trustees and Faculty who have assumed the direction and conduct of the Medico-Chirurgical College.

This college has been in existence for many years and its friends are entitled to view its present position with very much pleasure, yet I am greatly mistaken if its further progress and development are not to be much more ample in the future. We may consider the present organization and position of this college with exultant satisfaction. Still I apprehend that although very much has been done, yet much more must be done in the oncoming years.

For you know that a college is a place of aggregation where students come from every section for knowledge. It is a place where the best men of the profession are assembled. It is a place which attracts the young student by its renown. It is a place where inquiries are made, where discoveries are confirmed and mistakes exposed by the attrition of intellect with intellect.

Introductory address delivered at the opening of Medico Chirurgical College of Philadelphia, Sept. 22, 1913.

Our institution, with the thoroughness of instruction in theoretical and practical medicine, has grown with wonderful rapidity both in the acquisition and construction of laboratories and dispensaries. Each year imposes an increased amount of preparation upon the student before he can enter upon the study of medicine. Each year the courses of study are ever enlarging with the natural increment of the sciences. Each year after graduation you have still another year to devote to hospital experience before you can enter upon the practice of your profession. With these propitious surroundings our students will enter upon the study of medicine with unusual zeal and with the electric ardor of adolescence to keep in the difficult paths to be followed each year in the different sciences.

As a physiologist I wish to lay before you tonight the life of an extraordinary man. In doing this I will have to divert your minds to a small province upon the North Austrian border—a province which has produced the great warrior Wallenstein, who laid Gustavus Adolphus low in the battle of Luetzen; an evolutionist like Mendel of Bruenn; an actress like Janauscheck; and physiologists like Purkinje and John Nepomuck Czermack.

It is about the old physiologist Purkinje that I wish to dwell upon tonight. Purkinje lived eighty-two years, of which twenty-seven were spent at Breslau. Born at Libochowitz, in Bohemia, 1787, he was called from Prague to Breslau in Silesian Germany. He died in 1869 at Prague.

I have had the pleasure to visit the spot in Germany where its first laboratory was established in the semester of 1839 by Purkinje. It should be noted here that Magendie, of Paris, the prince of vivisectors, was then in the zenith of his fame. Hence you see that it is not a century since the founding of the Breslau laboratory, and you have now in Germany alone about twenty laboratories for physiology, many of them in elegant, large, separate buildings, well equipped with apparatus and endowed with sufficient means by the government to carry on original work. A separate chair of physiology was established at Breslau in 1811. It was held by Daniel Augustus Bartels, who was called from Marburg as ordinary professor of physiology. He was a good teacher, but was content with lecturing on the facts as then collocated. These facts, owing to the state of physiological science, were chiefly philosophical speculations. It must be remembered at that period in the domain of light in physiology there was mainly darkness, and in place of clear and distinct data there was variant and dubious discussion. In 1821, Marburg University recalled him as Professor of Internal Medicine.

It must be remembered that Magendie founded in this year, 1821, his Journal of Experimental Physiology, and during ten years it was a resume of all that was positive in physiology and in normal and morbid anatomy. He, however, had been publishing experiments from 1808. In 1839 he published his lectures upon the functions and diseases of the nervous system in two volumes.

Magendie at that time worked in a corner spoken of as "a damp, dark lair, a hiding place for a wild beast."*

The successor of Bartels at Breslau was John Evangelista Purkinje, a Czech of Prague. He accepted the chair January 11, 1823. Purkinje was an assistant in the anatomical institute at Prague. He was recommended for the position at Breslau by the anatomist Rust and by Alexander Humboldt. The poet Goethe had written some works on color vision. He invited Purkinje to visit him at Weimar. Goethe became interested in Purkinje by the reading of a work of his, a doctorate dissertation, "Beitrage zur Kentniss des Sehens in Subjectiver Hinsicht," 1819. Goethe recommended Purkinje to Humboldt, as the latter was not directly concerned in the work of the former. The salary of Purkinje was eight hundred thalers. His reception at Breslau was not very favorable, as he was not chosen by the Breslau faculty but by the ministry. It was not long after his teachings there that Otto, the anatomist, complained that Purkinje's language was not flowing and clear; that he often failed in his German expressions; that the current physiological views were not brought out in his lectures; that they were too philosophical. Otto's

*Claude Bernard. By Sir Michael Foster. p. 164.

opinion was that Purkinje might be useful as a Privat docent, that he had better lecture in Latin and not after his own resume but after the current compends of physiology. It must be remembered that Purkinje's mother-tongue was Czech, hence he had difficulty in lecturing in another language. But notwithstanding these deprecatory remarks of Otto, Purkinje remained professor at Breslau, and his name will continue to be remembered to the end of time, whilst the name of his critic and enemy, Otto, is dead—so thoroughly dead in the scientific world that it is doubtful if the angel Gabriel's horn will ever awaken it.

