Can the Section of the Splanchnic Nerves or the Removal of the Suprarenal Glands or their Medulla Modify the Glycaemic Effect of Adrenaline?

By

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Some writers, who found an exaggerated insulin hypoglycaemia on sectioning the splanchnic nerves, expected to see at the same time a diminishing of the adrenaline hyperglycaemia thereby; they were able, they stated, to have the data corresponding to their expectation. Rather an opposite outcome however seems to be likely from an analogy with the paradoxical pupil dilation on adrenaline.

If insulin and adrenaline be given in a few days after dividing the splanchnic nerves—this is done mostly on opening the abdominal cavity—, and an exaggeration of the insulin hypoglycaemia and a diminution of the adrenaline hyperglycaemia be obtained, one must take into account altered nutritive conditions causable by that operation, although there are some writers noting a no-lessening influence upon the magnitude of adrenaline hyperglycaemia even after some days of starvation.

In fact the view that sectioning the splanchnic nerves diminishes the magnitude of adrenaline hyperglycaemia was sometimes refuted. Inasmuch as some recent writers however seconded that view, I attempted to re-investigate and somewhat extend this problem, as the heading of this paper shows.

Double Splanchnicotomy: How dividing the splanchnic nerves modify the hyperglycaemic effect of adrenaline was first tested much later in comparison to a similar question on the rôle of suprarenal glands, as shown below.

I know only one reference, that of Hirayama¹⁾ before Dresel and

1) Hirayama, Nippon Igakukwaishi, 1922, 6, 31; Tohoku J. of Exp. Med., 1926, 7, 346.

O m o n s k y,²⁾ noting the adrenaline hyperglycaemia in the doubly splanchnicotomized rabbits. For the purpose of excluding the fastening diabetes, H i r a y a m a cut the splanchnic nerves two weeks or more before the adrenaline experiment, but he did not attempt to compare the magnitude of adrenaline hyperglycaemia there with that when the splanchnic nerves are remaining untouched. The figures on his Table II tell us the non-influence of the splanchnicotomy upon the magnitude of adrenaline hyperglycaemia, if they be compared with those reported everywhere.

D r e s e l and O m o n s k y demonstrated, they believe, that the splanchnicotomy largely diminishes the glycaemic response against adrenaline. The figures of Rabbit 2 correspond to the description, but those of Rabbit 1 should be taken on the contrary as showing non-effectiveness of the denervation. (It may be added that the ascending limb of I in Fig. 2 gives the impression that it is not so steep as I in Fig. 1, but this is largely due to the fact that it ascended much steeper 0.5 hour after injection in Fig. 2 than in Fig. 1.) They wrote: *Mehrfach vorgenommene Untersuchungen zeigten entsprechende Kurvenbilder; we must then question which of the types. The denervation was done per laparotomy; how long an interval of time was allowed to elapse between the operation and the adrenaline injection is not found in the paper.*

H i s a m o t o³⁾ came in next year to affirm, he stated, the results of D r e s e l and O m o n s k y, only the descending limb of the hyperglycaemia being cut short in his. The results of D. & O. are not similar, but different, as above discussed, in two rabbits, which are all that they published; and the data given in the paper of H i s a m o t o (Table 1-8) should be taken as showing non-alteration of the glycaemic response by the double splanchnicotomy of rabbits against adrenaline. His conclusion might have come about from his having been confused by the statement of the previous investigators.

The data which correspond to the statement of H i s a m o t o were published a few years later by I n o u y e⁴⁾; 13-15 days after sectioning the splanchnic nerves per laparotomy, rabbits were administered with adrenaline when the body weight was somewhat smaller.

N a k a t s u k a⁵⁾ was the first who mentioned non-influence of the double splanchnicotomy upon the intensity of adrenaline hyperglycaemia, the average of the maxima in 4 normal rabbits being 0.261% and that in 5 doubly denervated 0.257%. At least two weeks after the denervation, the adrenaline injection was done, as usual in both Laboratories, this one and Professor I. F u j i i's. In another set of experiments, 0.168% and 0.160% were the corresponding figures, on one and the same dose of adrenaline, viz. 0.15 mgrm. adrenaline hydrochloride subcutaneously.

