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THE PONTO-BULBAR HEAT CENTER.*

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Although our knowledge of the thermogenic mechanism is still in a formative state, we nevertheless have sufficient experimental data to warrant the conclusion that in the higher animals the heat formed arises in part as a product incident to the activities of all forms of vital processes, and in part as a specific product of specific heat-producing structures. The results of Rubner's researches leave no doubt as to the skeletal muscles possessing, besides their motorial properties, a specific thermogenic function, and, as a consequence, that these structures not only produce heat as an incident to repair, growth and motor activity, but also as a specific product. They further show that the quantity of heat which arises by virtue of this special function bears a reciprocal relationship to the amount formed as an incident to the activities of the body structures generally, increasing or decreasing in adjustment to the variations in thermogenesis caused by rest and activity, etc., and to the alterations in thermolysis which are dependent upon ever-changing internal and external conditions; so that as the output of heat incidentally produced increases or decreases, the quantity resulting from the specific thermal function of the skeletal muscles varies co-operatively in supplying the number of heat units required by the organism at any given time. Moreover, there can be no doubt that this specific thermal function is directly controlled by specific thermogenic centers, which are located in the cerebrospinal axis, although very little is known of their exact positions, functional relations and characteristics.

Since Tscheschichin¹ showed, thirty-five years ago, in an experiment upon a rabbit that injury of the base of the brain may be followed by a rapid and decided rise of body-temperature, considerable valuable information has been obtained from the researches of Bruck and Günter,² Eulenburg and Landois,³ Hitzig,⁴ Richet,⁵ Wood,⁶ Aronson and Sachs,⁷ Girard,⁸ Baginsky and Lehmann,⁹ Baculo,¹⁰ Ott,¹¹ White,¹² Tangl,¹³ Kemp,¹⁴ Schultz,¹⁵ Schreiber,¹⁶ and myself.^{17 18} A critical study of these contributions justifies the following conclusions:

1. That specific thermogenic centers exist in the brain and spinal cord, and that these centers are connected with each other and with various parts of the body,

- especially with the skeletal muscles and skin, by specific afferent and efferent thermogenic nerves.
2. That the centers in the brain are either thermo-accelerator or thermo-inhibitory.
3. That the center in the spinal cord is a general or reflex center.
4. That the brain centers probably affect heat production by acting upon the spinal center.
5. That the spinal center when separated by section from the brain centers is able to maintain the normal standard of heat production.
6. That the activities of these centers is largely influenced by the changes in the temperature of the blood, and by cutaneous impulses which are probably generated in the peripheries of the "heat" and "cold" nerves.
7. That the caudate nuclei contain an important thermo-accelerator center.
8. That the pons and bulb probably contain a thermo-accelerator center.
9. That a thermo-inhibitory center is located in the dog in the first cerebral convolution posterior to and in the vicinity of the sulcus cruciatus, and that possibly another such center extends downward from the junction of the supra-sylvian and post-sylvian fissures to the posterior fissure.
10. That there is no adequate evidence to lead to the belief that specific heat centers exist in any other part of the body than in those above noted.

The experimental study of the locations and functional peculiarities of heat centers is attended by many sources of fallacy, some of which are unavoidable and some so important as to materially modify or even entirely vitiate the results. Shock, hemorrhage, the pressure of a clot, circulatory and respiratory disturbances, the involvement of contiguous parts, etc., may be more or less potent disturbing factors, but shock is pre-eminent the most important. The sensitivity of the cerebrospinal axis to injury is very evident in the more or less marked disturbances of temperature, which almost invariably follow, and which sometimes are decided and persistent. In some instances a rise continues until death ensues from the excessive temperature, and in others there occurs a steady and rapid fall, which progresses until there is general functional collapse. Shock causes the temperature to decrease, and its influences may be so powerful as to not only prevent the decided rise, which ordinarily would be caused by irritation of the caudate nuclei, but even to bring on at once a rapid decrease. The ease with which the body-temperature is affected by even trifling injuries of the brain makes it necessary to be very guarded in reaching conclusions as to the specific connection of any given portion of the cerebrospinal axis with the heat mechanism, unless the effects of shock, vaso-motor palsy, etc., can be eliminated to a satisfactory degree, and the results obtained by the section, puncture, ablation, etc., be reasonably uniform and positive.

