How Atropine Interferes With the Epinephrine Secretion Causable by Morphine or Insulin?

By

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In the previous paper we have shown that atropine is capable of causing invariably a small acceleration in the epinephrine output rate in dogs, seldom preceded by a temporary depression. The present paper deals with the epinephrine discharge rate in the dog, when it is poisoned with morphine or insulin in addition to atropine. Both drugs act to accelerate the epinephrine discharge in a marked way through the central mechanism.

There are some papers dealing with similar question re atropine. Most of them dealt with the effect of stimulating the peripheral cut end of the splanchnic nerve.

Biedl collected the blood coming from the suprarenal veins into a pouch prepared with the inferior cava vein in curarized dogs. Stimulating the splanchnic nerve the pressoric power of the blood seldom increased. When atropine was given and the splanchnic stimulated, the active substance was also found, but Biedl was not able to speak of whether the amount was the same or not.

By giving atropine intravenously in doses of 0.003-0.01 grm. per kilo, Schwarz was able to nullify the pressoric effect of stimulating the suprarenal gland in the dog under chloroform. Within two hours the effect of atropine died away.

2) Sato and Ohmi, Ibid., 1933, 21, 411.
3) Yen, Aomura and Inaba, Ibid., 542.
4) Sato, Kanowoka and Ohmi, Ibid., 1933, 22, 7; Saizyo, Ibid., 1936, 30, 33.
5) Biedl, Pflügers Arch., 1897, 67, 480 f.
On giving atropine in doses of 5, 10 or 15 mgrms., Tscheboksaroff observed no inhibition of epinephrine secretion due to the splanchnic stimulation from a suprarenal gland in the dog under curara and some morphine, peptone being also given as an anticoagulant. Probably it is done only with difficulties to assume an accelerating influence of atropine from the figures given there.

Feldberg with his co-workers were not able to see on giving a small dose of atropine a very convincing reduction of the pressor effect, caused in an eviscerated spinal cat by splanchnic stimulation. Even after almost completely abolishing the effect of stimulation by large doses of nicotine, an intravenous injection of atropine is capable of only slightly but definitely reducing the remaining effect.

Lewis and Luduena saw abolishing of epinephrine discharge due to splanchnic stimulation by 5 mgrms. atropine sulphate in the suprarenal-jugular-anastomosis experiments on dogs under chloralose. This inhibitory effect lasts 15–20 minutes, and 2–3 mgrms. per kilo can only reduce the effect of splanchnic stimulation. They tried to explain this outcome without applying the view that the parasympathetic nerve controls the epinephrine discharge.

It may be added here, that atropine does not act to lessen the reduction of the epinephrine content in the suprarenal gland due to the splanchnic stimulation.

In the suprarenal-jugular-anastomosis experiments above cited, Lewis and Luduena observed no modification by atropine of the epinephrine discharge by nicotine, candicine chloride and tetramethylammonia, contrary to the case of splanchnic stimulation.

Katz and Katz, who experimented on cats eviscerated, and with restricted circulation, epinephrine output being estimated by the arterial blood pressure and nictitating membrane, saw a diminishing influence of atropine (2 mgrms. i.v.) upon epinephrine discharge caused by K and Ca, which lasts about 5 minutes.

In respect to the epinephrine content in the suprarenal gland Takahashi noted no influence of atropine (0.028–0.1 mgram per kilo) upon its reduction due to bleeding in rabbits. Though this was not seconded by Y. Wada, a recent investigator succeeded in duplicating the finding of Takahashi.

7) Tscheboksaroff, Pflügers Arch., 1911, 137, 94–95.
8) Feldberg, Minz and Tsudzimura, J. of Physiol., 1934, 81, 299.
All the materials, methods and procedures, applied in the present investigations are those described in our previous paper.\textsuperscript{1}

**DATA.**

In two dogs morphine was tried in addition to atropine, and in a dog, insulin. Both drugs act to accelerate the epinephrine output through the central nervous system; splanchnicotomy nullifies their accelerating effect.\textsuperscript{4}

**Morphine experiment.**

*Dog 1.* Male, 12.3 kilos.