Recently B e r n a r d i n i⁷⁾ denervated the suprarenals in grey rabbits, and

2) D r e s e l and O m o n s k y, *Z. ges. exp. Med.*, 1927, **55**, 371.

3) H i s a m o t o, *Okayama Igakkai Zassi*, 1928, 2476.

4) I n o u y e, *Nagasaki Igakkai Zassi*, 1930, **8**, 161.

5) N a k a t s u k a, *Mitt. med. Ak. Kioto*, 1932, **6**, 1351.

6) I d., *Ibid.*, 1427.

7) B e r n a r d i n i, *Rev. Pat. Sper.*, 1935, N.S. **3**, 15.

gave adrenaline intravenously in a dose of 0.1 mg, which resulted in a hyperglycaemia, but of much smaller magnitude. He took the average, initial as 0.100%, 0.190% 5 minutes after adrenaline, 0.175% 15 minutes, 0.161% 30 minutes and 0.143% 60 minutes for 8 normal rabbits, and 0.140%, 0.145%, 0.129% and 0.113% respectively for 2 rabbits after the unilateral denervation and the bilateral denervation together. It seems to me rather reasonable to regard the figures each for the unilaterally operated and for the doubly operated; the former is then 0.179%, 0.172%, 0.158% and 0.130% respectively, and the latter 0.125%, 0.134%, 0.118% and 0.106%. Therefore the unilateral denervation had no influence upon the adrenaline hyperglycaemia at all, but the bilateral acts to diminish to some extent the intensity of adrenaline hyperglycaemia. But it must be remembered that adrenaline was injected on that day of the last denervation or at length 4 days (or 5 days), probably a misprint in Experiment V (on p. 19), later. (Regrettably I was not able to have the paper where Bernardini described with a co-worker the method of denervation, since our Library lacks that volume.)

In this year Mori⁸⁾ reported a similar yield with Nakatsuka; 6-7 days were allowed to elapse after splanchnicotomy per laparotomy before injecting subcutaneously 0.15 mgrm. per kilo in rabbits.

Double Suprarenalectomy: Much earlier than that an endeavour was made to inject adrenaline into animals after double removal of the suprarenal capsules.

In dogs, Bierry and Malloizel⁹⁾ removed the suprarenals by the lumbar route, and a few hours later adrenaline was injected intraperitoneally; the hyperglycaemia occurred on a much reduced scale, compared with the normal animals.

Non-effectiveness of suprarenalectomy re adrenaline hyperglycaemia was reported by Kisch,¹⁰⁾ on injecting adrenaline in a subcutaneous dose of 0.5 mgrm. into rabbits long surviving double suprarenalectomy.

Shiozawa¹¹⁾ injected adrenaline in a dose of 0.1 mgrm. per 100 grms. in rats subcutaneously 2-7 days after double suprarenalectomy per laparotomy. The results show on the whole non-effectiveness of the suprarenalectomy upon the adrenaline hyperglycaemia.

Similar conclusion was reached by Mima, who left a small portion of the right suprarenal gland from excising in rabbits.¹²⁾

In enfeebled suprarenalectomized cats, Britton and Silvette¹³⁾ detected a small increase of the blood sugar content on applying adrenaline intraperitoneally.

Viale removed the suprarenals in dogs under chloral narcosis, through the lumbar route and they survived for 48-100 hours. On 1 mgrm. adrenaline the

8) Mori, Kumamoto Igakkai Zassi, 1937, **13**, 557.

9) Bierry and Malloizel, C. r. Soc. Biol., 1908, **65**, 232.

10) Kisch, Kl. W., 1924, 3. year, 1662.

11) Shiozawa, Zikken Igaku Zassi, 1926, **10**, 128.

