may be further support for a causal relation, as the father has had an unusual neurologic illness for nearly 30 years, originally diagnosed as "myositis." The blood of the patient's mother had no effect when tested against the phosphotransferase.

Of the total thiamine in the body, about 80 percent is in the form of TPP, about 10 percent is TTP, and the remainder is thiamine monophosphate (TMP) and thiamine (*6*). The coenzyme role of TPP is well documented, but virtually nothing is known about the function of TTP except for a report that it may be involved in the binding of TPP to an apoenzyme (*7*). However, in this study the activity of the three TPP-dependent enzymes in nervous tissue (pyruvate dehydrogenase, α-ketoglutarate dehydrogenase, and transketolase) was the same in the brain of the patient as the normal brain sample (*8*). A considerable amount of evidence has been accumulating to support the thesis that thiamine in some still unknown form has a specific role in ion movements in nervous tissue that is independent of its role as a coenzyme (*9*). It is thus conceivable that the neurophysiologically active form of the vitamin is TTP and that in SNE a factor is elaborated that inhibits the synthesis of TTP, the lack of which is ultimately reflected in the peculiar neurologic symptomatology that characterizes this condition.

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Traube-Hering Waves in the Pulmonary Circulation of the Dog

Abstract. *Although the pulmonary blood vessels receive an ample supply of nerves, it has been difficult to prove that these nerves operate in the regulation of the pulmonary circulation. In the present study, using the isolated lobe of the lung perfused in situ, waves in pulmonary arterial pressure were induced and were shown, as in the case of Traube-Hering waves in the systemic circulation, to be nervous in origin.*

The systemic arterial blood pressure is held remarkably constant by an elaborate system of control mechanisms. However, under certain experimental conditions, phasic and continuing fluctuations in systemic blood pressure occur either spontaneously or can be induced (*1*). One type of regular oscillations, synchronous with respiratory activity, was first described by Traube in 1865 (*2*) and subsequently by Hering (*3*). It has since been shown that these waves are nervous in origin and represent the phasic influence of respiratory activity on arterial and arteriolar tone produced by way of the vasomotor nerves (*4*).

The role of nerves in the control of the pulmonary circulation has been disputed for almost 100 years (*5*). If Traube-Hering waves did occur in the pulmonary circulation, they would constitute strong evidence in favor of a significant nervous control of the pulmonary blood vessels. However, waves in pulmonary arterial blood pressure have rarely been observed (*6*), and the opportunity for studying their genesis has been confined to the intact animal in which oscillations in systemic blood pressure coexisted (*7*). In a recent study in our laboratory (*8*), both systemic and pulmonary vasomotor waves were produced. However, it was not possible to prove that the vasomotor nerves to the pulmonary vessels were responsible for the genesis of these waves.

We have recently developed an isolated-lung preparation which proved to be ideal to settle the problem. This preparation makes it possible to perfuse, *in situ*, one lobe of a dog lung, by using levels and patterns of blood pressure and flow which approximate those which occur under natural conditions (Fig. 1). For the present experiments, a pulsatile flow pump was used to perfuse the left lower lobe with autologous blood. A tracheal divider separated the airway to the left lower lobe from the other airways; both sides were ventilated separately by constant-volume pumps. Airway pressure was recorded throughout the entire experiment and remained unchanged. The pulmonary artery and vein of the left lower lobe were cannulated with rigid L-shaped polyethylene tubing, and needles with three side holes (distal end obliterated) were passed through the walls of the cannula and connected to a strain gauge (Statham P23Db) to monitor blood pressure. Instantaneous flow was measured with a gated sine wave electromagnetic flow meter (Biotronex) by using cannulating transducers. The pulmonary vein cannula was connected to a water-jacketed blood reservoir which was kept at 37° to 38°C by a thermostated water bath. The level of the reservoir was monitored as hydrostatic pressure by a tap near the bottom which was connected to a Statham strain gauge (P23A) and calibrated for volume. In this preparation, stimulation of the sympathetic nerves to the lungs by way of the stellate ganglion elicits a characteristic pressor response, that is, an increase in systolic pressure but not in diastolic pressure (*9*).

With this preparation, synchronous fluctuations of systemic and pulmonary arterial blood pressure were induced during apneic oxygenation (by stopping, after preoxygenation, both mechanical

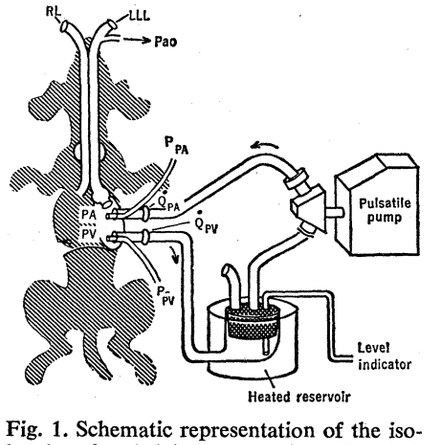

Fig. 1. Schematic representation of the isolated-perfused lobe preparation. The left lower lobe of a dog lung is perfused by a pulsatile pump, heated reservoir system, using autologous blood. A tracheal divider permits separate ventilation of the isolated lobe. *RL*, right lung; *LLL*, left lower lobe; *PA* and *PV*, cannulas in the left lower lobar artery and vein, respectively; P_{PA} and P_{PV}, pulmonary arterial and venous pressure taps; $\dot{Q}_{PA}$ and $\dot{Q}_{PV}$, electromagnetic flowmeters in series with the arterial and venous cannulas; P_{ao}, lateral tap on tracheal divider for measuring airway opening pressure.

