wing depressor. Thus, during flight the leg motor neurons in 6Br4 appear to be driven by both the wing depressor and elevator phases of the flight pattern generator. This establishes a near tonic level of 6Br4 activity, which helps maintain the proper leg posture.

Axons from sensory structures whose activity inhibits flight are located in leg nerve 5 (N_5) (*14*). To test whether these structures also provide the information for switching the GI-evoked motor output, we monitored levator axons in 6Br4.

We removed both pairs of prothoracic and mesothoracic legs, but left the metathoracic legs intact. Under these conditions, intracellular stimulation of a dorsal GI did not elicit motor outputs characteristic of flight (high-frequency levator bursts or wing movements) (Fig. 2A). Rather, the motor responses associated with turning and running were observed. Next, we cut the contralateral N_5 and again stimulated the same GI. Under these conditions, we occasionally observed slight wing movements and perhaps one or two weak bursts in 6Br4 motor neurons. Just as often there was no change. Finally, we cut the ipsilateral N_5 and again stimulated the GI. With both N_5's cut, the GI stimulation resulted in vigorous flight activity indistinguishable from that described above (Fig. 2B).

We have performed this experiment three times, twice with GI-5 and once with GI-7. In each case both N_5's had to be cut before vigorous flight could be evoked. This result suggests that sensory activity in N_5 prevents the dorsal GI's from initiating flight.

To further substantiate the role of activity in N_5, we again stimulated a GI after severing both N_5's, but this time the proximal stump of the ipsilateral N_5 had been drawn into a suction electrode for extracellular stimulation. As before, stimulation of the dorsal GI evoked flight activity. However, delivering four or more stimulus pulses to N_5 as the GI was stimulated prevented flight activity (Fig. 2C). Moreover, once flight was initiated, either by GI stimulation or by wind puffs, it could be immediately terminated by N_5 stimulation.

We conclude that the dorsal GI's are bifunctional interneurons that can initiate either flying or running; which movement occurs depends on whether any leg makes contact when the GI's are excited. During leg contact, sensory input via N_5 either allows or actively promotes one of the motor outputs generated by the GI's—turning and running. Removing this input promotes the alternative behavior—flight. This type of multifunctional interneuron provides an economical way for an animal to control diverse behaviors initiated by similar sensory cues but under different conditions. We expect that similar patterns of neural organization will be found in other systems.

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Thermoregulation in Doves (Columbidae): A Novel Esophageal Heat Exchanger

Abstract. *Key elements in avian thermoregulation at high temperatures are panting and gular flutter. Although these mechanisms are important, they are not sufficient to maintain body temperature below high ambient temperatures in doves. In the Columbidae, evaporative cooling from an inflated esophagus, driven by heat from a vascular plexus, is also essential.*

Many studies of heat stress in birds, including doves, have demonstrated that temperature regulation is accomplished by evaporative water loss from the upper respiratory tract (panting) and, in many species, from the pharynx and anterior esophagus (gular flutter) (*1*). Panting typically precedes, but is replaced by, the more energy-efficient gular flutter in species that use both. While engaged in an unrelated study involving surgery on the cervical region of the ringdove *Streptopelia risoria* (*2*), I noticed that the entire esophagus was rhythmically inflated when the doves were under the heat of surgical lights and that there was an unusual vascular plexus in the integument adjacent to the esophagus. These observations led me to reconsider the mechanisms of temperature regulation in doves.

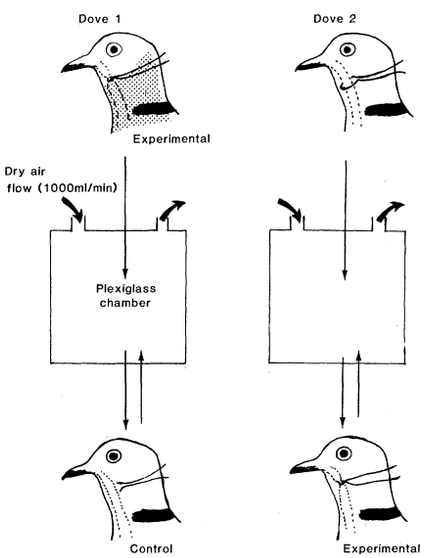

Fig. 1. The experimental design. Both chambers are submerged in a water bath (32° to 44°C). The shaded area on experimental dove 1 represents the vascular plexus in the integument. When inflated, the esophagus underlies this area.

