

## BLOOD FLOW CHANGES IN MUCOSA OF EMPTY AND DISTENDED CANINE AND HUMAN STOMACHS

by

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It is well known that the incidence of gastric carcinoma in the Koreans and the Japanese is much higher and that the younger age group is more involved than in other races (11, 12, 14). Various etiologic factors have been suggested without definite conclusions being reached. SEGI et coll. (1957) reported that rice or other cereals, irritative foods and drinks or certain condiments, seem to bear no relationship with the high incidence of gastric carcinoma in the Japanese although it was remarkably higher among big eaters and lower among small eaters. KIM & JAKOBSSON (1962) suggested that a certain degree of gastric distension may alter the normal well balanced physiology of a part of the stomach and predispose to carcinoma or other diseases. They investigated the quantitative blood flow in the mucosa of the empty and distended rat stomach and found that when the stomach was distended beyond a certain point the blood flow in the antral mucosa decreased significantly, more at the lesser curvature than at the greater curvature.

The present authors extended the research to determine whether the same phenomenon would occur in the human stomach as well as in the canine

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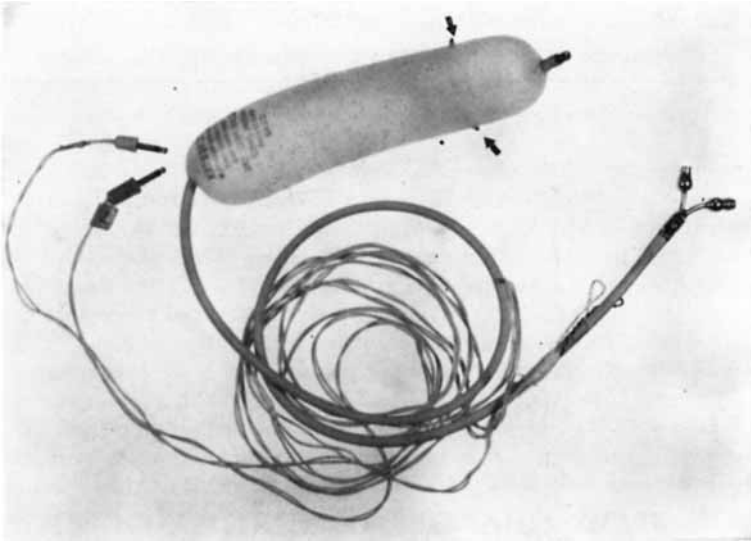


Fig. 1. Thermistor-balloon. The arrows indicate thermistors fitted onto the inner surface of a latex rubber balloon.

stomach. They have developed a device that accurately measures the temperature of the gastric mucosa to  $0.01^{\circ}\text{C}$  and records the change of the mucosal temperature as the stomach is distended to various degrees. The device consists of an intragastric balloon to which small thermistors are attached so that when the balloon is inflated the thermistors make contact with the surface of the gastric mucosa.

### Materials and Methods

*Measurement of the temperature of the gastric mucosa.* One or two of the pinhead-sized tiny Fenwal thermistors, type G 148, were fitted onto the inner surface of a latex rubber balloon and connected by means of fine cables to an amplifier and galvanometer through the larger hole of the Miller-Abbott tube (Figs 1 and 2).

The thermistor used has an electric resistance of about 2 000 ohm at about  $20^{\circ}\text{C}$ , the resistance decreasing as the temperature rises. Manganium line resistances were adapted so as to have electric resistances equal to those recorded when the thermistors were placed in  $30^{\circ}\text{C}$ ,  $37^{\circ}\text{C}$  and  $38^{\circ}\text{C}$  constant temperature waterbaths calibrated to within  $0.05^{\circ}\text{C}$ . When these resistances were substituted for the thermistors, the ammeter indicated the temperatures