Two hours after the left lumbar operation the epinephrine output rate was 0.00001 mgm. per minute per kilo (the blood flow through the gland 0.2 c.c. per minute, per kilo, 0.00005 mgm. epinephrine per c.c.). The blood sugar 0.109%. The heart rate 120 per minute, respiration 21 per minute, and the body temperature 38.3°C.

Atropine sulphate was then injected into the right saphena vein in a dose of 5 mgm. per kilo body weight, as in the foregoing experiment, 5 minutes later the blood sugar was found having increased to 0.133%, and ten minutes after atropine injection the epinephrine output rate was found as 0.0001 mgm. per minute per kilo. While the blood flow through the gland largely reduced, the blood contained much epinephrine (0.04 c.c. and 0.0024 mgm.). About ten times acceleration was thus noted on atropine in respect to the epinephrine output rate.

About a half hour after atropine injection, morphine hydrochloride was injected into the saphena vein in a dose of 4 mgm. per kilo. At this time, the atropine poisoning symptoms, viz. dilated pupils, increased heart rate, etc., were existing, of course.

10, 25, 60, 85 and 130 minutes after the morphine injection the output rate of epinephrine was measured as 0.00028, 0.00015, 0.00009, 0.0001 and 0.000016 mgm. per minute per kilo.

The blood flow was 0.06, 0.1, 0.1, 0.16 and 0.08 c.c. per minute per kilo. The rate at 85 and 130 minutes was measured somewhat smaller and possibly inexact, because the blood was very ready to clot. The epinephrine concentration in these samples was 0.005, 0.0015, 0.0009, 0.0006 and 0.0002 mgm. per c.c.
### TABLE.

