associated with the decrease in survival-time in *T. castaneum* (Figure). These results seem to contradict the conclusion arrived at in *Drosophila* by LINTS and LINTS[7], *viz.*, that 'a prolongation or a shortening of the duration of development results in an increase or in a decrease in the speed of the aging process'. This apparent contradiction may be due to the difficulty of comparing 'normal' life span with life span shortening after irradiation which may be due to lethal radiation syndrome not related to aging[8]. To compare lethality and life span shortening a lower radiation dose should be used. However, the present results indicate that lethality of a species as measured by survival-time is under the control of a genetic system. Most likely such a system has evolved as a result of the forces tending to prolong life and the environmental hazards tending to curtail it[9,10]. Other investigators have also recorded the effect of particular chromosomes on the variability of longevity in *Drosophila*[11].

In some of the populations (Table I) survival-time was found to be positively associated with survival rate (e.g., Kenya and France). This observation suggests the possibility of correlation between the 2 measurements of lethality, i.e., survival rate and survival-time after irradiation. However, inter-population correlation ($r = 0.16$, $P = 0.1$) indicates that this is not the case. Recently, BLAIR and BAXTER[6] have suggested that the 2 types of injury are mutually independent. The lethal injury resulting in reducing survival rate is mainly cytoplasmic, the damage is of a chemical nature and repairable; whereas reduction in survival-time is due to nuclear injury (chromosomal), which in these cases is not repairable. A theory based on loss of cellular function was also suggested by GARTNER[12] to explain radiation induced life span shortening.

Résumé. Après irradiation des pupes âgées de 2 jours, le temps de survie des adultes de *Tribolium castaneum* décroit avec l'âge de la pupation. Cette corrélation génétique négative indique que la vitesse de développement contrôle la létalité qui est maintenue à une valeur intermédiaire, peut-être à cause d'un jeu de forces opposées qui, elles, tendent à allonger ou à raccourcir le temps de survie.

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Table II. Inter-population correlation between fitness parameter and response after X-irradiation (Table I) in *Tribolium castaneum*

Traits	Survival-time (days)	Age-at-pupation (days)	Productivity (%)
Adult emergence (%)[a]	0.16	0.18	0.57
Survival-time	—	−0.87[b]	0.31
Age-at-pupation	—	—	−0.25

[a] After angular transformation. [b] Significant at $P = 0.01$.

[8] H. ATLAN, J. MIQUEL and R. BINNARD, J. Geront. *24*, 1 (1969).
[9] R. R. SOKAL, Science *167*, 1733 (1970).
[10] E. B. EDNEY and R. W. GILL, Nature, Lond. *220*, 281 (1968).
[11] D. MARINKOVIS and J. M. WATTIAUX, Nature, Lond. *216*, 170 (1967).
[12] L. P. GARTNER, Ph. D. thesis, Rutgers University, 1970; Int. J. radiat. Biol. *23*, 23 (1973).
[13] Thanks to Drs. R. R. SOKAL, R. C. BAXTER and F. LINTS for their comments and critical reading of the manuscript.

Intestinal Motility Increased by Tetrodotoxin, Lidocaine, and Procaine

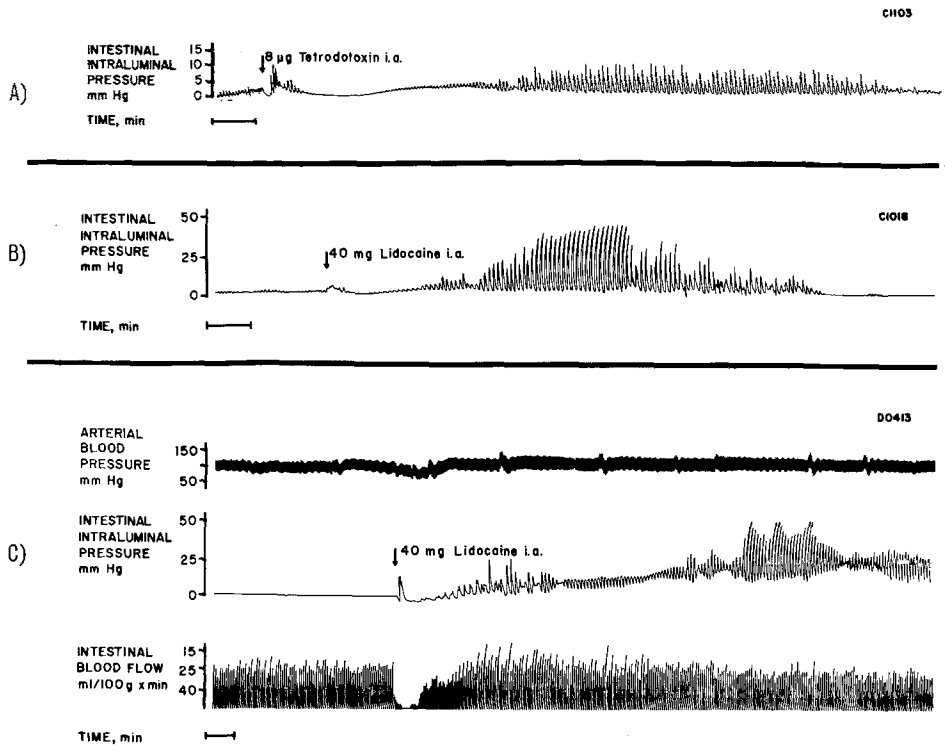
The existence of intrinsic intestinal inhibitory nervous mechanisms has been demonstrated[1]; but the extent to which intestinal motility is a result of myogenic activity and modified by intrinsic excitatory and inhibitory nervous factors is uncertain. An increased mechanical activity in cat intestinal circular muscle has been shown in vitro upon blockade of neuronal discharge in Auerbach's plexus and the possibility of a tonic inhibitory influence on circular muscle activity via intrinsic neurogenic elements has been postulated[2].

