Studies on the Temperature of the Gastrointestinal Tract

Fifth Report

Response of the Intra gastric Temperature to Various Drugs (Part I)

By

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In the previous reports¹⁾⁻³⁾, the responses of the intragastric temperature to bathing, local cooling and warming of the epigastrium, and ingestion of hot and cold water were studied. In this report responses of the said temperature to drugs acting on the autonomic nervous system and a gastric secretagogue are researched upon. Concerning this problem a report, in which histamine, acetylcholine, alcohol and typhoid vaccine were given to men, appeared by Thiessen and Snell⁴⁾.

EXPERIMENTAL

Methods and Materials

Adrenaline, pilocarpine and atropine were selected as drugs acting on the autonomic nervous system and histamine as a gastric secretagogue. To observe their actions as purely and correctly as possible, a large dose was applied and attention was paid to avoid, as far as possible, variations may arise from weather, surroundings, nourishment and so on. First a routine table for experiments was made by arranging at random 24 combinations of a man and a drug which are obtained by injecting 1 mg. of histamine and adrenaline hydrochloride and atropine sulphate and 10 mg. of pilocarpine hydrochloride respectively to each of six healthy males whose ages ranged from 24 to 29 years, and then the experiments were performed according to it. The intragastric temperature was measured by a thermometer⁵⁾, which was introduced into the stomach at 60 cm. from the incisor of the upper jaw in the fasting state at least 4 hours after meals. It became almost constant about 30 minutes thereafter. Then the drug was injected subcutaneously as above mentioned and for 60 minutes thereafter the intragastric temperature was continuously ob-

served. Simultaneously the axillary temperature was measured by a copper-constantan thermocouple and a potentiometer. Pulse rate and blood pressure were also determined at each 5 minutes to observe changes in the cardiovascular system, and gastric juice was aspirated at each 10 minutes through the Miller-Abbott's tube of the thermometer to observe response of the gastric secretion. The aspirated gastric juice was examined for the volume, free and total acidities by Toepfer's reagent and phenolphthalein solution and peptic power by Fuld-Levison's method⁶⁾. Room temperature was ranged between 15 and 18°C.

TABLE I

The Changes in the Intragastric Temperature after the Injection of Histamine, Adrenaline, Pilocarpine and Atropine