Purkinje clearly knew what the physiology of his day was, and what it should be, that is, lectures with explanatory experiments and original work to clarify and increase physiological knowledge. But both room and money were wanting to him. But with a strong will he followed his ambition. He obtained a room in the winter of 1824-25 in the old anatomical institute. The money for demonstrations and experiments had to come out of that princely salary of eight hundred thalers; but for his outlay, upon a requisition, he received from the curator fifty thalers. He also had not the necessary instruments for original work. For his optical and morphological work he needed a microscope. In 1830 Purkinje asked the curator for a microscope costing at that time two hundred thalers. The curator replied that the acquisition of so costly an instrument would require a petition signed by the physicist Steffens, the astronomer Jungnitz, the anatomist Otto, the botanist Nees van Esenbeck, and Purkinje. This instrument was to be used by all of the above petitioners. In 1832 he obtained the exclusive use of the instrument, but he was retarded by want of a suitable room. By a quarrel with his old enemy Otto he had to leave the anatomical building and could not lecture there. As a substitute he was given a room in the third story of the university building. This room was located between the residences of the professors and the lecture room of physics. Here his animals, instruments, collections and so on were brought. But the professors complained that unpleasant odors proceeded from Purkinje's laboratory, and they sought to have him evicted, but Purkinje was not a man to let go of a thing once attained. Besides, his lectures by this time had received so much acclaim and his scientific work obtained such a name that he was in an unassailable position in the university. He continued in Breslau his experiments upon the eye; as, for example, Purkinje's blood-vessel images and the Purkinje images reflected from cornea and lens. He studied the curvatures of the refracting surfaces of the eye with mirrors; besides, he had a method of lighting up the retina of the eye, thus anticipating the ophthalmoscope of Helmholtz. He also experimented upon the production of vertigo under different conditions; made the discovery of the Purkinje vesicle in the chick's egg;

the arrangement of the touch papilla in finger, experiments upon the path of fibres in the brain and the basket cells in the cerebellum.

Two years before Schwann he published the general idea of the cell; he also studied the structure of the skin, bones, nerves, Purkinje's interglobular layer in dentine. The dissolving action of acidulated infusion of the pancreatic juice on albumin was discovered by Purkinje and Pappenheim in 1836.

Prof. G. G. Valentin, at Berne, was for a long time a pupil of Purkinje.

In 1831 Purkinje asked the curator for (1) an independent physiological building, (2) a servant and an assistant, (3) a donation for the institute. The request never reached the ministry from the curator, who replied that even so rich a university as Bonn, not even any German university, not even Berlin, had a separate building for physiological work, with special physiological preparations, with special anatomical and surgical instruments, with chemical apparatus and special assistant and servants. Then Purkinje asked that he be given two rooms in the new anatomy institute for lectures and vivisections. But when the new anatomical institute was built, 1833-34, Otto claimed the anatomical building as his official residence. Thus Purkinje was left out in all these arrangements. But this did not paralyze Purkinje. As cholera deaths in the year 1831 had made his private residence empty, he made a physiological laboratory of it. Here he carried on a series of researches by himself and with his scholars. These experiments were mainly microscopical. The two hundred thaler microscope produced a new epoch in his work. He studied with great earnestness the whole domain of plant and animal histology. He used his eyes and those of his students in this work. He found himself urged on by the activity of young men and made many discoveries. In this way he discovered the ciliary movement in the respiratory organs and gonads of the higher animals and in man; their independence of the nervous system; the discovery of the sweat glands and their ducts; also the glands of the stomach.

But at length the curatorship was transferred to another man. He soon asked the ministry to give Purkinje two hundred thalers yearly for his demonstrations. In 1836 Purkinje again asked the new curator for a separate and independent physiological institute. In this application he gave the chief heads of his lecture courses:

(1) Morphology,
(2) Physiological physics,
(3) Physiological chemistry,
(4) Physiological dynamics,
(5) Physiological psychology;

these to be explained in great fulness, and in which he could use only the simplest means.