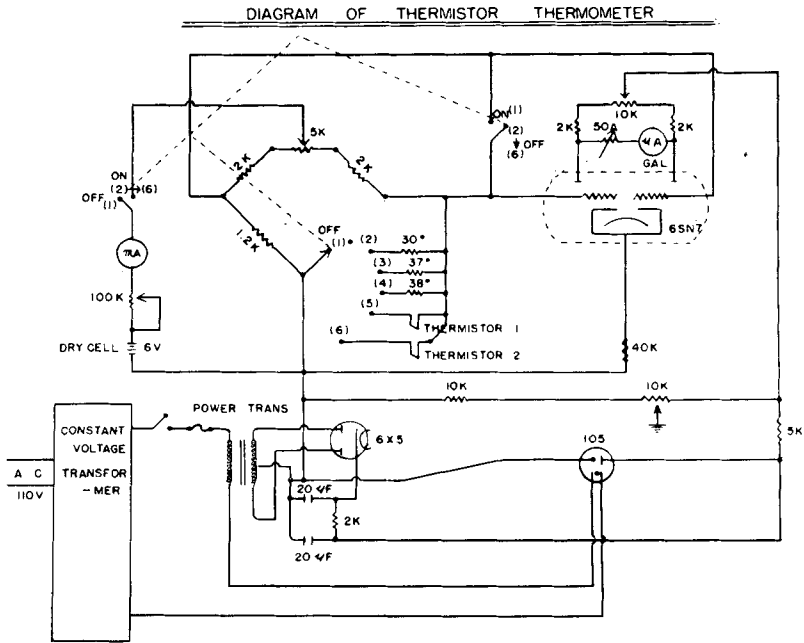


Fig. 2. Diagram of thermistor thermometer.

of  $30^{\circ}\text{C}$ ,  $37^{\circ}\text{C}$  and  $38^{\circ}\text{C}$ , respectively, The sensitivity of the ammeter was controlled so that its needle lay in a suitable position on the scale when the circuit was switched to the 3 and 4 positions (Fig. 2). The sensitivity of this electric 'thermometer' was made to show approximately a 3 cm needle deflection against a  $1^{\circ}\text{C}$  temperature difference so that  $0.01^{\circ}\text{C}$  temperature variation could be measured easily.

*Estimation of the degree of distension of the stomach.* The degree of distension of the stomach may be measured by the volume of air introduced or by the pressure inside the inflated balloon; the authors however estimated the degree of distension by the area of the stomach as evident in roentgenograms. The degree of the distension of the stomach was graded as minimal, moderate, marked and extreme. These, in canine experiments, correspond to  $60\text{--}80\text{ cm}^2$ ,  $100\text{--}120\text{ cm}^2$ ,  $140\text{--}160\text{ cm}^2$  and over  $200\text{ cm}^2$  of the areas of the stomach, respectively (Fig. 3), and in human experiments to  $80\text{--}100\text{ cm}^2$ ,  $140\text{--}160\text{ cm}^2$ , and over  $200\text{ cm}^2$ , respectively, with the exception of 'extreme distension', which was omitted in order to avoid any possible discomfort to the subject (Fig. 4).

