

In both groups of vagotomized rats the stomachs were dilated and contained food residue in spite of the 40 h isolation period. This food retention is presumably responsible for the gastric secretion obtained from these rats. Food retention, and gastric dilatation are expected following vagotomy due to absence of vagal motor stimulation. Body weight gain over the 14 days of injections was reduced following vagotomy ( $P < 0.05$ ) as compared to the sham operated rats.

**Discussion.** The results presented here show that abdominal vagotomy in rats prevents nicotine-induced gastric secretory stimulation. Chronic oral or parenteral nicotine administration has been shown previously to increase gastric juice volume and acid and pepsin outputs in rats<sup>3,8</sup>. The cause of this nicotine effect is not known but several possible mechanisms may be operating induction of histidine decarboxylase, histamine release, or central vagal activation. We have previously shown<sup>9</sup> that nicotine induces histidine decarboxylase activity and releases histamine in the rat stomach suggesting that these effects are responsible for the gastric secretory stimulation. Support for this concept is provided by KIM and SHORE<sup>10</sup> who reported that vagotomy inhibited or blocked depletion of gastric histamine by reserpine. However, recently GLICK et al.<sup>11</sup> have shown that

vagotomy and pyloroplasty in rats are followed by increased histidine decarboxylase activity in both fasted and fed animals.

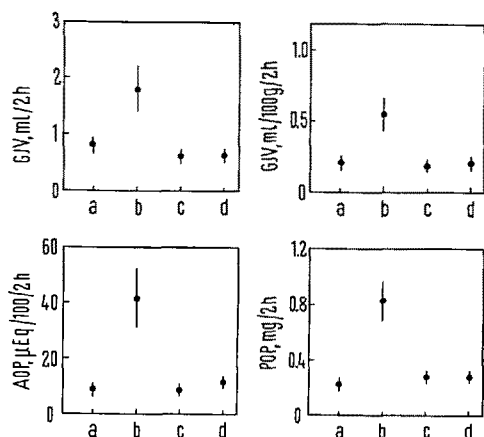
Gastric secretion in the rat is depressed by vagotomy<sup>7</sup>. Failure to show this here in the control rats is probably directly dependent upon the food retained in the stomach due to delayed gastric emptying, a sequelae of vagotomy<sup>12</sup>. Certainly, gastric histamine formation (of similar magnitude to that induced by gastrin or 2 deoxyglucose) has been shown in the rat following gastric distention<sup>13</sup>. The absence of nicotine-induced gastric secretory stimulation following vagotomy is not proof of a primary central vagal activation since the vagus has a 'permissive' effect on gastric secretion; vagotomy reduces the responsiveness of the parietal and chief cells to both histamine and gastrin, and reduces the release of gastrin from the gastrin antrum<sup>14,15,16</sup>.

In view of the deleterious effects of tobacco smoking on peptic ulcer disease in man<sup>1,2</sup>, and the frequency with which vagotomy is performed as part of surgical treatment, the results presented here are of great potential interest<sup>17</sup>.

**Résumé.** La sécrétion gastrique a été mesurée dans des rats mâles avec ligature pylorique de deux heures, après 14 jours d'injections sous-cutanées de nicotine ou de NaCl. Les résultats de l'administration de nicotine furent une augmentation du volume du suc gastrique, de la production d'acide et de la production de pepsine. La vagotomie abdominale bilatérale a prévenu la stimulation gastrique sécréteuse, provoquée par la nicotine.

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Gastric juice volume (GJV) and volume/100 g, acid output (AOP) and pepsin output (POP) in sham-operated and vagotomized rats. Each group is the mean  $\pm$  S.E.M. of 6 rats. Chronic NaCl (2.0 ml 0.85 g/100 ml w/v NaCl/kg) and nicotine (2000  $\mu$ g base/2.0 ml/kg) were given daily s.c. for 14 days commencing on the first post-operative day. Gastric secretion was collected in 2 h pylorus-ligated rats. There are no differences for any parameter between the vagotomized rats injected with NaCl or nicotine. Significant differences in the sham-operated rats are as follows: GJV and GJV/100 g ( $P < 0.025$ ), AOP ( $P < 0.05$ ) and POP ( $P < 0.01$ ). a) Sham operation: chronic NaCl. b) Sham operation: chronic nicotine. c) Vagotomy: chronic NaCl. d) Vagotomy: chronic nicotine.

## Effects of Acute Hypothermia on the Chick ERG

In the previous paper, OOKAWA and TATEISHI<sup>1</sup> reported the relation between gradually decreased body temperature and the electroretinogram (ERG) in the developing chick. Further investigation on the chick's ERG was made under the condition of dark adaptation during rapidly decreased body temperature using the ice-pack, as herein reported.