In the experiments recorded in the present contri-

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bution, essentially the same technic was pursued as in a preceding research¹⁸ on the effects of lesions of the base of the brain upon the heat processes. Dogs were used and were thoroughly anesthetized with a mixture of ether and chloroform (3:1), a tracheal canula was inserted, the skull was trephined on a level with the upper surface of the structure to be cut, and then a slightly bent, blunt-edged probe was pushed horizontally through the brain mass and withdrawn with a downward, sweeping movement, thus cutting all the nervous matter beneath, without, however, injuring any important vessels. Such section causes but trifling hemorrhage, and a variable amount of shock, which latter is indicated by immediate effects upon the respiratory movements and circulation, and in some cases by a fall of body-temperature. Artificial respiration was practiced throughout the experiments, even though it might have been possible for the ventilation of the lungs to have been carried on effectively by spontaneous respiratory movements.

When after the section a rise of temperature occurs, the result, eliminating any probable indirect effects due to the changes in the circulation and respiratory movements, is to be attributed to a cutting off of thermo-inhibitory impulses or to the generation of thermo-accelerator impulses. If due to the former, stimulation of the part of the brain involved in the section should lessen the temperature; while if the latter, the reverse. Inasmuch as section, puncture and other forms of stimulation of the striate bodies, crura cerebri and pons cause an increase of temperature, we are justified in the conclusion that the rise is due to an irritation of thermo-accelerator centers or nerves. In the research referred to it was found that sections of the striate bodies and pons were, as a rule, followed immediately, or within a few minutes, by a decided increase of temperature; and that section of the white matter anterior to the caudate nuclei, of the thalami, and of the crura cerebri, are either not followed by a rise or by one that is usually comparatively transient and not marked. The difference is such as to suggest that in the first instance thermo-accelerator centers were irritated, and in the other, thermo-accelerator fibers. Of 11 experiments in which the section was made of the striate bodies or pons, in 8 the increase of temperature ranged from 0.98 to 4.37; in 2 it was but 0.26 and 0.27, respectively; and in one the temperature fell. In one of the last 3, the section was 2 mm. posterior to the anterior extremity of the caudate nuclei and the effects of shock were greater than those of direct irritation of the thermo-accelerator cells; in the other 2 the animals suffered even more severely from shock, one dying within 45 minutes, and the other within 1 hour and 15 minutes. In a total of 24 experiments, in 2 of which the section was made through the white matter just anterior to the caudate nuclei, in 2 where it was made through the thalami, and in 20 through the crura cerebri, in 18 cases a rise was noted—in 12 of which it was transient—in 14 it was less than 1, and in only 4 was it over 1.

In another research¹⁷ in which the sections were made of the spinal cord at the level of the first and second cervical vertebræ, in 9 out of 10 experiments the temperature fell from the first. Probably the vasomotor palsy necessarily caused by these sections is almost solely accountable for the decrease. When sections are made of the bulb the effects are variable, and depend largely upon the extent to which the vasomotor center is involved, a fall of temperature occurring if the center is seriously affected, and a rise if not. If a rise occurs it is rarely

so decided as when the section is through the pons; and the temperature curves differ in other respects. These experiments show, in a word, that sections of the caudate nuclei and pons are followed by results which, as a whole, differ materially from those caused by sections of other portions of the cerebrospinal axis at any point between the white matter anterior to the striate bodies and the level of the first and second cervical vertebræ, and they are such as to indicate that thermo-accelerator centers are located both in the caudate nuclei and ponto-bulbar region.

The main results of the research (*loc. cit.*) upon the effects of sections of the basal parts of brain are summarized in the following table.

TABLE 1.—Summary of the chief results of the sections anterior to the striate bodies, striate bodies, thalami, crura cerebri and pons.

	Number of experiments.	Mean maximum rise of temperature. Degrees.	Mean time of occurrence of maximum rise of temperature. hrs. min.
Sections anterior to striate bodies . . .	2		
Sections of the striate bodies . . .	6	2.4	2:53
Sections of the thalami . . .	12	0.12	8
Sections of the crura cerebri . . .	20	0.8	1:20
Sections of the pons . . .	5	2.74	4