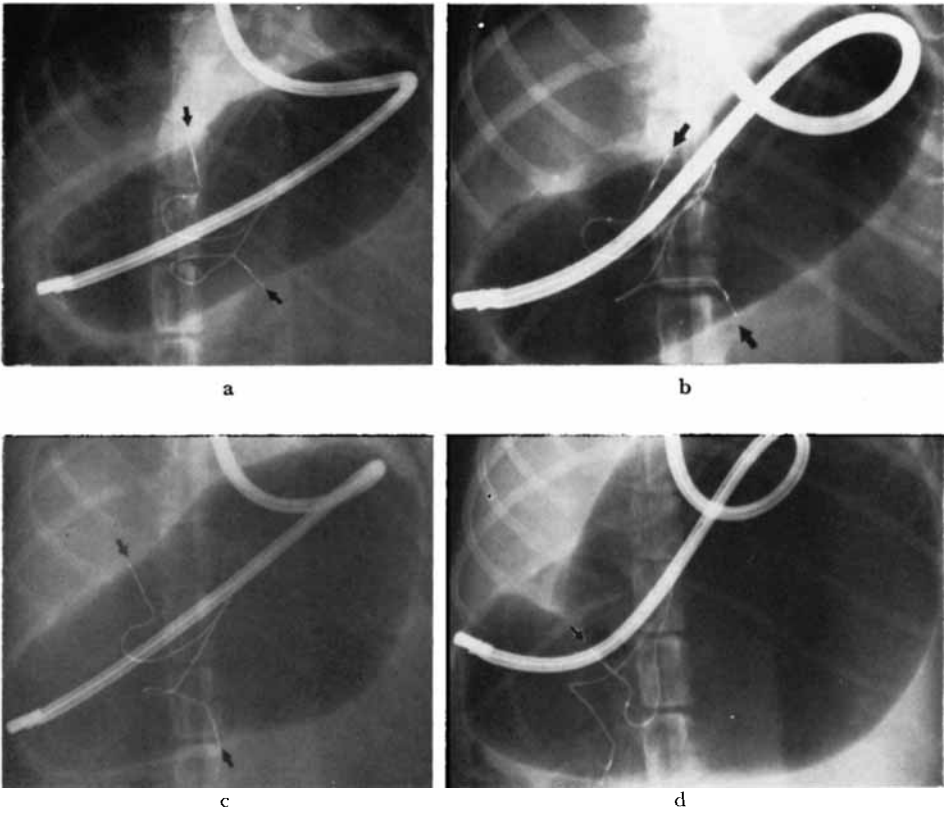


Fig. 3. Dog No. 7. Degrees of distension of stomach: minimal (a), moderate (b), marked (c), and extreme (d).

*Estimation of the temperature of the gastric mucosa.* Although the changes in the electric resistance with temperature usually take place within a few seconds, the galvanometer was read after it had become stabilized, usually at least 2 min after the stomach was inflated. A delayed reaction due to the intervening balloon membrane between the gastric mucosa and the thermistor and the plastic membrane covering the thermistor was always considered possible. The galvanometer was checked at  $37^{\circ}\text{C}$  and  $38^{\circ}\text{C}$  before the actual measurement of the temperature of the gastric mucosa, and thermistors 1 and 2 were then connected to the circuit. The temperature of the part of the gastric mucosa to be examined was indicated by the deflection of the galvanometer.

Because one scale of the galvanometer corresponded to  $0.03^{\circ}\text{C}$ , and about a quarter of the scale could be read, a temperature change as small as  $0.008^{\circ}\text{C}$