12) Mima, Nippon Naibunpigaku Zassi, 1927-28, **3**, 796.

13) Britton and Silvette, Am. J. of Physiol., 1931 (-32), **99**, 15.

blood sugar content did not increase.¹⁴⁾ Similar experience was reported by Carrasco-Formiguera; adrenaline was intravenously administered 22 hours after the last decapsulation which was conducted 10–15 days after the first.¹⁵⁾ (Some words may be written of the report of Kahn and Starkenstein.¹⁶⁾ They wrote in the text: Versuch VI zeigt die Wirkung subkutan eingeführten Adrenalins. Die Harnmenge ist vermehrt, die Glykosurie ist hochgradig, die Adrenalinosis wird ohne jede Störung ertragen. The protocol given on p. 185 shows rather contradictory figures re the amount of urine and sugar there.)

Lastly, a short account may be reported on the glycogen storage, mainly in rabbits, after splanchnicotomy and suprarenalectomy.

Double splanchnicotomy: A distinct decrease, such as by 40%, was noted by Morita in rabbits 6–24 days after the operation, when the body weight recovered nearly completely.¹⁷⁾ When a sufficient interval of time, such as a hundred days were allowed to elapse between the denervation and the glycogen assay, the liver and muscle glycogen of the operated rabbits were found only a little inferior to the normal values.¹⁸⁾ Nakatsuka's data¹⁹⁾ are similar to Morita, probably the rabbits were killed two weeks after the operation or later, as in Professor Fujii's laboratory, though actual data are not recorded there. The same question was attacked by Simizu on rabbits,²⁰⁾ Best's histological method being relied on. 58 days were found as sufficient to see a complete recovery of glycogen storage in the liver. A statement that 30 days interval is sufficient to see a complete recovery is repeated in his conclusion too, but the data given in the text tell clearly its insufficiency. It is scarcely necessary to note what significance can be attached to such a histological examination for estimating the glycogen content.

Sunaba²¹⁾ estimated the glycogen content of liver in rabbits, 6 hours, 2 days, 5–7 days and two weeks after double splanchnicotomy; about twenty to thirty per cent reduction was noted there everywhere. Otherwise expressed, two weeks interval is not sufficient to see a complete recovery.

Double suprarenalectomy: There is no room to cite the results of the animals which did not survive long enough double suprarenalectomy.

The liver glycogen content of a rabbit surviving the double suprarenalectomy over 8 months of Kahn and Starkenstein¹⁶⁾ (p. 189) was 6.1%. The same figure was obtained by Stewart and Rogoff²²⁾ in a rabbit surviving the last decapsulation over one month. The Cleveland physiologists who carried out a great number of experiments of various kinds upon the rabbits indefinitely sur-

14) Viale, Kl. W., 1933, 12. year, 467.

15) Carrasco-Formiguera, Ann. de Physiol., 1933, 9, 905.

16) Kahn and Starkenstein, Pflügers Arch., 1911, 139, 185 ff.

17) Morita, Tohoku J. of Exp. Med., 1921, 2, 423 & 436.

18) Mikami, Jap. J. Med. Sci., Pharm., 1926, 1, 125–129.

19) Nakatsuka, Mitt. med. Akad. Kioto, 1932, 6, 1427.

20) Simizu, Kyoto Igaku Zasshi, 1936, 33, 169.

21) Sunaba, Mitt. med. Akad. Kioto, 1936, 16, 1027.

22) Stewart and Rogoff, Am. J. of Physiol., 1918, 46, 90.

viving the suprarenalectomy, estimated usually the glycogen storage after ending the experiment and found no noticeable variations there from the animals without removing the glands. They are wholly correct in emphasizing the indispensability of estimating the glycogen content for denying the hyperglycaemic ability of an agent or manipulation under question.

