Lymphology 12 (1979) 158–164

# Lactic Dehydrogenase Activity in Lung Lymph During Hemorrhagic Shock, Resuscitation and Recovery

**G. Niehaus, Ph.D., J.A. Will, Ph.D., D.V.M., R.H. Demling, M.D.**

Departments of Surgery, Preventive Medicine and Veterinary Science
University of Wisconsin Center for Health Sciences, Madison, Wisconsin 53706

**Summary**

Lactic dehydrogenase activity was determined in lung lymph before, during and after hemorrhagic shock to determine if this insult produced pulmonary cellular damage. Lung lymph flow and lymph protein content, reliable indices of fluids filtration rate and microvascular protein permeability were also monitored. The experiment was performed in unanesthetized sheep with a chronic lung lymph fistula. Lymph flow, lymph LDH and protein content did not change during the period of shock. Lymph flow increased significantly during resuscitation but lymph LDH and protein content decreased in relation to plasma values indicating the sieving effect of the microvascular membrane for protein to be intact. The increased flow was most likely caused by an increase in microvascular hydrostatic pressure. Plasma LDH was significantly increased during the 72 hour recovery period with lymph flow, lymph protein and lymph LDH being normal. We therefore found that hemorrhagic shock produced a systemic cellular injury reflected in an increased plasma LDH activity. No pulmonary cellular damage was noted.

The estimation of intracellular enzymes in the lymph draining an injured tissue is considered to be a reliable method of assessing local cellular injury (1, 2). Lactic dehydrogenase (LDH) is an intracellular enzyme found in high concentration in the splanchnic system, heart and lung (3, 4). This enzyme is rapidly released from cells after injury and blood levels are used clinically to detect tissue damage (5). Of particular interest is that fact that blood LDH levels increase significantly after hemorrhagic shock (3). The contribution of the lung to this increase has not been determined and the actual effect of shock on the lung remains controversial (6).

Supported by NIH gram HL21076 and the College of Agriculture and Life Sciences.

The purpose of our study was to determine the extent of lung injury from hemorrhagic shock using lung lymph LDH levels and the ratio of lymph to plasma LDH as an indicator of cellular injury. We used the chronic lung lymph fistula in the adult sheep to monitor lung lymph flow, lymph protein and LDH concentrations before during and for three days after hemorrhagic shock.

## *Methods*

### *Chronic lung lymph fistula preparation*

Five adult sheep (50–70 kg) were prepared for collection of lung lymph according to the method of *Staub* (7). Briefly, this entailed three sequential procedures over two weeks. First a small right thoracotomy was made through the ninth intercostal space, the caudal mediastinal lymph node which drains approximately two-thirds of the lung lymph, was identified and its posterior portion resected. This eliminated any systemic contribution to this lymph node. One week later a catheter was placed in the left atrium through a left thoracotomy. A third procedure one week later consistent of making a right thoracotomy through the sixth intercostal space and identifying and cannulating the efferent duct of the caudal mediastinal node with a small silastic catheter (0.025 I.D. inches; Dow Corning, Midland, Mich.). This was tunnelled through the chest wall and secured externally. Polyvinyl catheters were then placed in the aorta and superior vena cava through a neck incision and a Swan-Ganz thermodilution catheter (Model 93A-131-7F Edwards Santa Anna, Calif.) was placed in the pulmonary artery through the jugular vein. A heparin penicillin

0024–7766/79 1500–0158 $ 02.00 

solution (1000 units/cc heparin, 10,000 units penicillin/cc) was placed in all vascular catheters daily to maintain catheter patency. All procedures were done with minimal manipulation of the lung. Animals were allowed to recuperate for five days prior to any studies to allow for a steady-state lymph and protein flow. All studies were performed in the unanesthetized state, the sheep unrestrained in a metabolic cage with free access to food and water.