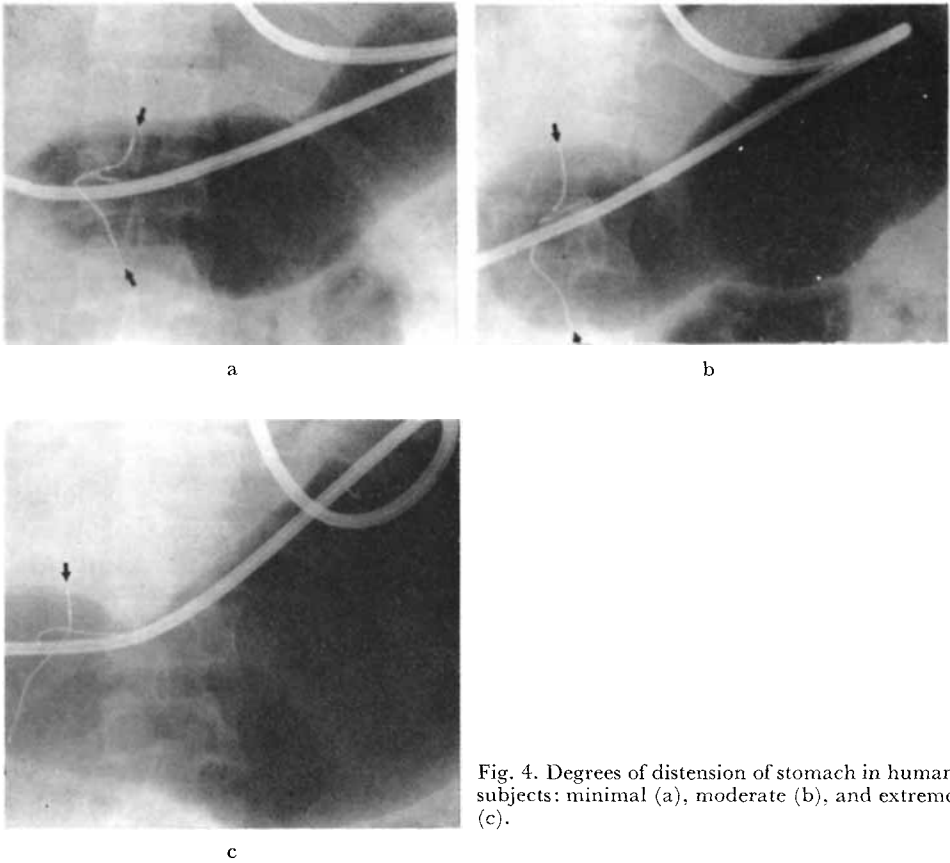


Fig. 4. Degrees of distension of stomach in human subjects: minimal (a), moderate (b), and extreme (c).

could be recorded. The instability of the device precluded however figures below  $0.01^{\circ}\text{C}$  from being considered reliable.

The cases in which the thermistors were incorrectly placed and remained at the lesser and greater curvatures of the stomach through the experiment, or those in which the thermistors were thought not to be in contact with the gastric mucosa because of remnant fluid or air in the stomach, were excluded.

*Experiments in dogs.* Healthy Mongolian dogs weighing 7.5 to 18.0 kg (mean weight 12.2 kg) and fasting overnight were used. After the dogs had been anesthetized with pentothal sodium, the thermistor balloon was inserted into the stomach, the tip of the tube being placed at the pylorus under roentgen control. The air and fluid contents of the stomach were removed through the tube to ensure that the balloon made contact with the gastric mucosa.

**Table 1**

*Degree of distension (increase) in 22 observations of the stomach of dog, in supine position, recorded in relation to the registered fall in temperature, °C, in the gastric mucosa — P indicates the significance level when compared with the temperature at minimal distension.*

<i>Degree of distension:</i>	<i>Site: Lesser curvature</i>			<i>Greater curvature</i>		
	Moderate	Marked	Extreme	Moderate	Marked	Extreme
Mean	0.07	0.17	0.29	0.01	0.04	0.06
Standard error	0.021	0.029	0.035	0.016	0.019	0.018
P <	0.01	0.001	0.001	0.6	0.05	0.01

The measurement of the temperature of the gastric mucosa was performed with four different degrees of distension of the stomach, i.e. minimal, moderate, marked and extreme, as already mentioned above, each measurement being repeated three times. Any difference in the temperature of the gastric mucosa produced by posture was observed by first taking a reading in the supine position and then in the right and left lateral positions.

The thermistor balloon was inflated as slowly as possible to avoid any sudden distension of the stomach and to lessen the influence of the temperature of the air introduced into the balloon; the galvanometer was read when the movement of the needle became stable. The experiments were performed with a small to a maximal degree of gastric inflation and each was repeated three times after the air had been removed.

Each experiment was carried out under roentgen control with roentgenograms to ensure the correct degree of inflation and the proper location of the thermistors.

*Experiments in human subjects.* Thirty-four apparently healthy men, all of them fasting for more than 12 hours, without any history of abnormality of the digestive organs, were chosen at random. The experiment was carefully explained to the examinees beforehand. The thermistor balloon was swallowed in a sitting position and when the tip of the tube had passed into the stomach the examinee was laid on the roentgen table and the tip of the tube advanced to the pylorus. The procedure of the experiment was essentially the same as in the dog experiments except for the exclusion of an extreme degree of inflation of the stomach for the reason mentioned previously. There was no significant distress or complication during or after the experiment.