The glycogen storage of 4 rats surviving the double suprarenalectomy 13-24 days, was found approximately the same as that in normal rats. It was only in trace in a rat, which was losing weight and killed 11 days after the operation. (The data re the glycogen storage in the cats, deprived of one suprarenal gland and the nerves of the other, are identical with the rabbits, doubly suprarenalectomized.²³⁾ The same conclusion was reached by subsequent workers in cats. The latter excised the suprarenal medulla of one gland besides the splanchnicotomy on that side and removal of the fellow gland.²³⁾

Catan, Houssay and Mazzocco²⁴⁾ measured a rather greater amount of the liver glycogen in two rabbits killed 89 and 35 days, after the double suprarenalectomy 2.14% against 1.40% of the normal being the figures. The liver glycogen was measured as 1.275% in 21 rabbits, 7-28 days after the double suprarenalectomy, against 1.519% of the controls.

Kisch¹⁰⁾ noted parenthetically a rich storage of the liver glycogen in a rabbit surviving double suprarenalectomy for some months.

Working on rats, Shiozawa¹¹⁾ estimated non-alteration of the liver glycogen storage by double suprarenalectomy. The absolute amount of glycogen of Shiozawa was far smaller than that of Stewart and Rogoff.

Artundo²⁵⁾ noted a diminution of liver glycogen in rats 3 and 8 days after the double decapsulation, and a considerably large amount (3.68%) in 14 days after the decapsulation, and the normal value 32 days after it (1.66%).

It may be noted further that there are papers reporting of non-influence of starvation extending for a week upon the magnitude of adrenaline hyperglycaemia, otherwise expressed, no direct relation between the latter and the glycogen storage of animals.²⁶⁾ Whether such a view can be taken as holding true is still questionable, inasmuch as we have, for instance, another recent paper¹⁹⁾ telling of a diminishing of the maximum increase of the blood sugar due to adrenaline in the rabbits starving for 6 days, or even for 2 days: this paper was probably overlooked by the latter investigator.²⁶⁾

METHODS.

Rabbits of good nutrition, male or non-pregnant female, were experimented on. They were fed on tofukara, dry straw and carrot of 30-40 grms. per diem. Some few days prior to the adrenaline experi-

23) Britton, Geiling and Calvey, *Ibid.*, 1928, **84**, 154.

24) Catan, Houssay and Mazzocco, *C. r. Soc. Biol.*, 1921, **84**, 164.

25) Artundo, *C. r. Soc. Biol.*, 1927, **97**, 411.

26) Yoshio, *J. of Biochem.*, 1937, **26**, 49 (Some previous references there).

ment, the ears were denervated for taking blood samples without pain and with ease. On the day before the adrenaline administration, the rabbit was brought into my laboratory room at just 2 o'clock in the afternoon, and thereafter no food was given.

The splanchnic nerves were bilaterally cut out about 7 cms. long per laparotomiam. Demedullation of the suprarenal glands was done through the lumbar route, as usual in this Laboratory. The suprarenal glands were excised through the lumbar way, about three weeks being allowed to elapse from removal of the right side to that of the left. No narcosis was resorted to at any operation.

The adrenaline administration was done while the animals looked wholly healthy, judging from their body weight, appetite and behaviour.

Blood samples were taken from the denervated ear vein, and estimated for sugar by the micro-method of Fujita and Iwatake,²⁷⁾ which has some invaluable merits not to be found in that of Hagedorn and Jensen, in that cadmium is used for preparing protein-free blood filtrate instead of zinc, whereby glutathione, ergothioneine, and uric acid are completely removed off, etc.

The rate of heart beat and respiration, the rectal and room temperature were noted from time to time. At the adrenaline experiment the animal was not fastened, and no narcosis was used. Adrenaline chlorid (1:1000) of Sankyo Co. was subcutaneously injected in a few seconds in a uniform dosis of 0.2 mgrm. per kilo. On this dose usually some symptoms became manifest: slight dyspnoea, mydriasis, widening of the palpebral fissurae, bradycardia, then tachycardia, etc.

DATA.

Normal rabbits.

As the control, 6 normal rabbits, 3 male and 3 female, were injected with adrenaline, in subcutaneous dose of 0.2 mgrm. per kilo, as above mentioned. The data are given in Table I.

