lence for deepening of a mixed layer.

With the estimates of τ_0 and ν_e, it is now possible to evaluate certain parameters in the CL model. The Langmuir number (*6*) is given by $La = (\nu_e k/Au_*)(\nu_e/\sigma)^{1/2}$, where A is the wave amplitude, k is the wave number of the surface waves, and $u_* = (\tau_0/\rho)^{1/2}$ is the friction velocity. For this experiment La = 0.59, compared to the value La = 0.01 used in the computations of (*6*) and (*7*). A smaller value of La implies faster growth of the cells. In the CL model the time scale for the growth of the cells is given by $T_d = (\nu_e\sigma)^{1/2}/\sigma u_* Ak$, and it is suggested (*6, 7*) that a time of 10 T_d is required for full development of the cells. For the experimental data it is found that T_d would be 29 seconds. The experimental response time for V^* was T = 12 seconds, a somewhat faster response than predicted by the theory, although there is some uncertainty in the value of ν_e and other assumptions.

The observed circulations are in general agreement with the CL model in that both wind and waves were necessary for the formation of the LC's and that the upwelling occurred beneath the traces of the wave crest intersections, as shown in Fig. 2. Trial reversals of the wind direction clearly reversed the circulation of the cells, a result that is also in agreement with the CL model, since the sign of the vorticity due to the wind stress was reversed. It is conceivable, however, that some wind-wave-turbulence interaction other than that of the CL model may also produce longitudinal rolls, and further experiments over a wide range of parameters will be required to definitively test the mathematical model.

Apart from the comparison with theory, the experiments have definitely shown that a light wind blowing over a pattern of waves of rather small amplitude can generate well-organized circulations. The characteristic time for the growth of surface cells in this case was about 18 wave periods. In a more complex pattern of waves it should be expected that circulations of many scales will be generated, perhaps with a dominant scale determined by the pattern of the dominant waves. Larger, secondary scales may then form by nonlinear interactions of the primary LC's and, as emphasized in (*1*), the larger scales may grow to dominate the entire pattern of flow. An alternative progression of events may occur through the instability recognized by Craik (*8*) and amplified by Leibovich (*9*).

Since the mechanism leading to the generation of LC's has not previously been well understood or well demonstrated, there has been a tendency for casual observers of the problem to equate LC's with thermal convective rolls, cloud bands, rolls in the laminar sublayer of turbulent boundary layers, or other mechanisms known to produce two-dimensional structures. It is now clear, however, that the interaction of the waves and the wind produces a distinctly different mechanism for the formation of longitudinal rolls, one that cannot be ignored by any serious student of the mixed layers of lakes and oceans.

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Left Ventricular Receptors Inhibit Brain Serotonin Neurons During Coronary Artery Occlusion

Abstract. *Acute coronary artery ligation in pargyline-treated rats decreased serotonin and increased 5-hydroxyindoleacetic acid in the medulla and posterior hypothalamus. Lidocaine applied topically to the left ventricle completely prevented these alterations. No changes in serotonin were observed in the other brain regions examined. These data suggest a reflex inhibition of bulbar and hypothalamic serotonergic nerves by left ventricular receptors following acute coronary artery occlusion in the rat.*

Experimental coronary artery occlusion may result in cardio-cardiac reflex alterations in autonomic nerve traffic (*1–4*). Afferent signals may arise in either mechano- or chemoreceptors (*4–7*) in the left ventricular myocardium and travel through vagal fibers (*1, 5*) or sympathetic afferents, or both (*3, 4*), to the central nervous system. Neural integration has been reported at both spinal (*3*) and supraspinal levels (*1, 7*). The resultant alterations in efferent autonomic nerve traffic are important both as determinants of hemodynamic state (*1–3, 8*) and as contributors to the enhanced vulnerability to lethal arrhythmias (*9*) accompanying acute myocardial infarction. The identification of neurotransmitters that participate in these reflexes is of therapeutic importance.