If now you will compare this lecture course with the arrangements at the Laboratory of Physiology at Berlin, where they have five professors in this branch, you will find that they lecture on

(1) Histology,
(2) Physics applied to Physiology,
(3) Physiological chemistry,
(4) Nervous system,
(5) Special senses.

What forethought, what remarkable prescience he had in giving lecture courses upon a plan laid down by Englemann about seventy years after Purkinje.

He measured the blood-pressure in the living animal, explained the mechanics of the circulation and respiration by models, measured the respiration long before Hutchinson with a spirometer, showed the effect of irritation on the muscles and nerves, etc. He was given three thousand eight hundred thalers for his independent physiological institute and a place in Catherine Street to build it. In 1839, November 8th, Purkinje gave to the world the first physiological institute. At this time the chairs of anatomy and physiology in Berlin were united and continued thus until 1858, for the first time separated after the death of Johannes Mueller. In 1877, Berlin University built an institute specially set apart for the purposes of physiology, whilst Purkinje about forty years previously had one erected at Breslau. But with the erection of the new laboratory Purkinje's important discoveries came to an end. The causes of this were that the state and donation of money in no way corresponded with the institute. As to the building itself, it was small, and later used as an academic prison. Purkinje was to have nine hundred thalers to furnish the laboratory, but instead he received only three hundred thalers for apparatus. The furnishing of the institute was a great source of anxiety, in which he exhausted his mental energy and desire for work. He spent a great deal of time in the preparation of microscopic objects, which was then new work in this direction. With the microscope he used Drummond's calcium light for projection purposes and made photographs of microscopic objects by means of Daguerre's method. With this work he was also actively engaged in the politics of the Czechs, and in 1850 was called to Prague to become entirely absorbed with them.

He shows us how a determined will and brains overcame all obstacles. Details of Purkinje's history have been so obscure that it is a pleasure to unearth them and bring back to our view one of the old masters in physiology. Farther, my own experiences in building up a laboratory have been on the same lines—pleasant ones, however. In the lecture room at Breslau they have erected a bust of Purkinje, and on the opposite side of the room one of his successors—Heidenhain. A similar statue exists in the German Physiological Institute at Prague.

I need not follow his life farther. I have related enough to illustrate the course of one who may be called the founder of the laboratory of physiology. Such, fellow students, was the life and career of a great man. He is a noble example to follow, in the victory over difficulties, in his triumphs over opponents, in the great discoveries he made, which will perpetuate his name through eons of ages.

Having considered the laboratory, let us next take up the work done in a laboratory of physiology. In the laboratory work the hand is trained in a progressive manner to perform the various technical manoeuvers. As Bernard has said, "A dexterous hand without a head to guide it is a blind tool. A head without a hand to realize its wishes is an impotent nothing." At the same time the eye is taught to note carefully and the mind is led to draw from the phenomena seen, logical deductions. The laboratory produces the habit of independent thought. No authority besides that of the five senses is appealed to, the student creates from his own experiments the conclusions to be derived therefrom. If his technique or observations or his conclusions are wrong, the law of nature will soon find his error. The manual dexterity, the quickness and acuteness of sight and flexibility of mind must in a greater or smaller degree be acquired by all who would undertake original work. In original work we do not know what result to expect and no one can tell what will ensue. We are traveling in a new country; we must be forewarned for every possible event and ready to meet every angle of view.

For the details of the life of Purkinje I have to thank Prof. Huerthle, who gave me his address at the unveiling of the bust of Purkinje, November 10, 1907, at Breslau.

Bernard used to say to those working with him, "Put off your imagination as you take off your overcoat when you enter the laboratory, but put it on again as you do the overcoat when you leave the laboratory. Before the experiment and between whiles let your imagination wrap you round; put it right away from yourself during the experiment itself lest it hinder your observing power."

Venturi in the fifteenth century very wisely stated, "Theory is the general, experiments are the soldiers. The interpreter of the artifices of nature is experience. She is never deceived." He states that "Nature begins from the Reason and ends in experience, but for all that we must take the opposite course, begin from the experiment and try to discover the Reason."

Scientific results are not made in a haphazard manner, but require often years of laborious experiment and observation. It is at the cost of time and strength that discoveries are made. It is the scientific knowledge which Germany has obtained in the laboratories which has mainly led to her preponderance in the promotion of medicine. It is their method of inquiry which, when applied to medicine, raises it from the state of an art to that of a science.