On adrenaline the blood sugar concentration increased from 0.097 grm. % (0.086-0.103) to 0.269 grm. % (0.235-0.300), which was measured 1-2 hours after the injection, so about 180% increase was thus established.

27) Fujita and Iwatake, *Biochem. Ztschr.*, 1931, **242**, 43; also in Fujita, *Manometric methods and their application* (Jap.), 1932 Iwanami, Tokyo, 95 ff.

TABLE

Effect of adrenaline injection upon the blood sugar

No.	Sex	Suprarenalectomy				Date of experiment and days after the last operation 1936	Body weight (kilos)	Blood sugar content (gram. per variation (in Italic))					
		R		L				before injection (min.)			after		
		Date	Body weight & weight of gland (kilos & mgrms.)	Date	Body weight & weight of gland (kilos & mgrms.)								
								20	10	30	60	90	120
C 3	♂	29. XI. 1934	1.45 113	15. IV. 1935	1.87 247	25. I. 285	1.89	0.100 98	0.102 100	0.207 203	0.254 251	0.258 253	0.278 272
C 5	♀	3. X. 1934	1.80 120	15. XI. 1934	1.90 160	25. I. 436	2.53	0.086 95	0.090 100	0.142 158	0.188 209	0.259 287	0.241 267
C 12	♂	3. X. 1934	1.75 132	15. IV. 1935	1.90 325	5. III. 325	1.92	0.100 93	0.107 100	0.230 215	0.255 238	0.257 240	0.283 266
C 15	♂	21. V. 1935	1.77 128	18. VI. 1935	1.75 155	5. III. 261	2.25	0.113 104	0.109 100	0.239 219	0.301 276	0.317 291	0.293 268
H 6	♀	6. VI. 1935	1.80 107	29. VI. 1935	1.59 180	10. II. 255	1.93	0.090 95	0.094 100	0.197 209	0.235 253	0.271 287	0.252 267
H 9	♂	27. VI. 1935	1.80 107	16. VII. 1935	1.65 132	12. V. 306	2.26	0.108 98	0.110 100	0.182 166	0.245 223	0.260 237	0.290 264
H 16	♂	28. IX. 1935	1.70 80	17. X. 1935	1.60 130	12. V. 208	2.44	0.096 107	0.090 100	0.171 190	0.227 252	0.235 260	0.254 282
Mean			1.72		1.75		2.17	0.099 99	0.100 100	0.194 194	0.244 244	0.265 265	0.270 269

The hyperglycaemic period covered at least 4 hours, seldom over 6 hours (No. C 19).

After elapsing of the hyperglycaemic phase, the blood sugar concentration had a tendency to diminish under the initial value; it was remarkable in No. C 72.

If the average figure be composed, the adrenaline hyperglycaemia reaches its maximum, 0.265 gram. % or an increase by 270 %, 2 hours after the injection, and the hyperglycaemic period extends for 5 hours. And the great hyperglycaemia period over 0.25 gram. % makes appearance one hour after the injection and lasts for 1.5 hours.

Doubly suprarenalectomized rabbits.

7 rabbits, 5 male and 2 female, were doubly suprarenalectomized, and 208-436 days later adrenaline injection was tried (Table II).

The initial blood sugar concentration was as a matter of course wholly normal (0.100 gram. %—from 0.09 gram. % to 0.11 gram. %).

II.

content in the doubly suprarenalectomized rabbits.