Although the integument of birds in general and doves in particular has been extensively studied (*3*), the circumcervical plexus has been mentioned (*4*) but not described. The plexus is located in the cervical subcutaneous fascia and forms a collar (incomplete at the dorsal midline) around the neck. It extends from at least the hyoid bone cranially to the crop caudally. Arterial supply is by way of the carotid arteries; venous drain-

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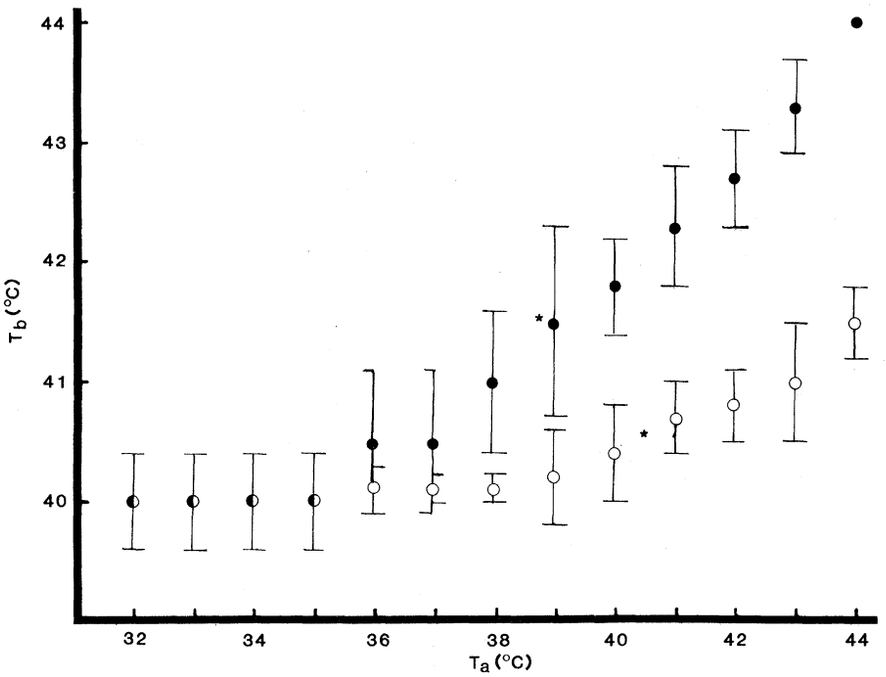

Fig. 2. Mean change in T_b with increasing T_a in doves with esophagi ligated (●) or patent (○). Bars represent 95 percent confidence limits. At $T_a \geq 38$°C, all differences are significant at $P < .01$ (paired Student's t-test). Asterisks indicate the T_a at which each group initiated gular flutter (also significantly different at $P < .01$).

age is by numerous tributaries to the jugular veins. Extensive arteriovenous anastomoses create a dense mat of vessels throughout the area (*5*). I have found this plexus in all doves examined to date (*6*), but not in noncolumbiform birds (*7*). Within doves there is some variation in the distribution of the plexus. For example, in *Columba livia* it extends beyond the hyoid onto the skull and is complete dorsally.

When the dove is stressed by heat, inflation of the esophagus with environmental air may stretch the already thin esophageal membranes and spread them beneath the plexus. The plexus is separated from the esophagus by only a thin sheet of striated muscle and subcutaneous fascia. [The striated muscle is in two layers, one circular and one longitudinal (*8*).] The large, moist surface area of the esophageal mucosa, heated by the blood of the plexus, could provide an ideal arrangement for evaporative cooling.