The studies made by various investigators of the thermal functions of the caudate nuclei are more numerous, extensive and convincing than those of the ponto-bulbar region, and the results are sufficient to justify the belief that these structures contain an important thermo-accelerator center. As to the ponto-bulbar region, the data upon which rests the belief that it contains a thermo-accelerator center is to be found mainly in the reports of the experiments by Tscheschichin,¹ Bruck and Günter,² Wood,⁶ Ott,¹⁹ and myself (*loc. cit.*). But little intrinsic value is attached to the results obtained by Tscheschichin, Bruck and Günter, and Ott. Tscheschichin found in a single experiment upon a rabbit, in which the pons was severed from the bulb, that the temperature rose from 39.7 to 41.2 (1.5) in 30 minutes. Bruck and Günter in 23 experiments upon rabbits, in which the ponto-bulbar section of puncture was practiced, noted an increase in 11. Ott in 10 experiments on rabbits, in which the pons was punctured at various points, recorded in 6 a transient rise, usually slight and ranging from 0.3 to 2.6; in the other 4 the temperature fell. In Wood's research upon dogs and rabbits it was found that "injuries of the medulla so situated as to paralyze the medullary vasomotor center, are followed by a decided fall of animal temperature; section of the medulla at the line of its junction with the pons in the dog, usually leads to an elevation of animal temperature, if the medullary vasomotor centers are not in any way impaired; section of the medulla at its junction with the pons is followed by increased heat dissipation and increased heat production, the increased heat dissipation usually not keeping pace with the increased production, so that the body temperature rises." In three experiments on dogs, in which the section—at the junction of the pons and bulb—was complete, the rises of temperature amounted to 3.25 in 1 hour and 30 minutes, 4.88 in 2 hours and 35 minutes, and 3.88 in 5 hours and 25 minutes. In 4 experiments in which the sections were incomplete, 2 being on dogs and 2 on rabbits, in 3 the section was at the junction of the pons and bulb and in one through the pons, an increase of temperature was observed in each, but the greatest rise was only 1.1.

TABLE 3.—Records of 14 experiments in which the sections were through the crura cerebri.

Number of experiment.	7	8	9	10	11		3	14	15	16	17	18	19
Level of the section.	Close to thalami.	Close to thalami.	Middle of peduncles.	Middle of peduncles.	Middle of peduncles.	Middle of peduncles.	Middle of peduncles.	Within 3 mm. of the pons.	Within 3 mm. of the pons.	Within 3 mm. of the pons.	Within 3 mm. of the pons.	Within 3 mm. of the pons.	Within 3 mm. of the pons.
Time after section. hrs. min.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.
0:00													
0:05	38.78	40.22	39.42			38.9	40.18	38.60	39.00	39.38	38.88		
0:10	.82	.68	.60	40.08	38.88	39.0		.70	38.88	40.35		39.23	
0:15	.80	.72	.75	.15	.92	.1		.78	.95		.40	.15	39.52
0:20	.60		.60	.18	.90		.3	.58	.85	.22		.05	.38
0:25		.86	.45	.08	.88			.55	.95		.37	38.94	.22
0:30	.38		.48	.10	.95	.2	.4	.45	39.03	.20		39.00	.13
0:35	.37	.95		.18	39.16		.7	.25	.08		.12	.00	.22
0:45			40.28	.15	.28	.3	.91	.32	.32	41.02	37.92	.03	.30
1:00	.51	41.22	.44	.15		.4	40.10	37.55	.58		.35	.85	.12
1:15	.53		.50	.15	.12		.22		.82		36.92	.80	38.50
1:30		.31	.62	.20		.6	.36		40.08	.45	.60	.70	.49
1:45	.52					40.0	.50	36.88	.30	.67		.78	.25
2:00		.90		.15	38.10	.55					35.65	.75	37.92
2:15		.71	39.83	.10		39.9	.00	.51		42.12	.10	.75	.50
2:30	.32						.70				34.70	.85	
2:45		.79	.42	.10		.4	.48	.10		.22	.42	.90	
3:00		.92	.18								.10	.87	
3:15			38.52			.3	.75	35.65		.50	33.82		
3:30							.80				.50		
3:45		.90				.2	.95	.48		.58	.10		
4:00							.90	.25		.62	32.82		
4:15		42.00								.60	.32		
4:30			37.95			39.0	.82	34.88		.72	.30		
4:45							.65			.80	31.85		
5:00		.60	.48			39.0	.40	.40		.90	.55		
5:15		.50					41.00			43.02			
5:30			36.40				40.70			42.90			
5:45		.28	35.10				.10			.75			
6:00		.30								.90			
6:15		43.16								.92			
6:30													
6:45													
7:00													
Max. increase of temperature	0.04	2.94	62.	0.12	0.4	1.1	0.82		1.3	3.64		0.62	
Time of maximum increase of temperature.	10 min.	7 hrs., 30 min.	1 hr., 30 min.	1 hr., 45 min.	1 hr.	2 hrs.	5 hrs., 45 min.		2 hrs.	5 hrs., 45 min.		3 hrs., 15 min.	