*Measurements*

Aortic, central venous, pulmonary artery and left atrial pressure were recorded (Gilson Model 1Ct-58 Polygraph) using calibrated pressure transducers (Statham P23db). Transducers were leveled at the point of the shoulder which we considered to be the level of the left atrium. Catheter were flushed each hour with 1 to 2 cc of lactated Ringer's solution containing 1000 units of sodium heparin per liter of fluid. Cardiac output was measured by the thermodilution method (Edwards Model 9520, Santa Anna, Calif.). Lung lymph was collected in heparinized graduated tubes measuring flow every 30 minutes. Arterial and venous blood specimens were obtained every two to four hours. Total protein (Biuret) and albumin concentrations (*Doumas,* 8) were determined on lymph and plasma samples and lymph to protein and albumin ratios calculated. Hematocrit, heart rate, respiratory rate and urine output were monitored. Baseline measurements were obtained for at least eight hours prior to hemorrhagic shock.

*Lactic Dehydrogenase Analysis*

Lactic dehydrogenase is an enzyme with a molecular weight of about 100,000. LDH levels were determined in samples of blood and lymph using the *Cabaud–Wroblewski* quantitative colorimetric technique (9) (Sigma Chemical Company, St. Louis). A Coleman Jr II Model 6/20 was used for determining absorbance. LDH was reported as Berger-Broida units/ml.

*Hemorrhagic Shock Study*

The study was performed on unanesthetized animals. Food and water were removed. After baseline measurements, sheep were bled from the arterial line into standard blood bags containing acetate, citrate, dextrose (ACD) solution (220 cc per 800 cc of blood), over a 15 to 30 minute period decreasing mean arterial pressure to a mean of 50 mm Hg. Blood was then removed as necessary over the next two hours (shock period) to maintain mean blood pressure between 50 and 60 mm Hg. After two hours of shock, 15 cc/kg of Ringers lactate was given intravenously over 15 to 30 minutes. The shed blood maintained at room temperature was then reinfused through a standard blood filter over the next 90 to 120 minutes until baseline left atrial pressure was reached. Sodium bicarbonate was given as necessary to correct severe acidosis. The resuscitation period was considered to be a three hour time period beginning with the Ringers lactate infusion. Animals were then monitored for the next 72 hours. Food and water were replaced in the cages 24 hours post shock.

Dextrose and one quarter normal saline was infused at a rate of one to two liters a day during the recovery period to maintain hydration if the animal was not drinking satisfactorily.

*Statistical Analysis*

Statistical analysis was done by the two-tailed Student's t-test on individual paired differences. We considered $p < 0.05$ as significant. Data were tabulated as the mean ± one standard deviation.

*Results*

Mean data for all the studies is shown in the Table.

*Baseline Period*

All animals appeared healthy during the baseline period with no evidence of respiratory problems. Animals appeared to be comfortable standing in the metabolic cage with a normal respiratory rate of 32 ± 6 heart rate of 90 ± 10