Nerve fibers, containing the neurotransmitter serotonin, have been demonstrated in brain regions (*10, 11*) believed to be important in cardiovascular control (*12*). Recent studies have supported a role for central serotonergic neurons in blood pressure regulation (*13*) and in the regulation of cardiac autonomic tone (*14*). The present studies were performed to determine whether central serotonergic neurons participate in the reflex alterations in neural activity associated with acute myocardial ischemia.

Three groups of six rats were exam-

Table 1. Serotonin concentration in rat brain regions. Results are expressed as mean ± standard error.

Region	Control (μg/g)	Ligated (μg/g)	Lidocaine-ligated (μg/g)
Thoracic cord	0.96 ± 0.03	1.02 ± 0.02	1.00 ± 0.04
Medulla	2.77 ± 0.13	2.44 ± 0.07*	2.90 ± 0.03
Pons-midbrain	2.69 ± 0.02	2.57 ± 0.13	2.69 ± 0.03
Posterior hypothalamus	2.92 ± 0.04	2.64 ± 0.06†	3.16 ± 0.10
Anterior hypothalamus	2.88 ± 0.11	3.06 ± 0.06	2.99 ± 0.11
Thalamus	2.14 ± 0.10	2.24 ± 0.05	2.21 ± 0.06
Cerebellum	0.49 ± 0.01	0.50 ± 0.01	0.50 ± 0.01

*Different from control at $P < .05$ and from lidocaine-ligated at $P < .001$. †Different from control at $P < .005$ and from lidocaine-ligated at $P < .001$ (Student's t-test was used).

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ined (*15*). In control animals the proximal portion of the left coronary artery was exposed and a suture needle passed under and removed. In a second group of rats a suture was passed under this portion of the artery and tied. A third group was treated in exactly the same manner as the ligated group except that, just prior to ligation, 2 percent lidocaine hydrochloride was administered topically to the left ventricle by means of a sterile cotton swab. The accumulation of serotonin and the decline of 5-hydroxyindoleacetic acid (5-HIAA), after monoamine oxidase inhibition, provides a reflection of serotonin turnover, a biochemical index of serotonergic neural activity (*16*). Thus we gave pargyline (75 mg/kg by intraperitoneal injection), a monoamine oxidase inhibitor, to each rat 1 minute before ligation or sham ligation. The rats were decapitated 90 minutes after ligation. Serotonin and 5-HIAA were measured (*17*) in thoracic cord, medulla, pons-midbrain, posterior hypothalamus, anterior hypothalamus, thalamus, and cerebellum.

Table 2. Concentration of 5-HIAA in rat brain regions. Results are expressed as mean ± standard error.

Region	Control (μg/g)	Ligated (μg/g)	Lidocaine-ligated (μg/g)
Thoracic cord	0.12 ± 0.01	0.12 ± 0.02	0.13 ± 0.01
Medulla	0.39 ± 0.04	0.46 ± 0.01*	0.34 ± 0.03
Pons-midbrain	0.57 ± 0.03	0.64 ± 0.04	0.62 ± 0.04
Posterior hypothalamus	0.37 ± 0.02	0.47 ± 0.02†	0.33 ± 0.01
Anterior hypothalamus	0.43 ± 0.02	0.38 ± 0.03	0.47 ± 0.03
Thalamus	0.37 ± 0.02	0.43 ± 0.02‡	0.43 ± 0.03‡
Cerebellum	0.09 ± 0.003	0.08 ± 0.003	0.09 ± 0.005

*Different from lidocaine-ligated at $P < .01$. †Different from control at $P < .01$ and from lidocaine-ligated at $P < .001$. ‡Different from control at $P < .05$ (Student's t-test was used).

Table 3. Hemodynamic data obtained from rats before and after coronary artery ligation. The blood pressure and heart rate of control rats, before and after sham operation, were identical to those tabulated under "Preligation." Postligation values represent maximum responses. Results are expressed as mean ± standard error.

Group	Mean arterial blood pressure (mm-Hg)		Heart rate (beat/min)	
	Preligation	Postligation	Preligation	Postligation
Untreated	156 ± 8	88 ± 10	339 ± 10	151 ± 30
Lidocaine-treated	152 ± 7	96 ± 10	341 ± 13	254 ± 10*

*Different from untreated at $P < .01$ (Student's t-test).