Drug	No.	Before inject. °C	After injection (minutes)								
			5 °C	10 °C	15 °C	20 °C	25 °C	30 °C	40 °C	50 °C	60 °C
Histamine	1	37.3	−0.15	−0.35	−0.55	−0.60	−0.55	−0.50	−0.30	−0.05	0.25
	2	37.4	−0.45	−0.50	−0.65	−0.65	−0.55	−0.45	−0.30	−0.15	−0.05
	3	36.8	−0.05	−0.40	−0.60	−0.65	−0.70	−0.65	−0.40	−0.15	−0.05
	4	37.8	−0.20	−0.35	−0.35	−0.35	−0.30	−0.25	−0.15	−0.05	0.05
	5	37.0	−0.50	−0.75	−0.75	−0.75	−0.65	−0.55	−0.40	−0.25	−0.20
	6	37.6	−0.20	−0.40	−0.50	−0.45	−0.45	−0.35	−0.25	−0.15	−0.05
	Sum	223.9	−0.92	−2.75	−3.40	−3.45	−3.20	−2.75	−1.80	−0.80	−0.05
	Mean	37.32	−0.15	−0.46	−0.57	−0.58	−0.53	−0.46	−0.30	−0.13	−0.01
Adrenaline	1	37.4	−0.10	−0.10	−0.10	−0.20	−0.25	−0.30	−0.35	−0.35	−0.35
	2	37.3	−0.10	−0.25	−0.25	−0.30	−0.35	−0.35	−0.30	−0.25	−0.25
	3	37.2	0	−0.15	−0.35	−0.45	−0.45	−0.50	−0.40	−0.35	−0.35
	4	37.4	0.05	0.05	0	−0.05	−0.10	−0.05	−0.10	−0.05	−0.05
	5	37.1	0	0	−0.05	−0.05	−0.10	−0.05	−0.10	−0.10	−0.05
	6	37.1	0	0	0	−0.05	−0.10	−0.15	−0.05	−0.10	−0.05
	Sum	223.5	−0.15	−0.45	−0.75	−1.10	−1.35	−1.40	−1.30	−1.20	−1.10
	Mean	37.25	−0.03	−0.08	−0.13	−0.18	−0.23	−0.23	−0.22	−0.20	−0.18
Pilocarpine	1	37.2	−0.05	−0.15	−0.25	−0.35	−0.45	−0.50	−0.55	−0.55	−0.45
	2	37.4	−0.05	−0.15	−0.15	−0.25	−0.35	−0.40	−0.50	−0.35	−0.25
	3	37.4	−0.05	−0.20	−0.35	−0.60	−0.70	−0.80	−0.85	−0.85	−0.80
	4	37.6	−0.05	−0.15	−0.50	−0.85	−0.85	−0.85	−0.70	−0.70	−0.65
	5	37.8	−0.05	−0.25	−0.45	−0.65	−0.65	−0.65	−0.60	−0.55	−0.45
	6	37.6	−0.05	−0.15	−0.25	−0.35	−0.45	−0.35	−0.35	−0.35	−0.35
	Sum	225.0	−0.30	−1.05	−1.95	−3.05	−3.45	−3.55	−3.55	−3.35	−2.95
	Mean	37.50	−0.05	−0.18	−0.33	−0.51	−0.58	−0.59	−0.59	−0.56	−0.49
Atropine	1	37.4	0	0	0.05	0	0.05	0.05	0.05	−0.10	−0.15
	2	37.4	0	−0.05	−0.05	−0.05	−0.05	−0.05	−0.10	−0.15	−0.10
	3	37.7	0	0	0.05	0.05	0.05	0.05	0.05	0	−0.05
	4	36.8	−0.05	0	0	0.05	0.05	0.05	−0.05	−0.10	−0.15
	5	37.4	−0.05	0	0.05	0.05	0.05	0.05	0	−0.05	−0.15
	6	37.5	0	0.05	0.10	0.10	0.10	0.05	0.05	−0.05	−0.05
	Sum	224.2	−0.10	0	0.20	0.30	0.25	0.20	0	−0.45	−0.65
	Mean	37.37	−0.02	0	0.03	0.05	0.04	0.03	0	−0.08	−0.11

Fig. 1. The changes in the intragastric and axillary temperatures after the injection of histamine (—), adrenaline (-----), pilocarpine (— · — · —) and atropine (-----).

Results

The data for the changes in the intragastric temperature after the injection of the 4 drugs are given in Table I and Fig. 1. In Fig. 1 the means of the changes in the intragastric temperature are shown together with those in the axillary. The means of the changes in the systolic and diastolic blood pressures and pulse rate are illustrated in Fig. 2 and those of the changes in the gastric contents, i.e., those in the volume, free acidity and pepsin in Fig. 3.

DISCUSSION

First the change in the intragastric temperature is discussed. Obviously in Fig. 1, following the injection of histamine the intragastric temperature began to drop abruptly and almost linearly reaching in the course of 15–20 minutes its maximum drop, -0.58°C on an average, and thereafter continued to rise also linearly recovering at 60 minutes after the injection. In cases of pilocarpine and adrenaline, it dropped almost linearly, reaching in the course of 30 minutes respectively the average maximum drops of -0.59 and -0.23°C and thereafter no significant change occurred. In case of atropine it at first rose then dropped on an average of -0.11°C in the course of 60 minutes. The above mentioned

Fig. 2

Fig. 3

Fig. 2. The changes in the pulse rate and systolic and diastolic blood pressures after the injection of histamine (—), adrenaline (-----), pilocarpine (— · — · —) and atropine (— — — — —).

Fig. 3. The changes in the free acidity, pepsin and volume of the aspirated gastric juice after the injection of histamine (—), adrenaline (-----), pilocarpine (— · — · —) and atropine (— — — — —).

drops and rises were all statistically significant. The types of the change (time series) were mutually also significantly different by the 4 drugs. The maximum drops by histamine and pilocarpine were almost equal (-0.58 and -0.59°C), that by adrenaline was about half of the formers, and that by atropine was about half of the latter. In these drops the differences between histamine and pilocarpine and between adrenaline and atropine were not significant. However, differences of the time for reaching the maximum drop between the said drugs were significant. Accordingly, among the 4 drugs significant differences were noticed in the combination of the maximum drop and the time for reaching it as well as in the type of the change. It is interesting that in general the change by histamine is transient in comparison with the drugs acting on the autonomic nervous system and that the changes by pilocarpine and atropine show mutually striking differences.