Table 1

| Sheep | Condition | $P_{pa}$ mm Hg | $P_{la}$ mm Hg | $P_{AO}$ mm Hg | C.O. l/min | Lymph Flow ml/1/2 hr | Lymph LDH units/ml | Lymph LDH units/1/2 hr | Venous LDH units/ml | Arterial LDH units/ml | Lymph/Plasma Ratio T.P. | Alb | LDH |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2116 | Baseline | 26 ± 2 | 6 ± 1 | 110 ± 5 | 7 ± 1 | 4.1 ± .2 | 521 ± 7 | 2447 ± 35 | 997 ± 11 | 1008 ± 29 | .5 | .6 | .5 |
| | Shock | 19 ± 4 | -3 ± 1 | 55 ± 0 | 3 ± 0 | 5.0 ± .5 | 228 ± 47 | 1250 ± 260 | 872 ± 30 | 743 ± 10 | .5 | .7 | .3 |
| | Resuscit | 30 ± 5 | 6 ± 2 | 110 ± 10 | 7 ± 1 | 6.0 ± .5 | 310 ± 6 | 1984 ± 80 | 1080 ± 52 | 960 ± 65 | .3 | .3 | .3 |
| | Rec 24 h | 25 ± 3 | 6 ± 1 | 110 ± 5 | 6 ± 2 | 4.5 ± .3 | 747 ± 36 | 2900 ± 140 | 1547 ± 18 | 1455 ± 45 | .5 | .6 | .5 |
| | 48 h | 26 ± 2 | 6 ± 1 | 115 ± 5 | 6 ± 1 | no lymph flow | | | 1544 ± 9 | 1513 ± 29 | | | |
| 177 | Baseline | 21 ± 1 | 5 ± 1 | 95 ± 5 | 5 ± 1 | 4.5 ± .3 | 444 ± 7 | 2230 ± 33 | 666 ± 30 | 800 ± 60 | .5 | .7 | .6 |
| | Shock | 10 ± 3 | -3 ± 2 | 50 ± 10 | 2 ± 0 | 3.9 ± .4 | 331 ± 55 | 1390 ± 23 | 349 ± 28 | 389 ± 19 | .6 | .7 | .9 |
| | Resuscit | 30 ± 5 | 6 ± 2 | 100 ± 10 | 5 ± 1 | 9.1 ± 1.1 | 344 ± 12 | 3200 ± 113 | 706 ± 40 | 675 ± 81 | .4 | .4 | .5 |
| | Rec 24 h | 21 ± 2 | 5 ± 1 | 95 ± 5 | 6 ± 0 | 4.8 ± .8 | 635 ± 81 | 2370 ± 50 | 1092 ± 46 | 970 ± 36 | .6 | .6 | .6 |
| | 48 h | 20 ± 2 | 4 ± 1 | 90 ± 5 | 5 ± 1 | 4.6 ± .5 | 424 ± 16 | 2035 ± 75 | 890 ± 24 | 913 ± 64 | .5 | .6 | .5 |
| 296 | Baseline | 22 ± 2 | 4 ± 1 | 90 ± 5 | 6 ± 0 | 8.0 ± .2 | 401 ± 17 | 3007 ± 127 | 846 ± 12 | 793 ± 37 | .3 | .5 | .5 |
| | Shock | 20 ± 4 | -2 ± 2 | 55 ± 5 | 2 ± 1 | 12.0 ± 1.2 | 300 ± 7 | 3600 ± 84 | 403 ± 35 | 419 ± 41 | .4 | .5 | .7 |
| | Resuscit | 40 ± 5 | 8 ± 3 | 100 ± 10 | 5 ± 1 | 28.8 ± 1.5 | 320 ± 7 | 7680 ± 168 | 490 ± 143 | 763 ± 45 | .4 | .3 | .5 |
| | Rec 24 h | 24 ± 2 | 1 ± 2 | 80 ± 5 | 7 ± 1 | 8.5 ± 2.1 | 1399 ± 87 | 9793 ± 600 | 2084 ± 10 | 2078 ± 17 | .6 | .3 | .7 |
| | 48 h | 22 ± 2 | 4 ± 2 | 80 ± 5 | 7 ± 1 | 12.0 ± 2.5 | 389 ± 41 | 5446 ± 514 | 1768 ± 38 | 1189 ± 408 | .3 | .2 | .2 |
| | 72 h | 22 ± 3 | 3 ± 2 | 80 ± 5 | 6 ± 1 | 10.0 ± 1.1 | 461 ± 55 | 4611 ± 550 | 1565 ± 31 | 1490 ± 150 | .4 | .3 | .3 |
| 130 | Baseline | 28 ± 2 | 13 ± 2 | 100 ± 5 | 5 ± 1 | 4.2 ± .2 | 566 ± 7 | 2320 ± 29 | 745 ± 117 | 783 ± 13 | .6 | .9 | .7 |
| | Shock | 10 ± 4 | -3 ± 5 | 55 ± 5 | 2 ± 1 | 3.5 ± .3 | 707 ± 63 | 2056 ± 183 | 771 ± 73 | 771 ± 73 | .7 | .9 | .9 |
| | Resuscit | 35 ± 10 | 13 ± 4 | 110 ± 5 | 6 ± 1 | 10.0 ± 2 | | | | | .5 | .5 | |
| | Rec 24 h | 30 ± 3 | 10 ± 3 | 110 ± 10 | 6 ± 1 | 4.0 ± .4 | 663 ± 6 | 2652 ± 17 | | | .6 | .7 | |
| | 48 h | 25 ± 2 | 10 ± 1 | 100 ± 5 | 5 ± 1 | 3.7 ± 1 | 569 ± 20 | 2276 ± 79 | 844 ± 99 | 865 ± 43 | .7 | .8 | .6 |
| | 72 h | 23 ± 1 | 11 ± 1 | 100 ± 5 | 6 ± 0 | 3.5 ± .5 | 552 ± 98 | | 987 ± 57 | 892 ± 90 | .7 | .9 | .6 |
| 195 | Baseline | 25 ± 2 | 3 ± 2 | 100 ± 5 | 6 ± 1 | 14.0 ± 1 | 401 ± 25 | 5614 ± 300 | 1274 ± 30 | 1312 ± 66 | .6 | .6 | .3 |
| | Shock | 15 ± 5 | -3 ± 2 | 60 ± 5 | | 12.0 ± 1.5 | 428 ± 36 | 5350 ± 432 | 1133 ± 93 | 1173 ± 156 | .6 | .6 | .4 |
| | Resuscit | 35 ± 5 | 8 ± 2 | 110 ± 10 | | 17.4 ± .4 | 302 ± 30 | 3451 ± 510 | 870 ± 25 | 839 ± 66 | .5 | .5 | .2 |
| | Rec 24 h | 26 ± 3 | 2 ± 1 | 95 ± 5 | | 11.2 ± .6 | 635 ± 20 | 6985 ± 220 | 1793 ± 133 | 1921 ± 43 | .7 | .6 | .3 |
| | 48 h | 25 ± 3 | 3 ± 1 | 95 ± 5 | | 12.5 ± .5 | 348 ± 19 | 4350 ± 237 | 1486 ± 70 | 1360 ± 66 | .7 | .6 | .2 |
| | 72 h | 22 ± 2 | 1 ± 1 | 95 ± 5 | | 9.0 ± 2.0 | 365 ± 25 | 2372 ± 150 | 1117 ± 114 | 1279 ± 47 | .6 | .5 | .3 |