TABLE 4.—Records of 10 experiments in which the sections were through the pons.

Number of experiment.	20	21	22	23	24	25	26	27	28	29
Level of the section.				Anterior margin of pons.	Anterior margin of pons.	2 mm. from the crura cerebri.	3 mm. from the crura cerebri.	4 mm. from the crura cerebri.	Middle of the pons.	Low margin of the pons.
Time after the section. hrs. min.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.
0:00		38.53								
0:05	39.42									
0:10	.50		39.82	38.91						
0:15	.50	.68		39.02		39.00	38.80			
0:20	.58		.93	.55	38.95	.12	.70	38.90	39.03	39.30
0:25	.62	.50								
0:30	.73		.98							
0:35	.90	.70		40.11	40.15	.22	.55	40.20	.08	.41
0:45		.70	40.08	.22	.60	.40	.55	.51	.40	.75
1:00	.98		.40	.35	.95	.60	.52	.89	.80	.99
1:15	40.08		.42	.55	41.28	.71	.50	41.30	40.35	40.35
1:30	.15		.80	.70	.38	.85	.50	.75	.85	.70
1:45	.62		41.07	.86	.45	.98	.60	42.20	41.32	.92
2:00	.88		.30	.93	.55	40.10	.70	.20	.80	41.15
2:15	41.28		.45	41.10	.70	.22	.80	.65		.35
2:30	.30		.62	.20	.75	.38	.90	.80	42.85	.60
2:45	42.20	41.40	.85	.20	.90	.49	39.00	43.05	43.00	.80
3:00	.43		42.00	.50	42.10	.68	.10	.19	.40	.90
3:15	.68		.15	.55	.33	.88	.17	.40		42.20
3:30	.95		.30	.52	.58	41.10	.21		.46	.63
3:45	43.00		.49	.61	.80	.45	.28			43.02
4:00	.23		.62	.65	43.00	.48	.30			.08
4:15	.52		.80	.70	.10	.70	.38			.12
4:30	.70		.95	.80	.15	.90	.42			.28
4:45	.90		43.20	.90	.25	42.00	.50			.90
5:00			.35	42.08	.40	.02	.52			44.08
5:15	.66		.70	.35	.53	.08	.60			.12
5:30			.80	.45	.62	.12	.68			.16
5:45			44.16		.70		.77			.10
6:00					.78		.88			43.95
6:15										
6:30										
6:45										
7:00							40.10			
Max. increase of temperature	3.48	2.87	4.34	3.54	4.83	3.12	1.3	4.5	4.43	4.86
Time of max. increase of temperature.	4 hrs., 45 min.	2 hrs., 45 min.	5 hrs., 45 min.	5 hrs., 30 min.	6 hrs.	5 hrs., 30 min.	6 hrs.	3 hrs., 15 min.	3 hrs., 30 min.	5 hrs., 30 min.

of the occurrence of the maximum increase varied from 2 hours and 45 minutes to 7 hours, the average being about 5 hours. In 7 experiments the observations were continued from 5 to 7 hours, and in 3 they lasted for

from 2 hours and 45 minutes to 3 hours and 37 minutes. It is to be noted that in every experiment but 2—Nos. 20 and 29—the temperature was still rising when the experiments were concluded. The mean increase of temperature in this series was not only more marked, but steadier and more persistent than in the previous series.

4. *Experiments in which the sections were through*

TABLE 5.—Records of 6 experiments in which the sections were through the bulb.