100 c.c. blood) and rate of the initial as 100					Duration of hyperglycaemia (hours)	Frequency of heart beat (per min.)		Frequency of respiration (per min.)		Beofore temperature (°C.)		Room temperature (°C.)
injection (min.)						before injection	after injection	before injection	after injection	before injection	after injection	
150	180	240	300	360								
0.268 263	0.266 262	0.195 191	0.144 142	0.105 103	6	270	240-324	102	84-120	38.9	38.0-38.8	12-14
0.239 265	0.225 250	0.167 185	0.102 113	0.084 93	5	222	216-288	78	66-108	38.3	38.3-39.3	12-15
0.273 255	0.257 241	0.165 154	0.088 82	0.090 84	4	252	276-312	48	42-60	38.3	38.2-38.6	13-16
0.271 249	0.250 230	0.130 119	0.111 102	0.095 87	5	264	240-324	210	60-228	38.4	38.4-38.9	13-16
0.246 261	0.240 254	0.167 177	0.099 105	0.087 92	5	240	264-312	72	60-120	38.0	38.0-38.3	13-16
0.302 275	0.300 272	0.221 201	0.137 125	0.086 78	5	192	180-300	66	48-96	38.4	38.5-39.1	16-22
0.243 270	0.225 250	0.158 176	0.086 96	0.088 98	4	180	168-240	36	36-78	38.6	38.1-38.8	16-22
0.263 262	0.252 251	0.172 172	0.109 109	0.091 0.091								

0.2 mgrm. per kilo adrenaline hydrochloride, subcutaneously applied, occasioned a hyperglycaemia, the highest of which was 0.280 grm. % (0.254 grm. %-0.319 grm. %) and the duration of which was 5 hours (4-6 hours). The hyperglycaemic phase was followed by development of hypoglycaemia of small degree.

The average figures are quite identical with those in normal rabbits. The maximum was 0.270 grm. %, the hyperglycaemic period lasted for 5 hours, the great hyperglycaemia period became manifest from 1 hour after the injection to 3 hours after it. Rather longer than in normal rabbits. The body weight of both series of experiments was almost the same.

Doubly splanchnicotomized rabbits.

7 rabbits, 3 male and 4 female, were excised of the splanchnic nerves in 7-10 cms. 70-320 days afterwards adrenaline hydrochloride was hypodermically given in the dose above stated (Table III).

TABLE

Effect of adrenaline injection upon the blood sugar

No.	Sex	Splanchnicotomy		Date of experiment & days after operation 1936	Body weight (kilos)	Blood sugar content (gram. per variations (in Italic), the					
		Date	Body weight (kilos)			before injection		after			
						20	10	30	60	90	120
C 26	♀	30. VII. 1935	1.58	6. VI. 320	2.41	0.107 102	0.105 100	0.212 202	0.242 231	0.260 248	0.262 250
C 60	♂	6. XII. 1935	1.68	6. VI. 183	1.87	0.108 104	0.104 100	0.160 154	0.220 211	0.226 217	0.233 223
C 67	♂	18. XII. 1935	1.72	26. II. 70	1.95	0.096 102	0.094 100	0.196 208	0.249 265	0.254 270	0.274 291
C 80	♀	18. XII. 1935	1.80	26. II. 70	2.13	0.094 99	0.095 100	0.175 185	0.222 235	0.242 254	0.260 274
C 88	♀	23. I. 1936	1.92	24. VI. 184	2.25	0.108 100	0.108 100	0.193 179	0.235 218	0.258 240	0.258 240
C 89	♀	23. I. 1936	1.70	24. VI. 184	2.01	0.108 97	0.111 100	0.152 137	0.211 190	0.243 219	0.243 219
C 94	♂	23. I. 1936	1.82	13. VI. 173	2.17	0.095 98	0.097 100	0.190 198	0.243 250	0.282 290	0.305 315
		Mean	1.74		2.11	0.102 100	0.102 100	0.182 180	0.231 230	0.252 248	0.262 259

The maximum sugar content of blood was then 0.280 gram. % (0.258 gram. % to 0.305 gram. %) or it exceeded the initial by 180% (140%–215%). The highest level appears commonly 2 hours after the injection, and the hyperglycaemic spell continued for 5–6 hours or more; that is, the highest level was practically identical with the rabbits normal or doubly suprarenalectomized, but the hyperglycaemic phase lasted somewhat longer. The hyperglycaemia over 0.25 gram. % continued only for 1.5 hours.