**Table 2**

*Degree of distension (increase) in 7 observations of the stomach of dog, in supine and left lateral positions, recorded in relation to the registered fall in temperature, °C, in the gastric mucosa — P indicates significance level when compared with the temperature at minimal distension.*

	Supine position						Left lateral position					
	Lesser curvature			Greater curvature			Lesser curvature			Greater curvature		
<i>Degree of distension:</i>	Mod.	Mark.	Extr.	Mod.	Mark.	Extr.	Mod.	Mark.	Extr.	Mod.	Mark.	Extr.*
Mean	0.11	0.22	0.33	+0.01	0.01	0.10	0.12	0.19	0.33	0.02	0.05	0.13
Standard error	0.037	0.062	0.053	0.008	0.022	0.028	0.049	0.054	0.042	0.029	0.029	0.036
P<	0.05	0.01	0.001	0.3	0.7	0.01	0.05	0.01	0.001	0.6	0.2	0.02

\* Only 6 observations

## Results

*Temperature of gastric mucosa examined in dogs in supine position.* The changes in the temperature of the gastric mucosa at the lesser and greater curvatures in the supine position, according to the four graded degrees of gastric distension, are shown in Table 1 and Fig. 5. As a matter of fact, the temperature in each degree of gastric distension should be compared with that of the empty stomach but because of the difficulty in recognising whether the thermistors made good contact with the gastric mucosa or not in an empty stomach, the temperature of the gastric mucosa at the minimal degree of gastric distension was taken as a standard. Temperature fall or 'rise' in this paper therefore means the temperature fall or rise from the temperature of the gastric mucosa at this minimal degree distension.

The mean temperature fall at the lesser curvature at moderate, marked and extreme degrees of gastric distension compared with a minimal degree were thus  $0.07^{\circ}\text{C} \pm 0.021^{\circ}\text{C}$  ( $P < 0.01$ ),  $0.17^{\circ}\text{C} \pm 0.029^{\circ}\text{C}$  ( $P < 0.001$ ) and  $0.29^{\circ}\text{C} \pm 0.035^{\circ}\text{C}$  ( $P < 0.001$ ), respectively, and the degree of temperature fall became marked as the distension increased. The fall of temperature at the greater curvature at moderate, marked and extreme gastric distension were  $0.01^{\circ}\text{C} \pm 0.016^{\circ}\text{C}$  ( $P < 0.6$ ),  $0.04^{\circ}\text{C} \pm 0.019^{\circ}\text{C}$  ( $P < 0.05$ ) and  $0.06^{\circ}\text{C} \pm 0.018^{\circ}\text{C}$  ( $P < 0.01$ ) respectively. The temperature fall at the greater curvature is much less than at the lesser curvature, the former being only about a fifth of the latter.

*Temperature of the gastric mucosa examined in the left lateral position.* The fall of mean temperature in the left lateral position at the lesser curvature in cases

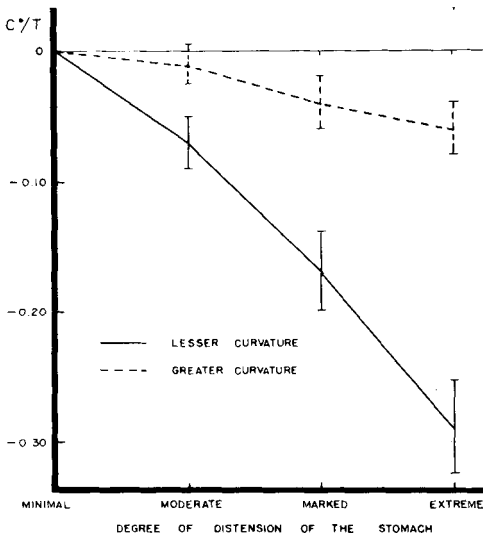


Fig. 5. Fall in temperature ( $^{\circ}\text{C}$ ) in the mucosa of the dog with increase in the degree of gastric distension, supine. Bars indicate 'standard error'.

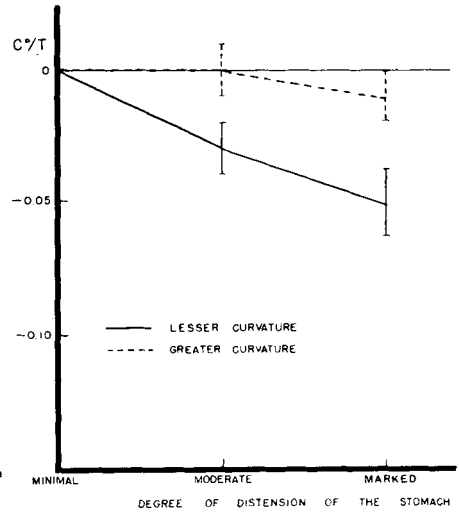


Fig. 6. Fall in temperature ( $^{\circ}\text{C}$ ) in human gastric mucosa with increase in the degree of gastric distension with air; supine. Bars indicate 'standard error'.