**The epinephrine output, blood sugar content, etc. after injection of morphine or insulin in atropinized dogs.**

<table>
<thead>
<tr>
<th>No. of Dog, date</th>
<th>Time (hour: minute)</th>
<th>Suprarenal vein blood</th>
<th>Epinephrine (mgram.)</th>
<th>Blood sugar content (%)</th>
<th>Heart beat per minute</th>
<th>Respiration per minute</th>
<th>Body temperature C.</th>
<th>Room temperature C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>30. VII. 1934. 12.3 kilos &amp;</td>
<td>(1) VI. 1934. D, L, D, dorsal spinal roots severed under ether-chloroform anaesthesia. 15.0 kilos Both hind limbs normal. 10:00—10:45 a.m. Left lumbar route, right saphena vein and left lumbar artery preparation; cannuulas inserted. 12:50</td>
<td>About 10 c.c. of arterial blood taken.</td>
<td></td>
<td></td>
<td>0.109</td>
<td>120</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>12:53</td>
<td>I</td>
<td>60</td>
<td>2.3</td>
<td>2.3</td>
<td>0.19</td>
<td>0.00005</td>
<td>0.00012</td>
</tr>
<tr>
<td></td>
<td>12:54</td>
<td>II</td>
<td>30</td>
<td>1.2</td>
<td>2.4</td>
<td>2.0</td>
<td>0.00006</td>
<td>0.00012</td>
</tr>
<tr>
<td></td>
<td>1:00</td>
<td>About 5 c.c. arterial blood taken.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:04</td>
<td>3.1 c.c. of 2% atropine-sulphate-Tyrols injected intravenously during 33 seconds, i.e. about 5 mgrams. per kilo.</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>1:09</td>
<td>7.2 c.c. blood taken from artery.</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1:15</td>
<td>III</td>
<td>120</td>
<td>1.2</td>
<td>2.6</td>
<td>0.05</td>
<td>0.0024</td>
<td>0.00128</td>
</tr>
<tr>
<td></td>
<td>1:17</td>
<td>IV</td>
<td>60</td>
<td>0.4</td>
<td>2.4</td>
<td>0.05</td>
<td>0.00024</td>
<td>0.00128</td>
</tr>
<tr>
<td></td>
<td>1:38—1:40</td>
<td>4.9 c.c. of 1% morphine-hydrochloride injected intravenously in about 2 minutes, i.e. 4 mgrams. per kilo.</td>
<td></td>
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<tr>
<td></td>
<td>1:42</td>
<td>2 c.c. arterial blood taken.</td>
<td></td>
<td></td>
<td></td>
<td>0.133</td>
<td>168</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>1:47</td>
<td>V</td>
<td>130</td>
<td>1.5</td>
<td>7.0</td>
<td>0.06</td>
<td>0.0035</td>
<td>0.00028</td>
</tr>
<tr>
<td></td>
<td>1:49</td>
<td>VI</td>
<td>60</td>
<td>0.7</td>
<td>7.0</td>
<td>0.06</td>
<td>0.0035</td>
<td>0.00028</td>
</tr>
<tr>
<td></td>
<td>2:05</td>
<td>VII</td>
<td>60</td>
<td>1.1</td>
<td>1.1</td>
<td>0.09</td>
<td>0.0015</td>
<td>0.00019</td>
</tr>
<tr>
<td></td>
<td>2:06</td>
<td>VIII</td>
<td>60</td>
<td>1.4</td>
<td>1.4</td>
<td>0.11</td>
<td>0.0015</td>
<td>0.00019</td>
</tr>
<tr>
<td></td>
<td>2:35</td>
<td>5.5 c.c. arterial blood taken.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2:36</td>
<td>IX</td>
<td>60</td>
<td>1.2</td>
<td>2.2</td>
<td>0.10</td>
<td>0.0009</td>
<td>0.00012</td>
</tr>
<tr>
<td></td>
<td>2:37</td>
<td>X</td>
<td>60</td>
<td>1.3</td>
<td>3.3</td>
<td>0.11</td>
<td>0.0009</td>
<td>0.00012</td>
</tr>
<tr>
<td></td>
<td>2:45</td>
<td></td>
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<td></td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>3:05</td>
<td>2 c.c. arterial blood taken.</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:05</td>
<td>XI</td>
<td>60</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:06</td>
<td>XII</td>
<td>60</td>
<td>2.0</td>
<td>2.0</td>
<td>0.16</td>
<td>0.0006</td>
<td>0.0012</td>
</tr>
<tr>
<td></td>
<td>3:21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:52</td>
<td>XIII</td>
<td>60</td>
<td>1.0</td>
<td>1.0</td>
<td>0.08</td>
<td>0.0002</td>
<td>0.00002</td>
</tr>
<tr>
<td></td>
<td>3:53</td>
<td>XIV</td>
<td>60</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:55</td>
<td>2 c.c. arterial blood taken.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4:10</td>
<td>About 50 c.c. arterial blood taken.</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4:15</td>
<td>The wound sewed up.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Soon after atropine, pupils dilated, respiration deep and rough; urination; the animal excited.

Sample III and IV dark. Colour of arterial blood at the time also dark as the vein blood. Samples IX, X, XI, XII, XIII and XIV easily coagulable. After the morphine the animal became very quiet. Salivation increased.

| 4. V. 1935. | 9:40—10:20 a.m. Left lumbar route operated. | | | | | | | | | | | | | | | | | | |
Atropine and Hyperepinephræmia by Morphine on Insulin

<table>
<thead>
<tr>
<th>No. of Dog, min.</th>
<th>Time of specimen collection</th>
<th>Duration of collection (sec.)</th>
<th>Quantity of blood flow (c.c.)</th>
<th>Epinephrine (mgram.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.6 kilos</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11:45</td>
<td>I</td>
<td>60</td>
<td>4.0</td>
<td>0.00005</td>
</tr>
<tr>
<td>11:46</td>
<td>II</td>
<td>30</td>
<td>2.5</td>
<td>0.00022</td>
</tr>
<tr>
<td>11:55</td>
<td>III</td>
<td>30</td>
<td>2.0</td>
<td>0.00012</td>
</tr>
<tr>
<td>11:56</td>
<td>IV</td>
<td>30</td>
<td>2.0</td>
<td>0.00015</td>
</tr>
<tr>
<td>12:00</td>
<td></td>
<td>4.5 c.c. of 2% atropine-Tyrode injected intravenously in about 30 seconds, i.e. about 5 mgrams. per kilo.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Soon after injection, the animal excited, heart beat became strong and large pupils dilated, hyperaemia appeared on conjunctiva and skin with light fur, respiration deep.