If the experiments were extended longer, there would be perceived a development of hypoglycaemic period.

Doubly medulli-suprarenalectomized rabbits.

7 rabbits, 6 male and 1 female, were removed of the suprarenal medulla, and 246 to 420 days later adrenaline was given in the above mentioned dose and manner (Table IV).

The initial blood sugar content was wholly the same as the normal rabbits. That bilateral interference of the splanchnic nerves, the suprarenal glands or the suprarenal medulla does not alter the blood sugar

III.

content in the doubly splanchnicotomized rabbits.

100 c.c. blood) and rate of initial, as 100					Duration of hyperglycaemia (hours)	Frequency of heart beat (per min.)		Frequency of respiration (per min.)		Body temperature (°C)		Room temperature (°C.)
150	180	240	300	360		before injection	after injection	before injection	after injection	before injection	after injection	
0.275	0.282	0.232	0.199	0.124	6	168	90-216	72	42-120	38.0	37.8-38.6	17-21
262	270	222	189	118								
0.237	0.255	0.247	0.233	0.210	6	216	240-312	96	84-144	38.0	37.1-38.1	17-21
228	245	237	223	202								
0.252	0.212	0.176	0.112	0.092	5	252	204-300	72	48-108	38.5	38.5-38.9	12-17
268	225	187	119	98								
0.230	0.203	0.124	0.103	0.079	5	300	240-300	60	42-72	38.4	38.6-38.9	12-17
242	214	132	109	83								
0.242	0.238	0.155	0.115	0.106	5	192	96-228	84	54-90	38.1	38.2-39.0	20-23
225	221	144	107	98								
0.270	0.272	0.291	0.252	0.177	6	216	120-228	60	48-78	38.2	37.7-38.5	20-23
243	245	262	227	159								
0.280	0.270	0.235	0.168	0.109	6	216	216-264	120	84-156	38.4	38.4-38.7	18-21
290	278	242	174	112								
0.255	0.247	0.208	0.169	0.128								
251	242	203	164	124								

concentration in the quiet state of animals, without disturbed carbohydrate metabolism, is a well established fact. It is quite superfluous nowadays to repeat such a statement.

Adrenaline injection brought about in these medulli-suprarenalectomized rabbits a hyperglycaemia of quite the same magnitude and duration, 0.271 grm. % (0.233 grm. %–0.294 grm. %) or an increase of 173% (133% to 167%) and 5 hours (4–6 hours) being estimated. The hyperglycaemia above 0.25 grm. % lasted in the average one hour. Hypoglycaemic phase was detected in almost all cases.

We are thus qualified to conclude non-effectiveness of double splanchnicotomy, suprarenalectomy or medulli-suprarenalectomy upon the magnitude and the course of hyperglycaemia due to adrenaline; in the present instance, investigations were carried out a considerable length of time after the operation. And the present outcome coincides with the results of previous investigators who were carefully observant as to the nutritious state of the animals. If one carries out the experiment when animals cannot be considered normal, excepting the necessary results occasioned by loss of the splanchnic nerves, suprarenals or suprarenal medulla itself; one will see a small hyperglycaemia or