**Method.** 8 male White Leghorn chicks (Goto-201 line), age 12–16 days after hatching, were used. For the purpose of rapid cooling, the ice-pack was placed on the back at the rectal temperature of 39 to 40°C. Body temperature was checked by the thermister placed in the rectum. Under local anesthesia (Benoxil, Osaka), both eyelids, the nictitating membrane and upper edge of the

<sup>8</sup> J. H. THOMPSON, C. A. SPEZIA and M. ANGULO, Res. Comm. Chem. Path. Pharmac., 7, 721 (1970).

<sup>9</sup> J. H. THOMPSON and D. AURES, Second Conference on Tobacco and Health, American Medical Association, Scottsdale, Arizona, May 1970, p. 3.

<sup>10</sup> K.-S. KIM and P. A. SHORE, J. Pharmac. 141, 321 (1963).

<sup>11</sup> D. GLICK, R. L. SWANK II, D. VON REDLICH and A. SINCLAIR, Gastroenterology 57, 385 (1969).

<sup>12</sup> H. SHAY, S. A. KOMAROV and M. GRUENSTEIN, Arch. Surg. 59, 210 (1949).

<sup>13</sup> G. KAHLSON, D. ROSENGREN and R. THUNBERG, J. Physiol., Lond. 190, 455 (1967).

<sup>14</sup> P. R. F. BELL, Gastroenterology 46, 387 (1964).

<sup>15</sup> S. EMAS and M. I. GROSSMAN, Am. J. Physiol. 212, 1007 (1967).

<sup>16</sup> S. EMAS and M. I. GROSSMAN, Am. J. Physiol. 213, 657 (1967).

<sup>17</sup> Supported in part by a grant from the American Medical Association Education and Research Foundation.

orbit were resected. The ERG was recorded with a platinum-ball electrode attached to a contact lens. The beak and the external meatus of the young chick were fixed with a holder. The reference electrode was a steel needle, inserted into the exposed orbit. The ERG was recorded with a dual-beam oscilloscope (Nihon-Koden, VC7) using a time constant of 2.0 sec. The ERG was simultaneously recorded with a 4-channel ink-writing system (Nihon-Koden) using a time constant of 1.0 sec. The xenon flash lamp (Nihon-Koden, MSP-2R), paralaxed with the optic axis, was used. The distance between the photostimulator and the eye was about 70 cm. The energy of the discharge was 20 J. An upward displacement in the record was taken as positive for corneal electrode. During the recovery phase, the chick was warmed by a thermoregulator.

**Results and discussion.** When the bird was cooled rapidly by an ice-pack and the body temperature had reached about 22°C, the ice-pack was removed, and the chick was warmed by the thermoregulator. Typical ERG

changes are represented in Figure 1 during the rapid cooling. The amplitude of the *b*- and *c*-waves decrease markedly with decreasing body temperature (Figure 1A). One component ( $a_2$ -wave) superimposed on the ascending phase of the *b*-wave appeared at about 30°C of rectal temperature. This component was accentuated when the amplitude of the *b*-wave decreased (Figure 1C). A new negative deflection in the  $a_1$ -wave was found with decreased rectal temperature between 22 and 24°C (Figures 1 and 2). In recovery phase a spitting of the  $a_1$ -wave disappeared (up to 25°C of rectal temperature). The ERG obtained after recovery phase showed normal waveform (Figure 1B).

One component ( $a_2$ -wave) on the *b*-wave might correspond to the  $a_2$ -wave reported by WITKOVSKY<sup>2</sup> and

<sup>1</sup> T. OOKAWA and T. TATEISHI, *Experientia* 26, 277 (1970).

<sup>2</sup> P. WITKOVSKY, *Vision Res.* 3, 341 (1963).