and temperature of 39 °C. Lymph was clear and yellowish in color. Mean vascular pressures in mm Hg were; $P_{pa}$ 24 ± 2.9, $P_{la}$ 6 ± 4.0, $P_{AO}$ 96 ± 8.0 with cardiac output being 6.0 ± .8 liters/min. Baseline lung lymph flow was 7.0 ± 4.2 ml per half hour for the group. Plasma total protein and albumin were 6.3 ± .85 g/100 ml and 2.9 ± .4 g/100 ml respectively. Lymph total protein and albumin were 3.5 ± .9 g/100 ml and 2.0 ± .5 g/100 ml respectively. Lymph to plasma total protein and albumin ratios were .5 ± .12 and .7 ± .15. Arterial, venous and lymph LDH values per ml and per time are found in the Table. The lymph to plasma (venous) LDH ratio (units/ml) was .5 ± .15 for the group.

*Shock Period*

Animals were intially quite agitated during the shock period lying down and standing up multiple times but they gradually became more lethargic. Heart rate increased to 190 ± 20. There was a significant decrease in vascular pressures and cardiac output with values; Ppa 15 ± 4.8, Pla -3 ± 0.3, $P_{AO}$ 55 ± 3.0 mm Hg and cardiac output 2.0 ± .50 l/min. Lymph flow decreased initially, then gradually increased toward baseline with lymph flow exceeding baseline values in 2 of 5 animals. Lymph to plasma total protein and albumin ratios were .6 ± .11 and .7 ± .15. Arterial, venous and lymph LDH levels decreased in 3 animals and remained relatively constant in 2 animals during the shock period. Lymph to plasma LDH ratio increased from .5 to .6 similar to that seen for total protein which also increased from .5 to .6.

*Resuscitation*

Animals remained lethargic through the three hour resuscitation period. Aortic pressure and left atrial pressure returned to baseline levels of 100 ± 10 and 8.0 ± 2.8 mm Hg. Pulmonary artery pressure was significantly increased over baseline with a mean pressure of 34 ± 4.1 mm Hg. Lung lymph flow was significantly increased in all animals from 50% to 300% over baseline and shock periods. Lymph to plasma total protein and albumin ratios were significantly decreased to .4 ± .08 and .4 ± .10 respectively. Lymph to plasma LDH ratio also decreased to .4 ± .15 (Figure 2). Lymph LDH in units/ml decreased in all five animals from baseline values (Figure 1), but when normalized for the increased lymph flow by calculating units/time, values were essentially unchanged from baseline except for one animal where levels increased. Arterial and venous LDH levels remained at baseline values with no gradient across the lung (Figure 1).