Coronary artery ligation resulted in a decrease in serotonin accumulation in the medulla and posterior hypothalamus (Table 1). The latter area also showed a smaller decrease in 5-HIAA concentration than in controls (Table 2). A smaller decrease in 5-HIAA was also seen in the thalamus. Ligation had no significant effect on the concentration of serotonin in any of the other brain regions studied. A decrease in serotonin accumulation and a lesser decline in 5-HIAA is consistent with a decrease in serotonergic neural activity (*16*). Thus it appears that acute coronary artery ligation, in the rat, leads to a decrease in the activity of bulbar and hypothalamic serotonergic nerves. The principal serotonergic input to the posterior hypothalamus is by fibers, traveling in the median forebrain bundle, which originate in serotonergic cell bodies localized in the raphe nuclei of the brainstem (*10, 11*). The majority of these nuclei lie in the midbrain and rostral pons. Recent evidence, however, suggests that a significant number of serotonergic fibers innervating the hypothalamus may originate in nuclei in more caudal brain regions (*11*). Thus, it is possible that our observations reflect a diminution in neural activity in a discrete bulbohypothalamic serotonergic pathway.

The reflex changes in autonomic nerve traffic to the heart and blood vessels after acute coronary occlusion appear to be mediated by afferent signals originating in both the heart and vascular tree. In order to determine whether the inhibition of central serotonin metabolism originates in receptors in the affected ventricle, we applied topical lidocaine to the left ventricles of one group of rats at the time of occlusion. Topical lidocaine treatment completely abolished the alterations in both central serotonin and 5-HIAA concentrations induced by ligation (Tables 1 and 2). These data suggest that an afferent signal originating in the ischemic left ventricle inhibited bulbar and hypothalamic serotonergic activity.

Immediately after left coronary artery ligation, heart rate slowed and blood pressure fell (Table 3). The maximum response occurred in 2 to 4 minutes; recovery of heart rate but not blood pressure occurred during the following 10 minutes. Similar alterations in heart rate and blood pressure have been reported to occur after coronary artery occlusion in other animal models (*1, 8*). The rats treated with topical cardiac lidocaine exhibited a significantly smaller peak decrease in heart rate but showed an identical recovery phase and blood pressure response (Table 3). It appeared that the afferent signal partially responsible for the postocclusion bradycardia also originated in the left ventricle.

There is an apparent parallelism between the alterations in heart rate and central serotonin metabolism. However, the difference in heart rate between ligated and lidocaine-ligated groups was lost with the relatively rapid recovery of heart rate to control levels in both groups. On the other hand, our data regarding brain serotonin would be expected to reflect alterations in regional serotonin metabolism over the first 90 minutes following ligation. It is possible that other central pathways [for example, bulbospinal catecholaminergic neurons responding to baroreceptor afferents (*1, 18*)] mediate the efferent signal for the recovery of heart rate in spite of the continuation of the serotonin-inhibitory afferent signal. Our experiments were not designed to delineate precisely the efferent cardiovascular autonomic activity mediated by central serotonin in the setting of myocardial ischemia.

We conclude that there is a reflex inhibition of bulbar and hypothalamic serotonergic nerves after left coronary artery ligation in the rat. The afferent limb of this reflex appears to arise from receptors in the ischemic left ventricle.

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Cryoprecipitate Reversal of Opsonic α_2-Surface Binding Glycoprotein Deficiency in Septic Surgical and Trauma Patients

Abstract. *Human opsonic α_2-surface binding glyoprotein (α_2SB-glycoprotein), a molecule having immunologic identity with an amino acid composition similar to cold-insoluble globulin, is concentrated in a cryoprecipitate of plasma. Septic surgical and trauma patients manifesting opsonic α_2SB-glycoprotein deficiency and associated reticuloendothelial system dysfunction were treated by intravenous infusion of cryoprecipitate. This therapy restored circulating bioreactive and immunoreactive opsonin and improved their septicemia, pulmonary insufficiency, and duration of recovery. Cryoprecipitate infusion may offer a new approach to the treatment of septic injured patients in preventing multiple organ failure; measurement of immunoreactive serum opsonic α_2SB-glycoprotein may provide a noninvasive index of reticuloendothelial system function and patient status during severe sepsis that follows trauma.*