I have visited in Europe twenty laboratories, French, German, Swiss, Austrian, Swedish, Dutch, Russian and English. And what did I see? That in all these countries men were working with all their powers at the problems of life.

Although it was warm weather and vacation time, yet the majority of them were at their posts. Certainly, gentlemen, it is a motif, and inspiration to us to push our efforts in the aid of our science. I know that American physiology is forging along to a prominent place in its world study of nature. With several laboratories well endowed with apparatus and money, with capable teachers we can not help bringing out the talent of this country to the cause of physiology. But the spirit of the times here, that success in a man's life means the acquisition of the "almighty dollar," is not as conducive as it is in Europe to invite talented men to live a life of investigation, with no pension on retirement, unless the Carnegie fund is extended to medical men as it is now to teachers in the colleges for literature. But as endowments increase, as scholarships are instituted, and the spirit of investigation stimulates the minds of the youth of this country, then will physiological investigation draw more workers to its side, and Americans will hold their own in physiological studies.

The quotations in foreign periodicals of the literature of American physiology are numerous. Besides, we have magnificent laboratories at Harvard, Columbia, University of Pennsylvania, Johns Hopkins, Western Reserve, and at the University of Chicago. Now what are the functions of a laboratory of this class? I might say that outside of chemical and microscopical work it is that of vivisection. In the twenty laboratories that I visited in Europe, I always found that a vivisection was being made. Now this subject is one reprobated, not by medical men, but by some of our good-hearted ladies. Let us see what some of the greatest minds have thought of this practice. Let us take the view of the discoverer of the circulation of the blood, Harvey, who wrote the brilliant first chapter in physiology. In his book, "De Motu Cordis et Sanguinis," published in 1628, he states, "When I first gave my mind to vivisection as a means of discovering the motion and uses of the heart, and sought to discover these from actual inspection and not from the writings of others, I found the task so truly arduous, so full of difficulties, that I was almost tempted to think with Fracastorius, that the motion of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place, nor when and where dilatation and contraction occurred, by reason of the rapidity of the motion which in many animals is accomplished in the twinkling of an eye, coming and going like a flash of lightning, so that the systole presented itself to me now from this point, now from that, the diastole the same, and then everything was reversed, the motions occurring, as it seemed, variously and confusedly together. My mind was therefore greatly unsettled, nor did I know what I should myself conclude, nor what believe from others. I was not surprised that Andreas Laurentius should have said that the motion of the heart was as perplexing as the flux and reflux of Euripus had appeared to Aristotle."

"At length, by using greater and daily diligence, having frequent recourse to vivisection, employing a variety of animals for the purpose, and collating numerous observations, I thought I had attained to the truth, that I should extricate myself and escape from the labyrinth, and that I had discovered what I so much desired, both the motion and the use of the heart and arteries. For the philosophers who are only eager for truth and knowledge never regard themselves as already so thoroughly informed but that they welcome further information from whomsoever and from whencesoever it may come. Nor are they so narrow minded as to imagine any of the arts or sciences transmitted to us by the ancients in such a state of forwardness or completeness that nothing is left for the ingenuity and industry of others. Very many, on the contrary, maintain that all that we know is still infinitely less than all that still remains unknown. For they know full well that to err is human, that many things are discovered by accident, and that many may be learned indifferently from any quarter, by an old man from a youth, by a person of understanding from one of inferior capacity."

Bacon, that illustrious man, not a physician, did not object to vivisection. In the New Atlantis he states "We have also parks and enclosures of all sorts of birds and beasts that thereby we may take light what may be wrought upon the body of man, wherein we find many strange effects, as containing life in them though divers parts which you account vital be perished and taken forth, resuscitating of some that seem dead in appearance and the like; we try also poisons and other medicines upon them, as well as of chirurgery as of physic."