Secondly the change in the axillary temperature is considered. It was generally parallel with that in the intragastric (Fig. 1). However, its magnitude was smaller and its onset was slower than the latter; and the ratio of the magnitudes of both temperatures was different from one another by the 4 drugs. The combination of the maximum change and the time for reaching it was, similarly as in the case of the intragastric, significantly different by the 4 drugs. As the axillary temperature is greater in individual variation and inferior in the accuracy of measurement than the intragastric, it is difficult to conclude from the change of the former comparing with the latter.

Thirdly the change in the cardiovascular system is considered. The pulse rate was significantly increased by histamine, pilocarpine and adrenaline, but by atropine it decreased as described in the monograph by Krantz and Carr⁷⁾ (Fig. 2). Onset of the change in the pulse rate precedes that in the intragastric temperature and among the 4 drugs significant differences are seen in the combination of the maximum change and the time for reaching it as well. The changes in the systolic and diastolic blood pressures were not directly related with those in the intragastric temperature as seen in Fig. 2. It is worthy of note that the change in the pulse rate was in a good contrast with that in the intragastric temperature. Namely, according to the increase or decrease of the pulse rate the intragastric temperature inversely drops or rises and between the magnitudes of both changes a good proportion is noticed. After the injection of histamine, the face and skin became flushed and the vessels of the skin dilated. Therefore, it is postulated that because the blood which is cooled peripherally at the body surface and the lungs returns to the heart and flows into the vessels of the stomach and its surroundings, the intragastric temperature is lowered; and that as the action of histamine

is relatively transient, the drop of the intragastric temperature will be also temporary. In case of the drugs acting on the autonomic nervous system changes in the cardiovascular system are more complicated, but it will be certain that the change in the blood flow is one of the most important factors. According to this assumption the change in the axillary temperature is also easily explained. Importance of the blood circulation in the change in the intragastric temperature was already stressed in cases of bathing and of cooling or warming of the epigastrium in the second and third reports¹⁾²⁾. From the present experiments the importance that the intragastric temperature is in intimate relation with the blood flow, is also evident.

Fourthly the change in the gastric juice is discussed. Among the changes shown in Fig. 3, only those in the free acidity by histamine and in the pepsin by histamine, pilocarpine and adrenaline are significant, owing to the lack of a reliable method for determination of the change in the gastric juice and the great individual variation. However, tendencies of the changes are noticed. Namely, the volume of the secretion and pepsin were increased by histamine and pilocarpine and the free acidity by histamine. It is interesting that by the drugs which intensely stimulate the gastric secretion, i.e., histamine and pilocarpine, the intragastric temperature is also remarkably lowered. Regarding to the relation between the intragastric temperature and the gastric secretion, many possibilities, for example, accelerated gastric blood flow, have been considered, but under the present state it is difficult without further studies to explain clearly the relation.

SUMMARY

Response of the intragastric temperature of healthy men to subcutaneous injection of histamine, adrenaline, pilocarpine and atropine was studied simultaneously with those of the axillary temperature, pulse rate, blood pressure and gastric juice; and the following facts were confirmed.

1. The intragastric temperature drops by the four drugs.
2. The drop by histamine is transient contrary to those by adrenaline and pilocarpine and the drop by atropine is preceded by a slight rise.
3. The maximum drop is large by histamine and pilocarpine and small by adrenaline and atropine.
4. Onset of the drop is more rapid by histamine than by pilocarpine and adrenaline and is slowest by atropine.
5. Combination of the maximum drop and the time for reaching it, is different by the four drugs.
6. Change in the axillary temperature is generally parallel with

that in the intragastric.

7. Change in the pulse rate is in intimate relation with that in the intragastric temperature. Blood flow is one of the most important factors in the change in the intragastric temperature.

8. By histamine and pilocarpine which strongly stimulate the gastric secretion, the intragastric temperature is intensely lowered.

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