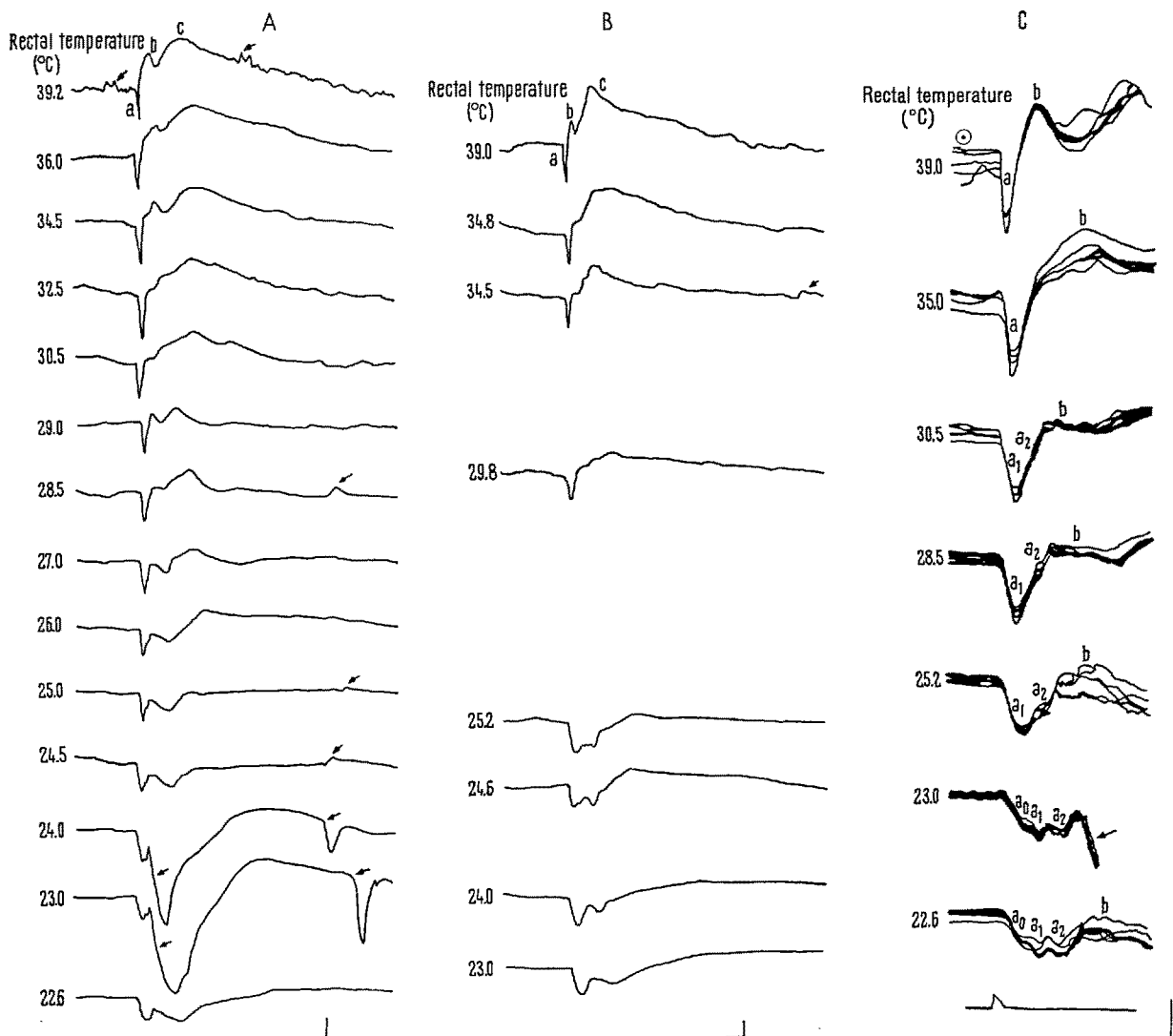


Fig. 1. Effect of rapid cooling on the ERG in a 14-day-old chick, age after hatching. The ERGs (A, B and C) are obtained from 1 chick in a series of experiment. Arrows indicate the artifacts induced by eye movement. Calibration marks: 100 msec, 100  $\mu$ V. An ice-pack was placed on the back when the body temperature was 39.2°C (A). After the body temperature reached about 22°C, the ice-pack was removed. Then, the chick was warmed by the thermoregulator and the ERG was recorded again during the recovery period (B). 5 successive sweeps have been superimposed in C record. ⊗ mark indicates the recovery phase from hypothermia.

OOKAWA and TATEISHI<sup>1</sup>. In addition, the author often observed the 2 components on the *b*-wave during the course of rapidly decreased body temperature as well as gradual cooling<sup>1</sup>. The double *b*-component, which is clearly evidenced during pentobarbital infusion, has been reported on the developing chick<sup>2-4</sup>, and it has photopic and scotopic properties.

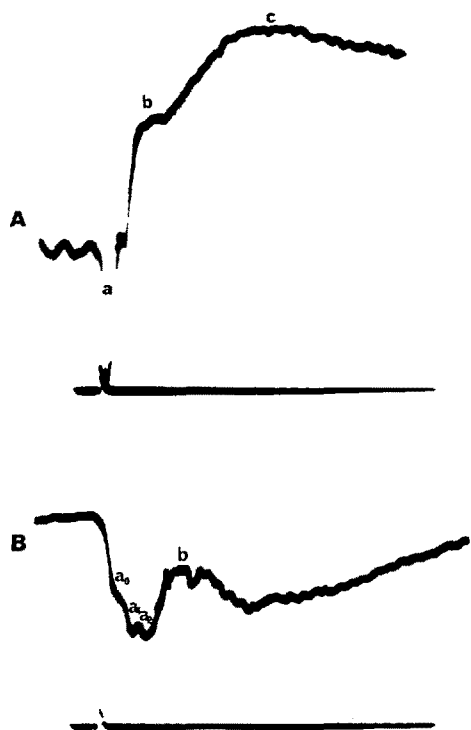


Fig. 2. ERG recordings from a 14-day-old chick at the rectal temperature of 39.2°C (A) and 22.5°C (B), respectively. For the details see the text.