Number of experiment.	30	32	32	33	34	35
Level of the section.	Close to the pons.	Close to the pons.	2 mm. from the pons.	2 mm. from the pons.	6 mm. from the pons.	3 mm. from the spinal cord.
Time after the section. hrs. min.	Deg.	Deg.	Deg.	Deg.	Deg.	Deg.
0:00						
0:05	38.84	39.78		39.66	39.25	
0:10		.64	39.59	.85	.22	38.42
0:15	58	.40	.62	41.10	38.87	.42
0:30				.60	.25	.32
0:45	.47	38.65	.95	41.00	.40	.30
1:00	.35	.05				
1:15	.08	37.48		.06	37.00	.49
1:30	37.80	36.80	40.12	.13	36.59	.52
1:45	.62	.10	.20	.29	.32	.40
2:00	.56	35.60	.18	.33	35.00	.30
2:15	.48	34.92	.18	.25	34.70	.31
2:30	.39	.50		.27		.32
2:45	.05	33.95	.21	.47		.22
3:00	36.83	.51	.12	.45		.20
3:15	.65	32.90	.18	.47	33.60	.11
3:30	.35		.29	.42	.88	.10
3:45	.08		.30	.41	.07	.10
4:00	.63		.30	.62	32.85	.05
4:15	.38		.33	.55	.65	37.99
4:30	.11		.33	.58	.40	38.05
4:45	34.89		.50	.83	.11	.05
5:00	.69		.56	.85	31.90	.08
5:15	.41		.58			
5:30	.17		.63	.81	.70	.10
5:45	33.85			.90	.47	.10
6:00	.74			42.10	.25	.10
6:15	.50			.25		.10
6:30	.23				.10	.11
7:00						
Maximum of increase of temperature.			0.68	2.59		
Time of max. increase of temperature after the section.			5 hrs. 30 min.	6 hrs. 30 min.		

the bulb.—In 7 experiments the sections were through the bulb at different levels. In 2 the temperature increased steadily for over 5 hours; in one the rise was 0.68 and in the other it was 2.59 (Table 5). In the remaining 5 there occurred a slow, steady fall, which in 3 cases continued until death, and in one slightly recovered after the lapse of 4 hours and 15 minutes. In the 2 experiments in which the rise occurred the sections were in each 2 mm. from the pons. Sections of the bulb must necessarily seriously affect the vasomotor center, and it is noteworthy, when it is remembered how rapid

TABLE 6.—Summary of main results of the sections of the caudate nuclei, crura cerebri, pons and bulb.

	Number of experiments.	Number in which a rise of temperature occurred.	Number in which a rise of temperature did not occur.	Average maximum rise of temperature. Degrees.	Average time after the section of the maximum rise of temp.
Sections of the caudate nuclei.	6	6	0	2.4	2 hr. 53 min.
Sections of the crura cerebri.	13	10	3	1.22	3 hr.
Sections of the pons . . .	10	10	0	3.73	5 hr.
Sections of the bulb . . .	7	2	5	1.64	6 hr.

is the fall of temperature caused by vasomotor palsy, that a rise of temperature ever occurs under such conditions. The most important results of these 4 series of experiments are summarized in Table 6.

A study of the results of these experiments shows that the effects caused by the sections of the caudate nuclei, crura cerebri, pons and bulb are in each case, as a whole, quite characteristic, and that thermo-accelerator centers certainly exist in both the caudate nuclei and the ponto-bulbar region. There can be no reasonable doubt that the cause of the rise of temperature when the caudate nuclei are injured is to be found essentially or solely in an excitation of a thermo-accelerator center, because similar irritation of parts in front of, above and beneath do not give rise to any notable increase of temperature, as should be expected if the nuclei merely represented a pathway of thermo-accelerator fibers which run to or from these parts. Starting then with the caudate nuclei as a point of origin of efferent thermo-accelerator fibers, it is evident that in order to directly or indirectly reach the thermogenic tissues they should be found running through the crura cerebri, pons and bulb into the spinal cord, and that their irritation at any point along this course might be followed by an increase of temperature providing that shock, vasomotor disturbances, etc., do not interfere; and, moreover, that irritation of this thermo-accelerator pathway should cause a less marked increase than when the thermo-accelerator center itself is irritated. A comparison of the figures which illustrate the main results of caudate and crura sections (Table 6) will show that in every one of the caudate experiments a rise of temperature occurred, while in only 10 of the 13 crural experiments was there an increase; and that the increase caused by caudate section was about double that following the section of the crura. The less marked and less rapid rise after crural section is logically to be attributed to one or more of three factors: 1, to the coincident irritation of hypothetical thermo-inhibitory fibers, which run from the cortical centers to the pons and parts below; 2, to the probably more marked vascular disturbances due to the section being nearer the cardiac and vasomotor centers, and 3, to the probable absence of thermo-accelerator cells from the crura. It is by no means likely that the irritation of thermo-inhibitory fibers has any important effect; while kymograph records show that the circulatory disturbances, although more marked as a rule the nearer the section to the bulbar centers, are not sufficient to explain the smaller rise caused by crural section. It seems therefore justifiable to assume that the increase of temperature caused by the section of the crura is due to the irritation of the thermo-accelerator fibers, and that the rise is less marked than when the caudate nuclei are irritated, chiefly because of the absence of thermo-accelerator cells in the former.