Let us take the views of Magendie. Claude Bernard was assisting him in an experiment when there entered a large man of an age demanding respect, clad in black and keeping upon his head a hat with a very large rim, wearing a coat with a stand-up collar, and knee breeches. By his costume it was easy to see that they were in the presence of a Quaker. He stated that he wished to speak to Magendie, who was pointed out to him. The Quaker continued, "I have heard of thee and I see I have not been deceived that you make experiments upon living animals. I come to demand of thee by what right you act in this manner and to state that you should cease these kind of experiments because you have no right to kill animals or to make them suffer, that you show a bad example, and that thee acquire habits of cruelty." The subjects of experimentation were removed from view and Magendie argued in justification of a vivisector. He replied to the Quaker "that there was another angle of view in judging of experiments upon living animals. It is certain that if experimentation did not have for its aim useful results to humanity it would be cruelty. But the physiologist who is imbued with the thought of making a discovery useful to medicine does not merit reproach. Your compatriot Harvey would not have discovered the circulation if he had not made experiments upon the dogs in the park of Charles the First. Who would dare deny that this discovery had not rendered the greatest benefit to humanity and who would dare to accuse Harvey of cruelty!" Magendie added that it was barbarous cruelty if you do not consider its end and the results to humanity. "Besides, what should be condemned is the chase, because the animals suffer and are killed solely for pleasure." "Certainly," interrupted the Quaker, "I condemn war, the chase and experiments upon living animals. In all these cases man assumes a right which he does not have, which I wish to prove and for which I made this voyage, to take out of this world three things —war, the chase, and experiments upon animals." No doubt the Quaker was not converted by Magendie, nor Magendie by the Quaker. When these intellectual giants have spoken it is needless to quote others.

And now I must say a few words to those students who are about entering upon the study of medicine. The question comes to you, how can you arrange your time, as you are attempting your life work, so as to make it useful and happy? In the first place you must keep yourself in good health. That means regular habits, exercise, cleanliness, simple food and moderation in eating and drinking. To be happy you must try to be cheerful. If you look at the world through spectacles of red glass all will be rosy, if through a blue glass everything will be blue. Do not complain. As Ruskin has said, "to read, to think, to love, to pray, are the things that make a man happy." You, gentlemen, are now commencing your studies under capable teachers. You have great opportunities and advantages. Let me give you the names of a few great men and tell you how they began life. Franklin was the son of a tallow merchant, Faraday of a blacksmith; Davy was a druggist's assistant; George Stephenson, who did so much for railways, was a miner and worked at two-pence a day and could not read until he was eighteen years of age. Galileo, Kepler, Cuvier, and many others were all children of poor parents and had not anything like the advantages in their education that you have today. Hence, it is reasonable to hope that some of you may take part in the progress of science.

But, fellow students, remember, as Gibbon has said, "Every one has two educations, one which he receives from others, and one more important which he gives himself."

To discover now it is not as in previous ages, when, as Ruskin has said, "The man who discovered the telescope and first saw heaven was paid with a dungeon, the man who invented the microscope and first saw earth died of starvation, driven from his home." I must remind you that the progress of science in the last century has been wonderful.. We not only are able to weigh and measure the stars, but by their spectrum to analyze them. We descend beneath the earth. We know how mountains rise and valleys are formed. It has given us anesthetics; it has enabled us to send messages without a wire across the sea; it has given us rays to accurately examine our deep-seated bony structures, the outlines of the internal organs; it has given us means to hear voices over a thousand miles distant; it has given us machines to fly through the air; it has given us metals like radium which show a constant bombardment of atoms. And yet how much remains to discover. What we know is an infinitely small fraction of what we know not. There is no plant or animal whose life history has been completely discovered. There is no element in nature, the uses and properties of which are completely investigated.

As the great Cardinal Newman has stated in his beautiful mastery of the English language, "We have familiar experience of the order, the constancy, the perpetual renovation of the material world which surrounds us. Frail and transitory as every part of it, restless and migratory as are its elements, never ceasing as its changes, still it abides. It is bound together by a law of permanence; it is set up in unity, and though it is ever dying it is ever coming to life again. Dissolution does but give birth to fresh modes of organization and one death is the parent of a thousand lives. Each hour as it comes is but a testimony how fleeting yet how secure, how certain, is the great whole. It is like an image on the waters which is ever the same though the waters ever flow. The sun sinks to rise again. The day is swallowed up in the gloom of night to be born out of it as fresh as if it had never been quenched. Spring passes into summer and through summer and fall into winter."

Or shall we quote Heine?

"By the sea, the dreary nocturnal sea,
Standeth a stripling;
His breast full of sorrow,
His head full of doubt,
And with gloomy lips he
asks the waters:—
'Oh solve me the riddle of life—
That harrowing world-old riddle—
Whereon many heads have
pondered and brooded—
Heads in caps hieroglyph-scribbled,
Heads in turbans and heads
in black beavers,
Heads periwigged and a
thousand others—
Poor aching human heads,
Tell me what signifies
Man—
Whence has he come?
Whither goes he?
Who dwells up in the golden stars?'"