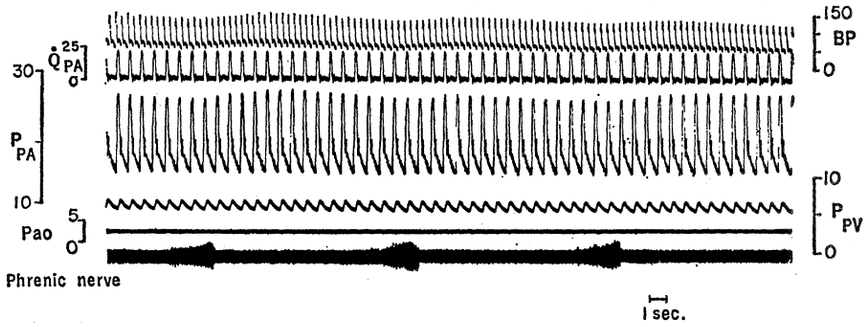

Fig. 2. Representative records of Traube-Hering vasomotor waves and phrenic nerve activity. The systemic arterial blood pressure (*BP*) and the pulmonary arterial blood pressure (P_{PA}) show regular oscillations of about 10 mm-Hg. The swings in pressure in both circuits are synchronous and are preceded by a volley of phrenic nerve activity. Blood flow through the isolated lobe ($\dot{Q}_{PA}$), pulmonary venous pressure (P_{PV}), and airway pressure (P_{ao}) are maintained constant. Pressures are shown in millimeters of mercury; $\dot{Q}_{PA}$, in milliliters per second.

respirators and connecting both sides of the tracheal divider to O_2 reservoirs). Since ventilation was arrested and airway pressure remained unchanged, the passive effects of lung inflation on pulmonary arterial pressure could not be involved in producing the waves in blood pressure. However, in order to determine whether the fluctuations in pulmonary arterial pressure were related to respiratory activity even though there were no respiratory movements, the neurogram of the cervical portion of the phrenic nerve, recorded with bipolar platinum electrodes, was used to indicate efferent respiratory activity.

Figure 2 shows an example of the cyclic variations in systemic and pulmonary artery pressure observed during apneic oxygenation in five dogs. Each wave in systemic and pulmonary artery pressure is preceded by a volley of phrenic nerve activity, indicating that the blood pressure oscillations are Traube-Hering waves (*10*). Figure 2 also shows that only the systolic pressure in the pulmonary artery is cycling while diastolic pressure remains constant. This is the characteristic pressor effect of sympathetic nervous stimulation on the pulmonary circulation, that is, an increase in pulmonary arterial systolic pressure despite constant pulmonary blood flow.

Except for potential anastomotic connections between the pulmonary and bronchial (systemic) vessels in the lungs, the pulmonary circulation in the isolated lobe was separate from the rest of the circulation. Such connections have never been shown to be of hemodynamic significance in the normal lung. Moreover, in the preparation used in the present study, ligation of the bronchial arteries consistently failed to produce any effect on the pulmonary arterial pressure. Conversely, during stimulation of the sympathetic nerves to the lungs, a pressor response could be demonstrated in the pulmonary circulation even though systemic blood pressure did not change (*9*). Because of the functional independence of the pulmonary and systemic circulations, and since pulmonary blood flow, pulmonary venous pressure, and airway pressure were constant, the pulmonary arterial pressor waves could not have been caused by the systemic arterial waves or by rhythmic changes in blood flow or by the passive mechanical effects of ventilation. Instead, they seemed to be caused by rhythmic changes in vasomotor tone, originating, as in the case of Traube-Hering waves in the systemic circulation, in the respiratory center and affecting the smooth muscle of the pulmonary arterial tree by way of the pulmonary sympathetic nerves.

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Mammary Tumor Virus Antigen: Sensitive Immunoassay

Abstract. *A rapid, sensitive immunoassay for mammary tumor virus antigen based on inhibition of passive hemagglutination has been developed. The method permits measurement of this antigen in mouse milk from which the fat has been removed.*

Quantitative biological assay of mammary tumor virus (MTV) involves the induction of nodules or tumors in virus-free mice after a latency period of several months. Other sensitive and specific in vitro immunological methods have been used to detect MTV (*1*), but none of these is adaptable to its titration. We developed a passive hemagglutination test in which tanned sheep erythrocytes coated with MTV antigen were agglutinated in the presence of antibody to the virus (*2*). The method provided a highly sensitive technique for measuring antibody in serums of animals immunized with purified MTV. We now describe the adaptation of this to a hemagglutination-inhibition test to measure MTV antigen.

The methods were based on those developed for the titration of a murine leukemia virus (*3*). The MTV antigen was prepared from samples of skimmed milk from C_3H/HeN mice by either of two methods. The first involves differential centrifugation and banding of MTV on Ficoll-sucrose density gradients (*2*); the second consists of rate-zonal centrifugation followed by isopycnic banding on linear gradients of Ficoll in heavy water (*4*). Examination of preparations with the electron microscope, especially with the latter technique, shows a preparation in which almost all of the observable forms are typical intact MTV B particles (Fig. 1).

For sensitization of the sheep cells, the purified virus suspension must be treated with ether at 4°C, three volumes of (anesthetic grade) ethyl ether being added to one volume of virus. The mixture was agitated for 30 seconds in a cyclomixer six times over a period of 30 minutes. Thirty minutes later, the ether was removed in a stream of nitrogen and the residual material was used for coating tanned sheep cells. Antiserums were prepared in rabbits or rhesus monkeys and absorbed with sheep erythrocytes and normal mouse tissues (*2*).

Cells coated with antigen at the optimum dilution of 1:2 were prepared and used on the same day. All titra-