of moderate, marked and extreme degrees of distension were  $0.12^{\circ}\text{C} \pm 0.049^{\circ}\text{C}$  ( $P < 0.05$ ),  $0.19^{\circ}\text{C} \pm 0.054^{\circ}\text{C}$  ( $P < 0.01$ ) and  $0.33^{\circ}\text{C} \pm 0.042^{\circ}\text{C}$  ( $P < 0.001$ ), respectively, while in the supine position they were  $0.11^{\circ}\text{C} \pm 0.037^{\circ}\text{C}$  ( $P < 0.05$ ),  $0.22^{\circ}\text{C} \pm 0.062^{\circ}\text{C}$  ( $P < 0.01$ ) and  $0.33^{\circ}\text{C} \pm 0.053^{\circ}\text{C}$  ( $P < 0.001$ ), respectively, (Table 2). These data suggest that the changes in temperature of the gastric mucosa do not alter with changes in the positions of the subject. The same is true at the greater curvature. The fall in mean temperature in the left lateral position when the stomach was inflated to the moderate, marked and extreme degrees were  $0.02^{\circ}\text{C} \pm 0.029^{\circ}\text{C}$  ( $P < 0.6$ ),  $0.05^{\circ}\text{C} \pm 0.029^{\circ}\text{C}$  ( $P < 0.2$ ) and  $0.13^{\circ}\text{C} \pm 0.036^{\circ}\text{C}$  ( $P < 0.02$ ), respectively, while in the supine position the mean temperature rose by  $0.01^{\circ}\text{C} \pm 0.008^{\circ}\text{C}$  ( $P < 0.3$ ) when the stomach was inflated to the moderate degree and fell by  $0.01^{\circ}\text{C} \pm 0.022^{\circ}\text{C}$  ( $P < 0.7$ ) and  $0.10^{\circ}\text{C} \pm 0.028^{\circ}\text{C}$  ( $P < 0.01$ ) respectively when the stomach was inflated to the marked and extreme degrees.

*Temperature of the gastric mucosa examined in the right lateral position.* The fall in mean temperature at the lesser curvature in the right lateral position at moderate, marked and extreme gastric distension were  $0.04^{\circ}\text{C} \pm 0.034^{\circ}\text{C}$  ( $P < 0.3$ ),  $0.17^{\circ}\text{C} \pm 0.069^{\circ}\text{C}$  ( $P < 0.05$ ) and  $0.27^{\circ}\text{C} \pm 0.077^{\circ}\text{C}$  ( $P < 0.02$ ), respectively, while in the supine position the mean temperature rose by

Table 3

*Degree of distension (increase) in 6 observations in stomach of dog, in supine and right lateral positions, recorded in relation to the registered fall or rise in temperature, °C, in the gastric mucosa — P indicates the significance level when compared with the temperature at minimal distension.*

	Supine position						Right lateral position					
	Lesser curvature			Greater curvature			Lesser curvature			Greater curvature		
<i>Degree of distension:</i>	Mod.	Mark.	Extr.	Mod.	Mark.	Extr.	Mod.	Mark.	Extr.	Mod.	Mark.	Extr.
Mean	+0.01	0.18	0.25	0.03	0.06	0.07	0.04	0.17	0.27	0.02	0.04	0.02
Standard error	0.025	0.061	0.088	0.050	0.056	0.050	0.034	0.069	0.077	0.054	0.065	0.043
P <	0.7	0.05	0.05	0.6	0.4	0.3	0.3	0.05	0.02	0.8	0.6	0.7

0.01° C  $\pm$  0.025° C (P < 0.7) when the stomach was distended to a moderate degree and fell by 0.18° C  $\pm$  0.061° C (P < 0.05) and 0.25° C  $\pm$  0.088° C (P < 0.05), respectively, when the stomach was distended to marked and extreme degrees. Here again no significant difference in the temperature changes between the supine and right lateral positions was evident (Table 3).