TABLE

Effect of adrenaline injection upon the blood sugar

No.	Sex	Demedullation				Date of experiment and days after last operation, 1936	Body weight (kilos)	Blood sugar content (grm. per variations, the					
		R		L				before injection (min.)			after		
		Date of demedullation	Body weight (kilos)	Date of demedullation	Body weight (kilos)			20	10	30	60	90	120
C 28	♀	11. XII. 1934	1.69	15. III. 1935	1.95	8. V. 420	2.18	0.093 102	0.091 100	0.176 194	0.235 258	0.278 305	0.272 300
C 29	♂	6. V. 1935	1.58	8. VII. 1935	1.65	12. III. 249	2.07	0.113 103	0.110 100	0.209 190	0.264 240	0.285 259	0.294 267
C 32	♂	13. V. 1935	1.55	8. VII. 1935	1.57	12. III. 249	1.90	0.096 102	0.094 100	0.186 197	0.230 244	0.254 269	0.261 277
H 3	♂	14. VI. 1935	1.75	9. VII. 1935	1.65	11. III. 246	2.20	0.118 106	0.111 100	0.214 193	0.225 202	0.283 255	0.287 258
H 4	♂	13. VI. 1935	1.78	2. VII. 1935	1.74	11. III. 253	2.05	0.085 102	0.083 100	0.186 224	0.245 295	0.267 323	0.292 352
H 5	♂	13. VI. 1935	1.70	2. VII. 1935	1.75	8. V. 311	2.01	0.119 104	0.114 100	0.207 182	0.252 222	0.245 215	0.236 207
H 18	♂	21. IX. 1935	2.13	14. X. 1935	1.99	17. VI. 247	2.17	0.109 109	0.100 100	0.180 180	0.201 201	0.233 233	0.204 204
Mean			1.73		1.76		2.08	0.105 104	0.100 100	0.194 194	0.236 237	0.263 265	0.264 266

none, as given in the inductory. Some writers failed to draw a proper conclusion from their correct data.

The findings, that double splanchnectomy, suprarenalectomy and medulli-suprarenalectomy do not act to alter the hyperglycaemic ability of adrenaline, while they intensify the hypoglycaemic action of insulin,²⁸⁾ can be at least chiefly explainable by the facts that the former has no accelerating action upon the epinephrine output rate,²⁹⁾ contrary to the latter.³⁰⁾

SUMMARY.

Adrenaline hydrochloride was given in the dose of 0.2 mgrm. per kilo of body weight into rabbits, long surviving bilaterally suprarenalectomized, medulli-suprarenalectomized or splanchnictomized and

28) Ohmi, Tohoku J. of Exp. Med., 1933, 21, 211.

29) Sugawara, Saito and Nemoto, Ibid., 1927, 9, 149.

30) Yen, Aomura and Inaba, Ibid., 1933, 21, 542.

IV.

content in the medulli-suprarenalectomized rabbits.

100 c.c. blood) and rate of initial as 100					Duration of hyperglycaemia (hours)	Frequency of heart beat (per min.)		Frequency of respiration (per min.)		Body temperature (°C.)		Room temperature (°C.)
injection (min.)						before injection	after injection	before injection	after injection	before injection	after injection	
150	180	240	300	360								
0.223 245	0.170 187	0.114 125	0.078 86	0.078 86	4	192	96-240	102	60-114	38.5	38.6-39.2	14-18
0.285 259	0.254 231	0.174 158	0.108 98	0.087 79	4	240	216-300	54	36-72	38.1	37.5-38.2	13-20
0.244 259	0.223 236	0.113 120	0.106 112	0.073 77	5	240	180-300	72	78-120	38.2	38.2-38.7	14-20
0.283 255	0.287 258	0.255 229	0.188 169	0.126 113	6	264	240-312	72	60-120	38.5	38.4-38.6	11-18
0.281 340	0.260 314	0.183 220	0.071 85	0.068 82	4	204	240-324	60	54-78	38.3	38.7-39.0	12-18
0.229 200	0.188 165	0.158 139	0.106 93	0.093 82	4	216	216-300	78	60-90	38.8	38.3-38.8	14-18
0.189 189	0.173 173	0.114 114	0.090 90	0.082 82	4	216	180-240	72	48-108	38.6	37.7-38.6	21-25
0.248 249	0.222 223	0.159 158	0.107 105	0.087 86								

living in good nutritive conditions.

In respect to the magnitude and course of hyperglycaemia, these animals did not differ at all from the normal control animals.

On thoroughly reviewing the previous reports, the present writer can point out why some of them arrived at a different conclusion. Some of the latter injected adrenaline when the animals were suffering from the operation itself, not from the loss of the nerves or glands, or when the animals were already moribund, and another made an erroneous conclusion in spite of correct data obtained.