This preliminary report describes observations in anesthetized cats where intraarterial injections of the nerve blocking drugs tetrodotoxin, lidocaine, and procaine to the extrinsically denervated intestinal vascular bed increases intestinal motility. It is suggested that this increased motility might be due to a supression of intrinsic nervous inhibition.

Methods. Experiments were performed on 10 cats weighing 2.0–3.8 kg and fasted for 24 h. Anesthesia was induced by ether followed by i.v. chloralose (50–60 mg/kg body wt.). Arterial pressure was recorded via a femoral artery cannula, and the left and right splanchnic nerves were sectioned. In some experiments all nerves running along the superior mesenteric artery were also cut and placed on a bipolar electrode for distal stimulation. A section of jejunum and its lymph nodes, together weighing 15–25 g, were placed in situ into a lucite chamber containing Tyrodes solution maintained at 38°C, and the rest of the intestine was removed. Venous outflow was recorded by means of an optical drop counter and jejunal motility as intraluminal pressure changes via an open-tipped saline filled cannula, both ends of the segment being tied. The following drugs were injected into the superior mesenteric artery via one of its small branches: 0.2–0.5 mg/kg body wt. atropine sulfate (6 cats), 2–6 µg/kg tetrodotoxin (3 cats), 10–20 mg/kg lidocaine chloride-Xylocaine, Astra (8 cats), and 10–20 mg/kg procaine hydrochloride (1 cat).

Results. Intraarterial tetrodotoxin, lidocaine, and procaine consistently induced an increase in rhythmic intestinal motility after a latency of 1–5 min and lasting up to 30 min, depending on the amount of drug given

[1] G. BURNSTOCK, G. CAMPBELL, M. BENNET and M. E. HOLMAN, Int. J. Neuropharmac. *3*, 163 (1964). M. R. BENNET, G. BURNSTOCK and M. E. HOLMAN, J. Physiol., Lond. *182*, 541 (1966). G. BURNSTOCK, G. CAMPBELL and M. J. RAND, J. Physiol., Lond. *182*, 504 (1966). H. W. KOSTERLITZ, Am. J. dig. Dis. *12*, 245 (1967). E. BÜLBRING, Rendic. R. Gastroent. *2*, 197 (1970).
[2] J. D. WOOD and C. L. PROSSER, Physiologist *12*, 398 (1969). J. D. WOOD, Physiologist *13*, 347 (1970). J. D. WOOD, Am. J. Physiol. *219*, 159 (1970).



Recordings from 3 cats illustrating the intestinal motility response to 8 µg tetrodotoxin (A) and 40 mg lidocaine (B), and the effect of 40 mg lidocaine on intestinal motility and blood flow (C). Note in (C) that the height of the blood flow ordinate is inversely proportional to the magnitude of blood flow.

(Figure). The motility increase was seen independent of the degree of spontaneous activity present prior to the drug injection. Intestinal motility was never increased by atropine, nor did atropine or complete sectioning of the extrinsic innervation alter the enhanced motility induced by tetrodotoxin, procaine or lidocaine. These drugs did not affect arterial pressure, and after an initial vasoconstrictor (tetrodotoxin) or vasodilator (lidocaine and procaine) response during drug injection, mean intestinal blood flow remained unchanged during the period of enhanced motility. Furthermore, after tetrodotoxin and lidocaine intestinal sympathetic nerve stimulation produced no vasoconstrictor response and did not affect the drug-induced motility increase.

Discussion. The present observations on the small intestine indicate that tetrodotoxin, lidocaine, and procaine increase intestinal motility independent of the intestine's extrinsic innervation. This effect could reflect a direct excitatory influence of the drugs on visceral smooth muscle, but might also reflect a blockade of intrinsic noncholinergic mechanisms that normally exert a tonic inhibitory influence.

Because transitory periods of either vasodilatation or vasoconstriction were initially induced by these drugs. the increase in motility is probably not a secondary effect to alterations in blood flow. Also, as the initial effects of the drugs on the vascular smooth muscle were quite transient, it seems less likely that the prolonged enhanced motility of the intestine should reflect a direct stimulatory effect of these drugs on the intestinal smooth muscle proper. Rather it is suggested that the motility increase is a consequence of the nerve blocking action of tetrodotoxin, lidocaine, and procaine, causing elimination of a local neurogenic inhibitory influence which normally supresses myogenic activity. Such an interpretation is also supported by recent in vitro studies on intestinal muscle strips[3] demonstrating an excitation of circular muscle by these drugs which is postulated to be mediated by their action on enteric neurons.

Current evidence would then imply that intestinal motor activity is exposed to a continual and variable inhibition via local neurogenic or neurohormonal mechanisms. Thus, what is often described as stimulated intestinal motility may in many cases actually represent a release from intrinsic inhibition. Additional experiments are in progress to elucidate further the nature of these inhibitory mechanisms[4].

Zusammenfassung. In Untersuchungen an Katzen in vivo wird eine bedeutende Zunahme der Dünndarm-Motilität nach lokalen intraarteriellen Injektionen von Tetrodotoxin, Lidocain und Procain demonstriert. Es wird diskutiert, dass diese Wirkung auf der Blockade eines lokalen neurogenen oder neurohormonalen Hemmungsmechanismus beruht, der an der normalen Kontrolle der Darmmotilität beteiligt ist.

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[3] J. D. WOOD, Am. J. Physiol. *222*, 118 (1972).

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