reactivate virus would be of importance not only in understanding the pathogenesis of herpetic lesions, but also in regard to the association of HSV-2 and cervical cancer (*5*, *16*). Our studies demonstrating both the establishment of HSV latency in lumbosacral ganglia after vaginocervical inoculation and the reactivation of the virus after nerve injury raise the possibility that latent HSV "activated" by the presence of a local tumor may travel down sensory nerves and secondarily infect tumor cells. This hypothesis is deserving of further investigation.

M. ANTOINETTE WALZ
Laboratory of Oral Medicine, National Institute of Dental Research, Bethesda, Maryland 20014

RICHARD W. PRICE
Medical Neurology Branch, National Institutes of Neurological Diseases and Stroke, Bethesda, Maryland 20014

ABNER LOUIS NOTKINS
Laboratory of Oral Medicine, National Institute of Dental Research

References and Notes

1. E. W. Goodpasture, *Medicine* **8**, 223 (1929).
2. J. G. Stevens and M. L. Cook, *Science* **173**, 843 (1971); J. G. Stevens, A. B. Nesburn, M. L. Cook, *Nat. New Biol.* **235**, 216 (1972).
3. R. Benda, J. Cinatl, S. Petrovic, J. Roubal, V. Plaisner, *Acta Virol.* **17**, 305 (1973).
4. F. O. Bastian, A. S. Rabson, C. L. Yee, T. S. Tralka, *Science* **178**, 306 (1972); J. R. Baringer and P. Swoveland, *N. Engl. J. Med.* **288**, 648 (1973).
5. A. J. Nahmias and B. Roizman, *N. Engl. J. Med.* **289**, 667, 719, 781 (1973).
6. R. A. Good and B. Campbell, *Proc. Soc. Exp. Biol. Med.* **68**, 82 (1948); J. R. Schmidt and A. F. Rasmussen, *J. Infect. Dis.* **106**, 154 (1960).
7. W. A. Anderson, B. Margruder, E. D. Kilbourne, *Proc. Soc. Exp. Biol. Med.* **107**, 688 (1961); P. R. Laibson and S. Kibrick, *Arch. Ophthalmol.* **75**, 254 (1966).
8. J. G. Stevens and M. L. Cook, in *Virus Research*, C. F. Fox and W. S. Robinson, Eds. (Academic Press, New York, 1973), pp. 437–446.
9. C. A. Carton and E. D. Kilbourne, *N. Engl. J. Med.* **246**, 172 (1952).
10. B. Hampar, A. L. Notkins, M. Mage, M. A. Keehn, *J. Immunol.* **100**, 586 (1968).
11. Two strains of mice were purchased from Jackson Laboratories, Bar Harbor, Maine; strain A was used only for corneal inoculation, while strain BALB/c was used for all other experiments.
12. M. L. Cook and J. G. Stevens, *Infect. Immun.* **7**, 272 (1973).
13. R. H. Kaufman, H. L. Gardner, W. E. Rawls, R. E. Dixon, R. L. Young, *Cancer Res.* **33**, 1446 (1973); H. Stalder, M. N. Oxman, D. M. Dawson, M. J. Levin, *N. Engl. J. Med.* **289**, 1296 (1973).
14. The sensitivity of the homogenization procedure was assessed by reconstruction experiments. When a known amount of HSV-1 was added to uninfected ganglia and homogenized, approximately 80 percent of infectivity was lost.
15. A. R. Lieberman, *Int. Rev. Neurobiol.* **14**, 49 (1971); E. Pannese, *Z. Zellforsch.* **63**, 568 (1964); R. W. Leech, *Neurology* **17**, 349 (1967).
16. S. Sprecher-Goldberger, L. Thiry, I. Gould, Y. Fassin, C. Gompel, *Am. J. Epidemiol.* **97**, 103 (1973); W. E. Rawls, E. Adam, J. L. Melnick, *Cancer Res.* **33**, 1477 (1973).
17. We acknowledge the assistance of C. Wohlenberg.

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Taurine Concentrations in Congestive Heart Failure

Abstract. *The concentration of taurine in the left ventricular muscle of hearts of patients who died of chronic congestive heart failure was twice that of patients who died of other causes and had no cardiac pathology. There was no corresponding difference in taurine concentrations in aortic tissue between the two groups. Stress-induced hypertension in rats also led to an increase in taurine concentration in the heart, whereas that in skeletal muscle and brain showed no significant alteration when compared to unstressed animals. Spontaneously hypertensive rats, of the Wistar-derived Okamato strain, showed a similar elevation in cardiac taurine compared to age-matched control Wistar rats.*

Taurine (2-aminoethanesulfonic acid) is abundantly present in mammalian heart, yet its possible function there is undefined despite much speculation. Reed and Welty postulated that it has a role in ion movement in the heart (*1*), and reported that taurine reverses digoxin and epinephrine-induced arrhythmias (*2*). It increases the retention of calcium by the heart (*3*), and potentiates the inotropic effect of strophanthin-K (*4*). Since little is known about taurine in human heart, or how it is affected by drug treatment or disease states, we undertook the study described below.