12:09—12:10 9 c.c. of 2% morphine injected subcutaneously, i.e. about 10 mgrams. per kilo, on the other lumbar side.

12:15 V 30 2.0 4.0 0.23 0.00015 0.00005 0.000042 0.0115 225 14 38.3 17
12:16 VI 30 2.5 5.0 0.23 0.00022 0.00024 0.000014 0.0090 162 12 38.8 16
12:17 VII 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:18 VIII 30 2.5 5.0 0.23 0.0003 0.00024 0.000014 0.0090 162 12 38.8 16
12:19 IX 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:20 X 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:21 XI 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:22 XII 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:23 XIII 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:24 XIV 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:25 XV 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
12:26 XVI 30 2.0 4.0 0.23 0.00005 0.00024 0.000014 0.0090 162 12 38.8 16
3:00 About 120 c.c. of arterial blood was shed.
3:15 The wound sewed up.

About 10 minutes after morphine, animal quiet, pupils large, reflexes increased, hyperaemia disappeared before long. 1.5 hour later it seems the animal quite normal.

(2. III. 1935 D_23 L_2 dorsal spinal roots severed under morphine-ether-chloroform anaesthesia. 10.0 kilos. Both hind legs somewhat atactic.

9:50—10:30 a.m. Left lumbar route preparation.
3:05
3:10 I 30 1.8 3.6 0.39 0.00005 0.00019 0.00002 0.098 158 24 40.2 33
3:11 II 30 2.0 4.0 0.43 0.00005 0.00019 0.00002 0.096 158 24 40.2 33
3:15 III 30 1.9 3.5 0.41 0.00005 0.00019 0.00002 0.096 158 24 40.2 33
3:16 IV 30 2.0 4.0 0.43 0.00005 0.00019 0.00002 0.096 158 24 40.2 33
3:20—3:21 2.3 c.c. of 2% atropine-Tyrode injected intravenously, i.e. about 5 mgrams. per kilo.

Soon after the injection, hyperaemia appeared on conjunctiva and skin with light fur, pupils dilated, the animal excited a little.
3:30 V 30 1.8 3.6 0.39 0.00015 0.00057 0.000061 0.107
3:31 VI 30 2.0 4.0 0.43 0.00015 0.00057 0.000061 0.107
3:33—3:45 6.5 c.c. of insulin, i.e. 7 units per kilo, was injected intravenously
3:45 VII 30 2.1 4.2 0.45 0.0010 0.0047 0.00050 0.082
3:46 VIII 30 2.6 5.2 0.56 0.0010 0.0047 0.00050 0.082

(Continued on p. 399)
Intestine tracings (reduced to \(\frac{3}{5}\)) for Dog 1.

In all the intestine tracings, at the mark "x" atropine-Tyrod's solution, in which the rabbit intestine segment was beating rhythmically, was replaced by indifferent blood solution, and at the "numeral" by the indifferent blood solution to which a certain quantity of adrenalin chloride of Sankyo Co. was added, or by the specimen solution. All the blood solutions were prepared by diluting with 4 volumes of Tyrod's solution, and the quantity of the blood employed for an assay was 0.5 c.c.

The numeral of specimen and the quantity of adrenalin solution, which is showed in c.c. and in concentration, were added to each observation. For example, "0.1/2000" shows "0.1 c.c. of adrenaline solution with the concentration of 1:2 000 000 in 1 c.c." i.e. 0.00005 mgrm. adrenaline.

To show the I specimen, we used the numeral "I".

In all tracings, time intervals are 30 seconds.