The fall in mean temperature at the greater curvature in the right lateral position at moderate, marked and extreme degrees of gastric distension were 0.02° C  $\pm$  0.054° C (P < 0.8), 0.04° C  $\pm$  0.065° C (P < 0.6) and 0.02° C  $\pm$  0.043° C (P < 0.7), respectively, while in the supine position they were 0.03° C  $\pm$  0.050° C (P < 0.6), 0.06° C  $\pm$  0.056° C (P < 0.4) and 0.07° C  $\pm$  0.050° C (P < 0.3), respectively.

*Experiments in human subjects.* The changes in the temperature of the gastric mucosa according to the degrees of gastric distension in the supine position are shown in Table 4 and Fig. 6. The mean fall in temperature of the mucosa at the lesser curvature at moderate and marked degrees of gastric distension were 0.03° C  $\pm$  0.009° C (P < 0.01) and 0.05° C  $\pm$  0.012° C (P < 0.001), respectively. The temperature fall at the greater curvature was not so marked as at the lesser curvature, that is, the mean temperature remained the same when the stomach was moderately distended while the mean temperature fell by 0.01° C  $\pm$  0.011° C (P < 0.4) in the marked degree of gastric distension; this is not significant statistically. The difference in temperature fall, however, between that at the lesser curvature and the greater curvature with a marked degree of distension was significant (P < 0.05). These data suggest that the changes in temperature of the gastric mucosa in human subjects follows more or less the same tendency as observed in the experiments in canines.

**Table 4**

*Degree of distension (increase) in human subjects, supine position, recorded in relation to the fall in temperature, °C, in the gastric mucosa — P indicates the significance level when compared with the temperature at minimal distension*

<i>Degree of distension:</i>	<i>Site: Lesser curvature*</i>		<i>Greater curvature**</i>	
	Moderate	Marked	Moderate	Marked
Mean	0.03	0.05	0.00	0.01
Standard error	0.009	0.012	0.009	0.011
P <	0.01	0.001		0.4

\* 34 observations

\*\*22 observations

### Discussion

The incidence of gastric carcinoma in the Japanese has been reported to be higher among big eaters and lower among small eaters (11), as previously stated. KIM & JAKOBSSON (1962) performed an experiment in rats to investigate changes of blood flow as the stomach is distended and found a considerable decrease in blood flow in the gastric antrum, especially at the lesser curvature when the stomach was distended beyond a certain degree. They suggested that this might contribute at least in part to the development of carcinoma and other gastric diseases that prevail in the antrum and at the lesser curvature of the stomach. Their method was not nowever applicable to human subjects.

The present authors developed a thermistor device that could measure precisely a minute variation in temperature and thus register changes in the temperature of the gastric mucosa in human subjects and dogs in vivo. This change in temperature, as will be discussed later, reflects the changes in blood flow of the stomach in various degrees of distension.

The mucosal temperature of the stomach, i.e. the blood flow of the stomach, in the experiment in the dog dropped significantly as the stomach was distended with air, the temperature fall becoming greater as the distension of the stomach was increased; the rate of fall was more marked at the lesser than at the greater curvature. This phenomenon was also observed, although to a lesser degree in the human stomach and was similar to that observed by KIM & JAKOBSSON in the rat stomach. The temperature fall in the dog, at marked and extreme degrees of gastric distension compared with a minimal degree of gastric distension, were 0.17° C (P<0.001) and 0.29° C (P<0.001), and in the human

subject the temperature fall at a marked degree of gastric distension compared with a minimal degree of gastric distension was  $0.05^{\circ}\text{C}$  ( $P < 0.001$ ).

The fall in temperature in this experiment may indicate the decrease of blood flow, although, because there is no way of recording the actual temperature gradient between the temperatures of the gastric wall and the core body, the exact amount cannot be determined quantitatively. The present method may not be exactly a quantitative one but is a practical and reliable means of estimating the blood flow change. Furthermore, the thermistor used in this experiment has the advantage of high sensitivity to temperature by its instant reaction and the high temperature coefficient of the electric resistance.