To test this hypothesis, I recorded cloacal temperatures from doves prepared in the following manner (Fig. 1). Suture thread was looped around the cranial end of the esophagus so that, when tied, the ligature prevented esophageal inflation but did not occlude blood vessels or hinder gular flutter. Each test involved two birds subjected to both experimental and sham procedures. In sham-operated controls, the ligature was not tied (the esophagus could still be inflated); in experimentals the esophagus was ligated. Thus the opposite condition could be established in the same bird by removing or tying the ligature. Experimental and control birds were tested simultaneously by placing each in a separate, sealed, plexiglass chamber supplied with a constant flow of dry air (1000 ml/min). The chambers were submerged in the same water bath, and the temperature of the bath was increased from 32° to 44°C at the rate of about 1°C per minute. Cloacal and chamber temperatures were monitored with Bat 4 thermocouples (Bailey Instrument), and behavior was observed through the transparent covers of the chambers. When the temperature reached 44°C, both birds were removed, the ligature was cut from the experimental dove (now the control) and tied in the control dove (now the experimental bird), and the test was immediately repeated. Four such paired tests were conducted with eight different birds. The procedure controlled for variables such as age, sex, weight, rate of temperature increase, and time of day.

At the starting temperature of 32°C, all the doves were erect, alert, and attentive. At about 37°C, the control birds began a slow, shallow pulsation of the esophagus with the bill closed. This was not panting, since panting does not involve the esophagus, nor was it gular flutter, since flutter does not involve this area of the esophagus and is more rapid. The motion was subtle, somewhat masked by the feathers, and easily overlooked but for the close comparison with ligated doves, which could not do it. At about 38°C, a marked change occurred, with both the control and experimental birds actively panting with open bills. The control birds, however, continued their shallow pulsation of the esophagus. At this and higher temperatures, all the doves erected their auricular feathers. In the control doves, panting was augmented by gular flutter at about 40.5°C, and esophageal pulsation became rapid, deep, and much more evident. The experimental birds, prevented from engaging in esophageal pulsation, began gular flutter sooner than the controls (at about 39°C). As the temperature was increased further, the wings of the doves in both conditions began to droop.

The auricular feathers cover the locus of another vascular plexus, the rete mirabile ophthalmicum, which helps to keep the temperature of the brain lower than that of the body (*9*). Cooling of the arterial blood to the brain may be augmented by the erection of the auricular feathers, increasing airflow over the area and allowing for convective heat loss between the air and the blood. [These feathers are already modified, having widely spaced barbs and reduced barbules—presumably to improve sound penetration, and to direct sound to the external auditory meatus (*3*).]

Mean cloacal temperature in both the control and experimental birds was maintained at 40°C when the ambient temperature (T_a) was less than 38°C (Fig. 2). With $T_a > 38$°C, the experimental birds exhibited a steep increase in body temperature (T_b). With $T_a = 44$°C and their esophagi ligated, none of the eight birds was able to maintain T_b below 44°C. Control birds also showed an increase in T_b with increasing T_a, but the increase was more gradual—and significantly less than when their esophagi were ligated ($P < .01$). The cloacal temperatures of the control birds never reached 44°C.

The ligated doves, unable to inflate their esophagi, seemed to compensate for this loss by initiating gular flutter at lower T_a's than the controls (Fig. 2). Indeed, at the time gular flutter began, the T_b of the experimental birds was already higher than the highest measured in most of the controls.

In conclusion, doves regulate body temperature by evaporative cooling from their inflated esophagus when the ambient temperature is high. This mechanism involves more than the anterior portion of the esophagus used in gular flutter, since the inflation extends caudally as far as the crop. Heat presumably

is transferred from the warm blood of the subcutaneous vascular plexus to the cooled esophageal membranes. This mechanism is coupled with panting, gular flutter, and postural adjustments. The latter mechanisms cannot, alone, maintain body temperature in the ringdove.