Septic complications after multiple trauma, burn injury, and major surgery are a major clinical problem despite advances in surgical techniques, antimicrobial therapy, and patient monitoring (*1, 2*). Resistance to septicemia involves both nonspecific and specific factors; however, recent studies have emphasized the function of the reticuloendothelial system (RES) as a determinant of survival after severe trauma and shock (*3–5*). The RES is depressed after major surgery (*4–7*), blunt trauma (*4, 5, 8*), burn injury (*4, 5*), and hemorrhage (*4, 5*); and therapeutic techniques to reverse systemic RES failure have not been developed.

Previous studies (*4, 9–11*) have implicated opsonic α_2-surface binding glycoprotein (α_2SB-glycoprotein) as a key determinant of RES phagocytic function. The amount of this protein in the serum is decreased after trauma, a decrease which contributes to the observed RES phagocytic depression (*4*). Reticuloendothelial (RE) cells in the liver and spleen remove bacteria, microaggregates of fibrin, injured platelets, denatured protein, and immune complexes from the blood, and thus serve as a selective filter or clearance mechanism to protect the pulmonary and systemic vascular beds from potential microembolization and injury (*3, 4*). Immunologic and biochemical analyses of purified human opsonic α_2-SB-glycoprotein (*12–14*) have revealed that it is identical to cold-insoluble globulin or plasma fibronectin, a major protein fraction recoverable in human plasma cryoprecipitate.

In our study, we intravenously infused fresh plasma cryoprecipitate into severely ill, septic surgical and trauma patients with marked opsonic deficiency and RES failure, and tested for augmented systemic defense against persistent septicemia and associated pulmonary insufficiency. Opsonic replacement was quantified by bioassay (*5, 15*) and immunoassay (*10, 13*), and the clinical course of the patients before and after cryoprecipitate therapy was monitored.

The bioassay for opsonic activity in serum was measured relative to Kupffer cell phagocytosis by liver slice assay (*6, 8, 15*) with the gelatinized ^{131}I-RE test lipid emulsion and heparinized serum (*5, 9, 14, 15*). Immunoreactive opsonic α_2SB-glycoprotein from serum was measured in micrograms per milliliter by electroimmunoassay or rocket immunoelectrophoresis (*10, 13, 16*) with monospecific antiserum (*9, 11, 13*). Isolation of the protein from serum involves a series of steps (*9, 11, 13*), including ammonium sulfate fractionation, high-voltage free-flow electrophoresis, and Sepharose 4B gel filtration. An alternative purification with a gelatin-Sepharose affinity column in the presence of mercaptoethanol is also effective. Immunochemical purity of the protein was tested by electroimmunoassay with unabsorbed, polyspecific antiserum, and homogeneity was ascertained by gradient polyacrylamide gel electrophoresis (*10, 11, 13*).

Cryoprecipitate (*17*) was intravenously infused as a continuous dose throughout a 60-minute interval. Both biologically active and immunoreactive serum opsonic α_2SB-glycoprotein were measured before and at least at 1/2 4, and 24 hours after infusion. Circulating white blood cell levels, body temperature, blood and tissue fluid bacterial cultures, arterial blood gas determinations, and standard cardiopulmonary measurements were recorded.

Patients displayed elevated α_2SB-glycoprotein in their serum during the 1/2- to 4-hour interval after cryoprecipitate infusion. The three patients presented in this study (*18–20*) showed an average increase in immunoreactive opsonic protein of 94 μg/ml above preinfusion levels by 30 minutes after treatment. By 4 hours, the average level of α_2SB-glycoprotein in the serum, determined by electroimmunoassay increased by (on the average) 172 μg/ml. Patient 2 (Fig. 1) experienced a phase of rapid serum depletion

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