Fig. a. I+II: Stronger than indifferent blood, and weaker than 0.00005 mgrm.
Fig. b. I+II: Almost the same with 0.000025 mgrm. III+IV: Far stronger than I+II.
Fig. c. (III+IV)/6: Almost as strong as 0.0002 mgrm. and a little weaker than 0.00025 mgrm.
Fig. d. V+VI: Far stronger than 0.00025 mgrm. (V+VI)/5: Far stronger than 0.00003 mgrm.
Fig. e. (V+VI)/5: About the same with 0.0005 mgrm. (VII+VIII)/5: Weaker than (V+VI)/5.
Fig. f. (VII+VIII)/5: Weaker than 0.0004 mgrm. and 0.0003 mgrm. (IX+X)/3: Stronger than 0.0001 mgrm. and weaker than 0.0002 mgrm. (Obs. 28).
Fig. g. (IX+X)/3: Stronger than 0.0009 mgrm. and almost as strong as 0.0003 mgrm.
Fig. h. XII: Stronger than 0.0002 mgrm. and almost as strong as 0.0002 mgrm. (IX+X)/3: Stronger than 0.0001 mgrm. and weaker than 0.0002 mgrm. (Obs. 28).
Fig. i. XIII: Weaker than XII (0.0003 mgrm.), about the same with 0.0001 mgrm. and a little weaker than 0.00015 mgrm.
To sum up:

I+II: Stronger than indifferent blood, and weaker than 0.00005 mgm. Almost the same with 0.000025 mgm. It was assayed at 0.00005 mgm. in 1 c.c.

III+IV: Far stronger than I+II. (III+IV)/6: Almost as strong as 0.0002 mgm. and a little weaker than 0.00005 mgm. The 6 times diluted specimen was assayed at 0.0004 mgm. per 1 c.c. That is, (III+IV) was taken as 0.0024 mgm. in 1 c.c.

V+VI: Far stronger than 0.00025 mgm. (V+VI)/8: Far stronger than 0.0003 mgm. About the same with 0.0005 mgm. The 5 times diluted specimen was assayed at 0.001 mgm. per 1 c.c. That is, the original sample was taken as 0.0005 mgm. per 1 c.c.

VII+VIII: (VII+VIII)/5: Weaker than (V+VI)/5. Weaker than 0.0004 mgm. and 0.0003 mgm. Weaker than 0.0002 mgm. and stronger than 0.0001 mgm. The 5 times diluted one was assayed at 0.0003 mgm. per 1 c.c. That is, the original specimen will be 0.0015 mgm. per 1 c.c.

IX+X: (IX+X)/3: Stronger than 0.0001 mgm. and weaker than 0.00002 mgm. (Obs. 28). The 3 times diluted specimen was assayed at 0.00003 mgm. per 1 c.c. That is the original one was taken as 0.00009 mgm. per 1 c.c.

XII: Stronger than 0.0002 mgm. and almost as strong as 0.0003 mgm. It was taken as 0.0006 mgm. per 1 c.c.

XIII: Weaker than XII (0.0003 mgm.), about the same with 0.0001 mgm. and a little weaker than 0.0002 mgm. It was taken as 0.00015 mgm. per 1 c.c.

(Continued from p. 397)

The output rate of epinephrine occurring 10 minutes after morphine was 0.00028 mgm. per minute per kilo and the highest in this experiment. In a previous experiment (on Dog 5, of Satô and Ohmi,2)
p. 430), the same dose of morphine caused an accelerated secretion of epinephrine such as 0.00022 mgm. per minute per kilo, the basal rate being about 0.00002 mgm. The hyperepinephrinaemia lasted there about two hours; on double dosage the acceleration was also much larger, and on a half dosage much smaller, 0.00058 mgm. against 0.00003 mgm. of the basal rate, and 0.00007 mgm. against 0.00001 mgm. respectively. In these experiments with morphine alone, the blood flow through the gland did not alter much, or occasionally it tended to increase though not largely. In the present case, the blood flow was largely effected by atropine, so that it is difficult to analyze how morphine had influence thereupon.

The blood sugar was not further increased on morphine administration, but the hyperglycaemic period existed so long as the epinephrine secretion was accelerating.

The heart rate further increased, the respiration, and the body temperature too.

Dog 2. Male, 17.6 kilos.