Certain observations on the morphology of the empty although not distended stomach (1, 2, 3, 4, 5, 6, 10) should be mentioned. BARLET (1924) and COLE (1929) reported that the arteries of the lesser curvature of the human stomach are much more sparse than those of the remainder of the stomach and are predisposed to occlusion. REEVES (1920) reported that the sub-mucosal arterioles at the lesser curvature are not only remarkably thinner and longer but also lie, without anastomoses, near the mucosal layer; thus a greater resistance to the blood flow in this region results in a decreased blood flow and consequent risk of thrombosis. DORAN (1951) suggested, however, that in the normal stomach and in cases of duodenal ulcer no significant difference in the vascular density between the lesser curvature and other parts existed and KEY (1950) stated that the vessels of the mucosa of the lesser curvature of the normal stomach are profuse and complex. According to BENTLEY et coll. (1951), there is no difference in the vascular density between the lesser curvature mucosa and that lining the rest of the stomach.

In view of the possibility that blood stasis in the dependent portion of the stomach due to gravity may influence the local temperature, the change in the mucosal temperature of the greater and lesser curvatures of the stomach when the examinee was changed from the supine to the right and left lateral positions were studied. The result indicated that there was no significant difference in temperature as the position of the body was changed.

The fall in temperature of the gastric mucosa when the stomach is distended beyond a certain degree may be attributed to local ischemia due to decrease in the local blood flow. This local ischemia might cause a derangement of the normal function and a decrease in tissue resistance in that area, and subsequently might predispose that area to certain disease such as carcinoma. From this viewpoint, the reports of ORR (1935), PEACOCK (1943) and TANNENBAUM (1954) are of interest.

ORR (1935) stated that the induction of tumours of the skin in mice by local tar was appreciably accelerated by procedures interfering with the normal

vascular supply. PEACOCK suggested that tissue of normal resistance does not react to a carcinogen unless its equilibrium is in some way disturbed. TANNENBAUM (1954) reported that in animals fed on restricted diets the tumour incidence is strikingly decreased, and the time at which neoplasms appear is delayed. He also pointed out that statistical evidence indicates a similar factor in man, as individuals who are overweight are more likely to die of carcinoma. (General restriction in diet should be clearly distinguished from deficiency diets which may give rise to conditions predisposing to carcinoma.)

The fact that the results of the experiments of ARVBEHETÝ et coll. (1959), DEMLING & WACHSMANN (1961), and others who studied the blood flow of the stomach morphologically or quantitatively, are not in keeping with the present authors' work seems to be due to the circumstance that the experiments of the former were performed in empty state, i.e. in the fasting of the morbid stomach.

### Acknowledgements

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### SUMMARY

The difference in temperature of the gastric mucosa between minimal and other degrees of distension were compared in dogs and human subjects by means of a sensitive intragastric thermistor. Distension of the stomach beyond a certain degree appeared to produce a marked fall in the temperature of the mucosa of the lesser curvature as compared with the greater. The significance of this in the etiology of pathologic conditions, such as carcinoma, in human subjects is discussed.

### ZUSAMMENFASSUNG

Mit Hilfe eines höchstempfindlichen „Thermistor-Thermometer“ wurde die Temperatur der Magenschleimhaut an Menschen und Hunden bei verschiedenen Ausdehnungsgraden des Magens gemessen. Bei grösserer Magenausdehnung zeigte sich ein stärkerer Temperaturfall an der kleinen Krümmung als an der grossen Krümmung. Die Bedeutung dieses Befundes für die Entstehung von Magenerkrankungen, wie z. B. des Karzinomes, wird erörtert.

### RÉSUMÉ

Les différences de température de la muqueuse gastrique suivant que l'estomac est plus ou moins distendu ont été comparées chez l'homme et chez le chien grâce à un « thermistor-thermomètre » intragastrique sensible. La distension de l'estomac au delà d'un certain degré paraît entraîner un abaissement marqué de la température de la muqueuse de la petite courbure par rapport à la grande courbure. Les auteurs étudient l'importance de ce fait dans l'étiologie de certaines maladies telles que le cancer chez l'homme.

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