The content of taurine in the left ventricle of the heart was compared in patients who died from congestive heart failure to patients who died from other causes not involving myocardial pathology (Table 1, groups 1 and 2). Patients with congestive heart failure had twice the taurine content of other patients. Samples of heart tissue received varied widely in terms of degree of hydration, fibrous nature, and percentage of fat content, making it desirable to report in several ways the specific concentrations of taurine.

Patients were diagnosed as having had congestive heart failure if they had clinical signs and symptoms of chronic congestive heart failure, secondary to rheumatic or atherosclerotic heart disease, of not less than a week and more typically of months or years duration. These diagnoses were made independently by clinicians and were confirmed by pathologists at autopsy. For most samples, analyses were performed without any knowledge on our part of the patient's medical history. Subjects less than 10 years old were excluded from the study because of the high taurine levels in the newborn (*5*) and in young children. Also excluded from groups 1 and 2 were subjects who had had any myocardial abnormality not clearly definable as chronic congestive heart failure. Infarcted or scarred muscle was not included in samples taken for analysis. All the subjects having congestive heart failure were males, but even if females were excluded from the control group, taurine concentrations in the congestive heart failure group were still significantly higher (group 3 compared to group 1).

The age at death for congestive heart failure subjects (group 1) ranged from 53 to 88 years, whereas for the controls (group 2) it ranged from 12 to 77 years. The mean age of death for group 1 was 10 years higher than that for group 2. However, a regression analysis showed no correlation between taurine concentration and age (correlation coefficient .08). This indicates that the difference in taurine concentration between group 1 and group 2 is not due to the age difference. There was no difference in

Table 1. Taurine content of left ventricular muscle of human heart. In a number of cases the sample was too fibrous and caused too much light scattering to permit a protein determination. "Wet weight" refers to sample weight as received from the morgue. Acid precipitate refers to material precipitated by trichloroacetic acid, after homogenization of the sample. Protein was determined by the biuret procedure (*9*). Numbers in parentheses are numbers of samples. Data are reported as means ± S.E.M. The significance of differences was measured by Student's *t*-test, groups 2 and 3 being compared to group 1.

Group	Sex	Age (years)	Taurine (μmole/g)		
			Wet weight	Acid precipitate	Protein
		Congestive heart failure			
1	M	65.8 ± 4.5	13.2 ± 2.1 (13)	36.7 ± 3.3 (13)	47.3 ± 8.4 (9)
		No congestive heart failure			
2	M and F	55.8 ± 3.7	5.6 ± 0.5* (23)	18.2 ± 1.6* (23)	23.6 ± 3.5† (18)
3	M	65.3 ± 3.3	5.9 ± 1.0 (8)	17.4 ± 2.9* (8)	17.4 ± 3.5‡ (7)

* $P < .001$; † $P < .005$; ‡ $P < .025$.

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Table 2. Ratios of taurine to protein in stress-induced hypertensive male rats. The group size for brain is 3, and for other groups 5.

Group	Heart weight (g)	Systolic blood pressure (mm-Hg)	Taurine (μmole per gram of protein)		
			Heart	Muscle	Brain
Stress-induced hypertension	1.33 ± 0.06*	161 ± 3*	224 ± 10*†	41.1 ± 1.9	16.1 ± 2.3
Stress-induced mild hypertension	1.32 ± 0.05*	138 ± 2*	172 ± 12	45.5 ± 9.2	
Unstressed	1.15 ± 0.04	122 ± 2	166 ± 11	52.3 ± 9.3	18.2 ± 1.2

* $P < .05$ when compared to unstressed group. † $P < .025$ when compared to mildly hypertensive group.

age at death between group 1 and group 3.

Samples of aorta from patients with or without congestive heart failure showed no difference in taurine concentrations. In congestive heart failure, the mean value was 5.3 ± 0.8 μmole per gram of material precipitable by trichloroacetic acid ± standard error for six samples; the mean for the controls was 4.3 ± 0.3 μmole (six samples). This suggests that the increase in ventricular taurine found in congestive heart failure may be specific to the heart, and is not part of a general increase in body taurine.