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6. Doves examined were *Columba livia*, *Zenaida macroura*, *Leptoptila verreauxi*, and *Goura crista*. The plexus is absent in the sand grouse *Pterocles decoratus*, whose position within the Columbiformes is often disputed.
7. The description of a "nape-cheek rete" in the helmeted guinea fowl *Numida meleagris* by T. M. Crowe and A. A. Crowe [*J. Zool.* **188**, 221 (1979)] is intriguing, but insufficient for comparison with the plexus described here.
8. Both male and female doves inflate the esophagus when cooling. During cooling, the internal choanae appear to be blocked by the tongue (A. S. Gaunt and S. L. L. Gaunt, unpublished observation). How the esophagus is inflated and how the inflation is maintained with an open bill during heat stress is not readily apparent. The striated muscle of the integument may be involved in the pulsations of the inflated esophagus.
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Bladder Cancer and Artificial Sweeteners: A Methodological Issue

The appropriate conclusions to be drawn from the data on artificial sweetener use and bladder cancer reported by Wynder and Stellman (*1*) are quite different from those stated in the report.

The authors say that "these findings are essentially in agreement with results obtained during an earlier phase of the study." In October 1977 [reference 15 in (*1*)] Wynder reported a "crude" relative risk (*RR*) of 1.87 for 260 males with bladder cancer. Later, for a series of 420 cases including the original 260, he found the crude *RR* to be 1.85. When a series of "adjustments" was made the *RR* fell to 1.43. A matched-pair analysis incorporating additional adjustment cut the *RR* further to 1.13. In a later sample of 312 male bladder cancer patients—the study reported in the main text (*1*)—the *RR* is 0.93, on the basis of similarly matched controls. While the adjusted values may be in agreement, the drastic reduction of the *RR* from the values first reported can hardly be called "essential agreement."

There are two explanations of what the statistical adjustments have done here. One is that they have removed a spurious effect. The other is that they have thrown out the baby with the bath water. As is well known, "matched pairs" such as the Miettinen procedure (*2*) used here can produce a serious loss of statistical "power" (ability to detect effects). Miettinen has emphasized this in previous arguments with me (*3*). The Mantel-Haenszel test (*4*) has the same weakness (*5*). This loss of power is especially severe when the covariables are "confounded" (related to each other). While the issues are generally discussed in statistical jargon, the point can be made in plain English.

The problems are especially acute in these data. Cigarette smoking is known to be a major factor here. It is a factor in both the cases and the controls. Thus 61 percent of the controls have cancer, 23 percent at a site which is more closely related to cigarette smoking than bladder cancer is. This confounding is especially troublesome when, as here, the authors propose to study "cocarcinogenesis" (the combined effect of smoking and artificial sweetener). Moreover, they are dealing with a series of hospitals where both the cases and the controls are markedly different in character from one hospital to another.

In a situation like this, matching on confounded variables (for example, hospital and hospital room status, as was done here) can easily match out the effect that is under study or can introduce random effects that will overwhelm weak real effects (when the *RR* is less than 2) (*6*).

The progression of the *RR*'s from 1.87 down to 0.93 strongly suggests that this is exactly what has happened here.

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The downward shift of the adjusted *RR*'s in our earlier study [reference 15 in (*1*)] typifies the classical effect of adjustment for confounding variables in "removing a spurious effect," which is the straightforward explanation we favor for the changes in *RR*. Furthermore, we now know the source of the confounding: it arose from the selection bias that resulted from oversampling controls from lower socioeconomic county and Veterans Administration hospitals, while the cases came largely from upper socioeconomic hospitals, such as Memorial Hospital in New York. On the other hand, it is difficult to see how "overmatching," a rare enough artifact in epidemiological studies of this magnitude, could have affected that study, inasmuch as matching was not employed in the initial selection of controls but only in a post hoc analytical procedure to control for several confounding variables at once.

Our second study (*1*) was carried out in a substantially more homogeneous set of hospitals and with rigorous matching of controls to cases prior to interview. The distributions of usage, quantity, and duration of tabletop sweetener consumption among these controls so closely resemble the corresponding distributions in a much larger and geographically diffuse stratified population sample, as reported by Hoover and Strasser (*2*) in a separate study of bladder cancer and artificial sweetener use, that it would be difficult to maintain that prematching forced an unusual distribution on them; therefore, the possibility that overmatching occurred in our second study is remote.

In all population strata in that study, sweetener use among controls slightly exceeded that among cases; that is why the *RR*'s were all below 1.0. Point estimation of *RR*'s as the ratio of discordant

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