This view receives additional support in the results of the experiments in which the sections were made through the pons and upper part of the bulb. In pontine section, as in section of the caudate nuclei, an increase of temperature was not only invariably observed, but it was generally more marked and much more persistent than after sections of the latter, notwithstanding the nearness of the section to the vasomotor center, and the consequent vasomotor weakness and resulting rapid heat loss. The differences in the temperature effects caused by injuries of these two bodies can not apparently satisfactorily be explained except by admitting, as previously stated, the existence of a thermo-accelerator center in the pons and bulb, and that this center is even more powerful than that in the caudate nuclei. In fact, the center must be more potent than is indicated by the actual temperature records, because the rise was undoubtedly more or less

interfered with by the effects of the depression of the vasomotor center. That the center extends for some distance in the bulb is rendered probable by the fact that a marked rise of temperature may still be observed when the section is close to or at the junction of the pons and bulb. In several experiments in which the lobes cerebellum or the cerebellar peduncles were cut, no temperature changes were in any case noted which were at all comparable to those caused by pontine section.

Not only do the mean rises in temperature vary in degree in accordance with the region affected, but the temperature curves exhibit distinct characteristics, and such as to indicate the organ involved. Thus, after section of the caudate nuclei, the temperature tends to increase for approximately three hours on an average and then subside. In the sections of the crura cerebri the mean maximum rise is reached in about the same time, but the temperature curve rises only half as rapidly. In the pontine experiments the rise is not quite

Chart of temperature curves during first three hours after the sections. The broken line is the temperature curve of the caudate series; the unbroken line of the pontine series; and the dotted line of the crural series.

so rapid as in the caudate series, but there is a marked tendency to a steady increase for from 6 to 7 hours or more, or until fatal hyperpyrexia is established. These differences can be better appreciated by a glance at the accompanying chart in which are exhibited composite temperature curves of the caudate, crural and pontine experiments. The marked differences in the mean temperature curves of the caudate and pontine sections indicate that the thermo-accelerator centers in these structures differ at least in power—the latter being the stronger—if not in other important features. That they are functionally different has been shown conclusively in experiments in which I have injected powerful pyretics and antipyretics in large doses after the sections. For instance, after section of the caudate nuclei, and after section of the crura cerebri, the administration of cocain and morphin has no effect upon the temperature changes caused by the section: cocain neither increases the rise nor hinders the fall; nor does morphin hinder the rise or hasten the fall, unless given in such quantities as to seriously affect the circulation, etc. It seems

from this that the direct action of both cocain and morphin upon the heat mechanism is upon the thermo-accelerator center in the caudate nuclei. This subject has, however, so important a bearing upon febrile processes, and is of such scope, that a further consideration must be left for a special article.

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DISCUSSION.

DR. R. O. BEARD, Minneapolis—Referring to Dr. Reichert's conclusions I would suggest a possible source of error in his sections arising from the stimulation incident to section of afferent as well as efferent fibers related to the thermotaxic centers. The fillet from the ascending lateral tract of Gowers, which is believed to carry impressions of temperature to these centers, passing upward through the bulb and pons, might easily be involved in Dr. Reichert's pontine and bulbar sections; while lying in the lateral fillet, beyond the pons, it might escape in his sections of the crura. Section has always been a doubtful method of localizing centers.

PERNICIOUS ANEMIA—THE STATISTICS OF A SERIES OF FORTY CASES.*

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This paper is a report of a series of 40 cases of pernicious anemia which have occurred in the service of Dr. Osler in the Johns Hopkins Hospital. No attempt will be made to discuss in any detail the features of the disease or to give any extended notes of the histories of the patients. Cases in which there was any doubt as to the diagnosis have not been included. These 40 patients were among approximately 12,500 general medical admissions.

Incidence.—There were 32 males and 8 females, a rather unusual ratio for which no explanation can be given. The general admissions are about 5 males to 4 females. Large series show little difference in the number from each sex. As to age, the distribution was: 1 to 10 years, 1 case; 11 to 20, none; 21 to 30, 7 cases; 31 to 40, 6 cases; 41 to 50, 13 cases; 51 to 60, 7 cases; 61 to 70, 6 cases. It will be observed that four-fifths of the patients were over 30 years of age. The youngest was aged 10 and the oldest 66 years. In regard to race there were only 2 colored patients in the series, a proportion of 1 to 19, while the general ratio of admissions is about 1 colored to 7 white patients.

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