*Recovery*

All animals survived the three day recovery period. Pulmonary vascular pressures, cardiac output and lung lymph flow returned to baseline values in the first 24 hours of the period. Arterial and venous LDH levels were significantly increased over baseline during the first 48 hours of recovery with a return toward baseline at 72 hours. There was no a-v gradient noted across the lung (Fig. 1). Lymph LDH in units/ml also increased but to a lesser degree than plasma values. When normalized to units per time, lymph LDH levels were essentially baseline except for one animal (296) where there was an increase comparable to that in the blood values. Lymph LDH levels returned to baseline by 48 hours. Lymph to plasma LDH ratio remained at or below the baseline value of .5 during the entire recovery period. The correlation between lymph to plasma LDH and total protein ratios for the entire study period was 0.9 (Fig. 2).

*Discussion*

The effect of hemorrhagic shock on the lung remains controversial. Major issues are whether pulmonary damage actually occurs from an episode of shock and if it does, whether the injury occurs during shock or in the post shock period (6, 10). *Hillen* (11) noted no ultrastructural damage to the lungs from untreated shock but did note edema after resuscitation. *Demling* (12) described no change in lung lymph flow, protein transport or lung water in an anesthetized preparation during shock. *Moss* (10) noted interstitial edema but no cell damage in baboons prior to resuscitation. Others (13) have described severe damage

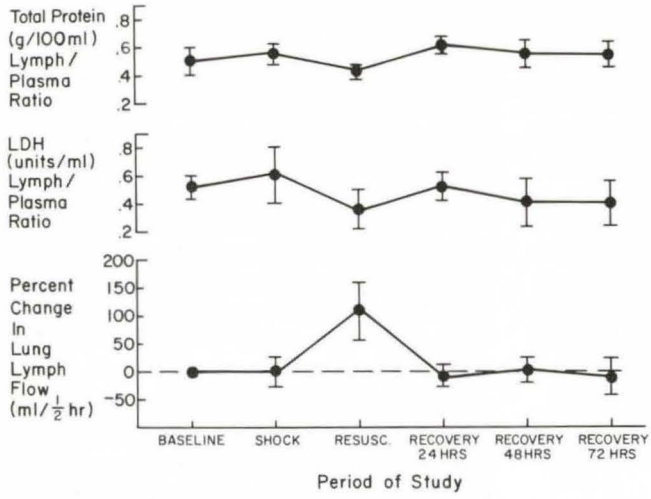


Fig. 1 Changes in lung lymph LDH during the study period are compared with arterial and venous LDH levels. There was no difference between central venous and aortic LDH levels indicating no gradient across the lung. Plasma LDH levels were significantly elevated during the recovery period. Lymph LDH increased to a lesser degree than plasma, during the early recovery period

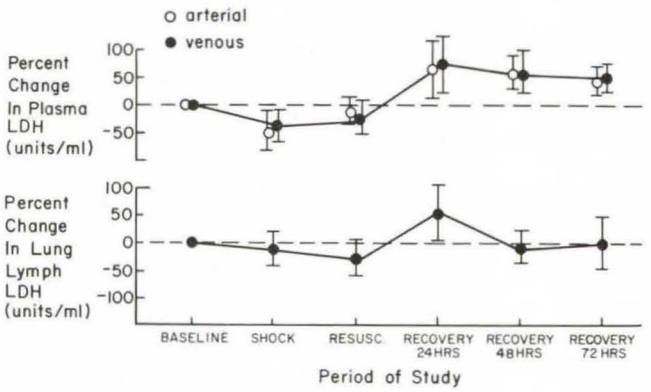


Fig. 2 Changes in lung lymph flow during the study are compared with similar changes in lymph to plasma LDH and total protein ratios. These ratios varied inversely with changes in lung lymph flow indicating the sieving effect of the microvascular membrane for protein was intact. The LDH lymph/plasma ratio decreased when lymph flow was maximally increased

to microvascular endothelium with edema and hemorrhage in the lung during the shock period.