COBB and MORTON<sup>5</sup> found that the human ERG showed several rhythmic wavelets on the ascending phase of the *b*-wave. Similar oscillations have been found in many species, and have been designated as the 'oscillatory potential' by YONEMURA<sup>6</sup>. YONEMURA et al.<sup>6,7</sup> mentioned that the rhythmic wavelets in the bird's ERG are similar in waveform to the oscillatory potential in mammals. The minor components superimposed on the ascending phase of the *b*-wave were also reported on the bird's<sup>3,8</sup> ERG. The *a*<sub>2</sub>-wave and the double *b*-wave component observed in the chick in the present experiment may be comparable to a part of the rhythmic wavelets or the oscillatory potential<sup>9</sup>.

*Zusammenfassung.* Mit der Abnahme der Körpertemperatur verminderte sich gleichzeitig die Amplitude der *b*- und *c*-Wellen des ERG. Zwei kleinere, von den *a*- und *b*-Wellen abgespaltene Komponenten wurden während der Abkühlung festgestellt, während nach Wiederherstellung der Hypothermie das ERG die normale Wellenform registrierte.

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<sup>3</sup> N. W. SCHOLES and E. ROBERTS, *Biochem. Pharmac.* 13, 1319 (1964).

<sup>4</sup> T. OOKAWA, *Poultry Sci.*, in press.

<sup>5</sup> W. A. COBB and H. B. MORTON, *J. Physiol., Lond.* 123, 36 (1954).

<sup>6</sup> D. YONEMURA, Y. MASUDA and M. HATTA, *Jap. J. Physiol.* 13, 129 (1963).

<sup>7</sup> Y. MASUDA, *Acta Soc. ophthal. jap.* 66, 1420 (1962).

<sup>8</sup> H. BRONSCHER and K. TANSLEY, *Experientia* 17, 185 (1961).

<sup>9</sup> K. T. BROWN, *Vision Res.* 8, 633 (1968).

<sup>10</sup> The author is greatly indebted to Prof. I. HANAWA for his valuable advice and encouragement during this study. The author is also indebted to the Goto Hatchery Ind., Gifu City, for supplying the chicks.

## The Ontogenetic Development of the c-Wave in the Chick ERG

In the mouse ERG, there is no appreciable *c*-wave in the youngest animals, whereas it becomes very predominant in the 21st postnatal day<sup>1</sup>. In the youngest chick, the absence of the *c*-wave is reported by WITKOVSKY<sup>2</sup>, though he suggested that one unexplored possibility is that the *c*-wave may be present in older chicks by analogy with findings in rats<sup>1</sup>. Recently, BLOZOVSKI and BLOZOVSKI<sup>3</sup> reported that the *c*-wave appears at 6 days old in the hatched chick. In the present investigation, the authors observed that the *c*-wave was seen just before and after hatching.

*Materials and methods.* 40 White Leghorn chicks (Goto-201 and -202 line) were used for this experiment. The head of the embryos were exposed by a removal of a portion of the shell. The beak and external acoustic meatus of the chick was fixed with a holder. During the ERG recording, body temperature of the bird was kept as normal as possible, using a thermoregulator. The body temperature was checked by a thermistor placed in the rectum (about 1 cm from the cloaca). Under local anesthesia (Benoxil, Osaka), upper and lower eyelids, the nictitating membrane and the upper edge

of the orbit were cut. General anesthesia was not employed in this experiment.

The ERG was recorded with an electrode (platinum-ball) attached to a contact lens, and the reference electrode of a steel needle was inserted into the exposed orbit. The ERG was registered with a dual-beam oscilloscope (Nihon-Koden, VC7) and photographed. The upper beam of the oscilloscope was used for displaying an ERG response and the lower one for the sign of photic stimulus. A comparison was made simultaneously between penwriter records (Nihon-Koden, 4 channel system) and those obtained from the above-mentioned oscilloscope, and it revealed no significant differences in the waveform. The ERG was recorded with a time constant of 2 sec on the oscilloscope and of 1 sec on the penwriter record. An upward displacement in the record was taken

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<sup>2</sup> P. WITKOVSKY, *Vision Res.* 3, 341 (1963).

<sup>3</sup> D. BLOZOVSKI and M. BLOZOVSKI, *J. Physiol., Paris* 60, 33 (1968).