One and half hours after preparing for collecting the suprarenal vein blood, the output rate of epinephrine was 0.000014 mgm. per minute per kilo. Atropine was then intravenously injected in the dose of 5 mgm. per kilo, the animal excited, the heart beat strong, the respiration became deep the pupils dilated and the conjunctiva and skin hyperaemic. Some minutes later morphine was injected, this time subcutaneously in the dose of 10 mgm. per kilo, as in Dog 1 in the experiment of Sato and Ohmi.2) This time the blood flow through the gland underwent no alteration; such course was also seen in a case in the previous experiments with atropine alone,1) and in almost all cases with morphine alone.2) The epinephrine output rate was estimated as 0.00004 mgm. per minute per kilo about 5 minutes after morphine, 0.00017 mgm. 35 minutes, 0.00007 mgm. 65 minutes, 0.00006 mgm. 95 minutes, 0.00007 mgm. 125 minutes, and 0.00002 mgm. 155 minutes. The highest velocity was seen about a half hour after morphine and as 0.00017 mgm. per minute per kilo.

The blood sugar concentration increased, its acme 0.133% being noted one hour after morphine, and the hyperglycaemic period covered two and half hours at least. The tachycardia did not show signs of dying out at the end of observation, that is two and half hours after atropine and morphine; the body temperature tended to decrease a little.
The rate of the accelerated secretion of epinephrine and the time when it appears coincides well with those noted in Dog 1 of Sato and Ohmi, which received the same dose of morphine. The magnitude of hyperglycaemia was somewhat smaller in the present case.

The rate of the accelerated secretion in this case is somewhat greater than those in the previous report, which were occasioned by intravenous 5 or 10 mgrms. atropine alone.

**Insulin experiment.**

**Dog 3.** Male, 9.3 kilos.

The basal output rate of this dog was 0.00002 mgrm. per minute per kilo, and the blood sugar content 0.097%. 5 mgrms. per kilo was the atropine dose. The animal excited a little, the pupils dilated, the conjunctiva and skin hyperaemic. 10 minutes after atropine the output rate was estimated as increased to 0.00006 mgrm. per minute per kilo, and the blood sugar to 0.107%; the blood flow through the gland remained unaltered.

A few minutes later insulin-Toronto was intravenously injected in the dose of 7 units per kilo, the animal looked weak and excited a little. The epinephrine output rate was found 10 minutes after insulin to have increased to 0.0005 mgrm. per minute per kilo, the flow rate of blood being measured a little increased; that is the increase was due to an enormous increase of the concentration of epinephrine. The blood sugar was going down.

15 minutes later the output rate was estimated as 0.00012 mgrm. per minute per kilo, thirty minutes further later 0.00026 mgrm., thirty minutes and one hour still later 0.00014–0.00013 mgrm. The acceleration is due to the increase of the concentration of epinephrine. The hypoglycaemia was occurring simultaneously.

The pulse rate was somewhat accelerating and the body temperature underwent a small reduction.

The magnitude of acceleration in the epinephrine output rate roughly corresponds to that by Yen, Aomura and Inaba on giving only insulin, or it is clearly larger than that obtained with the same dose of hormone, viz. 7 units per kilo. If the largest rate of 0.0005 mgrm. per minute per kilo in the present case be taken out from consideration, the figures in both experiments coincide rather well.

And the greatest magnitude of acceleration of the discharge in the present case, 0.0005 mgrm. per minute per kilo and the next one
0.00026 mgrm. exceed largely that obtained in the former experiments, where atropine only was given. It is out of the question on the one hand, that the acceleration in this case can be taken as not to be elicitable by atropine alone, and on the other hand it was at least non-inferior to those producible by similar doses of insulin.

SUMMARY.

In the dogs, which were prepared for obtaining the suprarenal vein blood without fastening, narcotizing, laparotomizing or evoking pain, atropine was intravenously administered, which was followed by morphine or insulin. Epinephrine was estimated by means of the rabbit intestine segment.

The epinephrine output rate was accelerated, and the magnitude of acceleration nearly corresponds to that producible by those doses of morphine or insulin alone. Or at least the acceleration was not so large as to account for it as the sum of that elicitable by atropine and morphine or insulin, though it seemed somewhat likely with the latter.

At least we failed to gather any evidence of atropine inhibiting the acceleration in the epinephrine output rate due to morphine or insulin. This finding also stands against the view that only the para-sympathetic nerve fibres control secretion of epinephrine from the suprarenal gland, and atropine paralyzes its termination, while the accelerating action of morphine and insulin upon the epinephrine discharge is annulled by splanchnicotomy.