Hypertensive rats show an increase in the ratio of taurine to protein in the heart similar to that observed in human congestive heart failure. Rats exposed to environmental stress (loud noises, flashing lights, and cage oscillation) develop hypertension (*6*). Table 2 shows that mild and marked degrees of hypertension produced in this way are associated with cardiac hypertrophy. In addition, the markedly hypertensive animals show an elevation of taurine relative to protein in the heart. There is no corresponding alteration in taurine in skeletal muscle or brain. The ratio of taurine to protein is also increased in the hearts of spontaneously hypertensive male rats of the Okamoto strain (*7*) by comparison with age-matched Wistar controls. In hypertensive rats the mean concentration of taurine in the heart was 351 ± 44 μmole per gram of protein (seven animals) compared to 163 ± 12 μmole in the controls (seven animals, Student's *t*-test between the two groups, $P < .001$). Taurine concentrations have also been shown to be increased in the right ventricles of dogs with experimentally induced right ventricular failure caused by constriction of the pulmonary artery (*8*).

The analyses for taurine was performed by homogenization of the tissue sample in five parts of water. A sample was taken for protein determination (*9*). One volume of 20 percent trichloroacetic acid was added to the remainder, and the precipitated protein was separated by centrifugation. The supernatant was extracted with ether to remove the trichloroacetic acid, and the aqueous layer was taken to dryness on a rotary evaporator. The residue was refluxed with 5 ml of 6*N* HCl for 15 minutes to hydrolyze phosphoethanolamine, which otherwise interferes with the taurine assay. The sample was evaporated to dryness and the residue was taken up in 1 ml of water and layered on an ion-exchange column containing AG 50 H^+ cation exchange resin (5.5 by 0.7 cm) layered over an equal quantity of AG 1 Cl^- anion exchange resin. The taurine was eluted from the column with water and assayed by a ninhydrin procedure (*10*). The loss of taurine was corrected as described (*11*) by the recovery of tracer amounts of [^{14}C]taurine added at the beginning of the procedure. Certain samples of human tissue were analyzed again to determine whether there were differences between sites. The repeated analyses fell into two groups. One group (six samples) differed by an average of 0.5 ± 0.1 μmole of taurine per gram (wet weight) from the first analysis, but another group (four samples) showed a variation of 3.9 ± 0.7 μmole. Analyses of samples frozen for as long as a year have shown no differences in taurine concentrations, demonstrating that taurine in autopsy samples is stable.

Nothing explicitly is known about the function or functions of taurine in the heart. The ultimate significance of our observation that taurine concentrations are elevated in human congestive heart failure cannot be assessed at present. It may be involved in the pathophysiology of heart disease or it may be a secondary and unimportant consequence of the disease. The observation is of interest, however, in that chemical changes have rarely been demonstrated in human heart failure.

RYAN HUXTABLE
RUBIN BRESSLER
Department of Pharmacology, Arizona Medical Center, Tucson 85721

References and Notes

1. W. O. Read and J. D. Welty, in *Electrolytes and Cardiovascular Disease*, E. Bajusz, Ed. (Karger, New York, 1965), pp. 70–85.
2. ———, *J. Pharmacol. Exp. Ther.* **139**, 283 (1963); J. D. Welty and W. O. Read, *ibid.* **144**, 110 (1964).
3. P. Dolara, A. Agresti, A. Giotti, G. Pasquini, *Eur. J. Pharmacol.* **24**, 352 (1973).
4. A. Guidotti, G. Badiani, A. Giotti, *Pharmacol. Res. Commun.* **3**, 29 (1971).
5. N. Okumura, S. Otsuki, A. Kameyama, *J. Biochem.* **47**, 315 (1960).
6. W. J. Hudak and J. P. Buckley, *J. Pharm. Sci.* **50**, 263 (1961).
7. K. Okamoto and K. Aoki, *Jap. Circ. J.* **27**, 282 (1963).
8. M. B. Peterson, R. J. Mead, J. D. Welty, *J. Mol. Cell. Cardiol.* **5**, 139 (1973).
9. A. G. Gornall, C. J. Bardawill, M. M. David, *J. Biol. Chem.* **177**, 571 (1949).
10. W. Troll and R. K. Cannon, *ibid.* **203**, 803 (1953).
11. R. Huxtable and R. Bressler, *J. Nutr.* **102**, 805 (1972).
12. Supported by PHS grant HL-13636. We thank members of the pathology department, Arizona Medical Center, for making autopsy material available, and Drs. Perhatch and Amer of Mead Johnson Research Center for animal samples.

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Thyroid Hormone Action: In vitro Demonstration of Putative Receptors in Isolated Nuclei and Soluble Nuclear Extracts

Abstract. *Saturable binding activities for triiodothyronine were demonstrated in vitro with isolated nuclei and soluble nuclear extracts of rat liver, kidney, and cultured GH_1 cells. The binding activity can be extracted from nuclei in soluble form with no significant change in hormone affinity and has properties of a nonhistone protein.*

Thyroid hormones appear to regulate a wide variety of biological processes in higher organisms, varying from oxygen consumption to cell growth and differentiation. Studies of thyroid hormone effects on amphibian metamorphosis and RNA polymerase activity in rat liver suggest that the diverse biological effects of these hormones may result from a primary effect on the control of gene expression (*1*).

We have demonstrated that triiodo-