Several factors have produced these discrepencies. First, most studies have been performed under a variety of general anesthetics. Anesthetics (14) have major cardiopulmonary effects which may alter results. Secondly, most studies have been performed over a short time course either including only shock or shock and early resuscitation. Any delayed effects of shock will be missed and a distinction cannot be made as to whether these early pathologic findings are transient or progressive in nature. And lastly, for the most part, conclusions have been based on post mortem histology. This may not accurately reflect physiologic change (15, 16). *Meyers, Meyers* and *Baue* (6) suggested that significant differences in histology can be produced by differences in tissue handling and fixation and pre-existing lesions may be difficult to differentiate from induced pathologic damage. Significant changes in fluid filtration and protein permeability also can occur with no apparent histologic change (15, 16). This is probably due in part to the efficiency of the pulmonary lymphatics in handling high fluid and protein flows while maintaining a normal fluid content in the lung (17).

In our experiment we utilized a preparation where we could avoid anesthesia and study

the effects of shock over a long time course incorporating shock, resuscitation and recovery. We monitored lung injury by measuring lung lymph flow, lymph to plasma protein ratio and lymph and plasma LDH contents. The first two measures are sensitive and reliable indicators of endothelial cell injury with lymph flow measuring transvascular fluid filtration rate and lymph protein content monitoring microvascular protein permeability (18). LDH is a measure of any cellular injury both endothelial and epithelial (4, 19). Since LDH is released rapidly after cell injury (5), an increase indicates when, in the time course of the study, the cell is injured as opposed to the physiologic parameters of lymph fluid and protein dynamics which may change at varying time periods after actual cell injury.

The technique of measuring lymph intracellular enzymes for determining cellular injury has been used effectively for tissues other than the lung both for shock as well as other injuries. *Lewis* (1) noted a marked increase in lymph LDH draining a thermally injured limb with peak increase occurring within 20 minutes of injury when blood levels were only slightly increased. *Berman* (20) studied the lysosomal enzyme concentration of thoracic duct lymph and noted a significant increase after hemorrhagic shock. Others (21) have demonstrated that many of these enzymes reach the circulation through the lymphatics and therefore concentration is highest in the local lymphatics.

We studied lung lymph LDH content in order to measure lung injury after hemorrhagic shock. We noted a significant increase in plasma LDH as previously described by *Vesell* (3), after hemorrhagic shock indicating a significant cellular injury. The increase was not seen until the early recovery period and persisted for the 72 hour study. The delayed increase could be explained by the fact that the damaged tissues were not adequately perfused until several hours post resuscitation at which time the released enzymes were washed into the circulation. Lung lymph LDH remained at normal or less than normal levels for the period of shock and resuscitation. Lung lymph flow was significantly increased during the resuscitation period but the microvascular sieving effect for protein remained intact as lymph to plasma protein ratio decreased (Fig. 2). Lymph to plasma LDH ratio decreased in a similar manner, LDH being a protein of 100,000 molecular weight. The increased lung fluid filtration rate as reflected in the lymph flow was most likely due to an increase in microvascular hydrostatic pressure (18) since no protein permeability change was evident. A generalized increase in permeability to smaller solutes would also explain the findings, but the fact that no evidence of cellular injury was found as lung lymph LDH was normal, suggests that this is less likely.

Lymph LDH did increase in the early recovery period but to a lesser degree than the plasma increase (Figure 1). This increase was most likely due to a passive reequilibration of the interstitial space with the increased plasma concentration. We would anticipate a much higher content of LDH in lung lymph inrelation to plasma if any significant cell injury occurred. The lack of a venous to arterial LDH difference across the lung substantiates the fact that the increased lymph LDH was not secondary to direct lung injury.

We therefore found no evidence of direct cellular injury after pure hemorrhagic shock to the degree studied, using lymph LDH as an indicator, with the increased plasma LDH coming from tissues other than the lung. This conclusion is supported by the lymph fluid and protein measurements which indicated that the physiological functions of the microvascular membrane remained intact. The correlation between lymph fluid and protein dynamics and enzyme content appears to be a very effective means of studying tissue injury.

## *References*

1 *Lewis, G.P.:* Intracellular enzymes in local lymph as a measure of cellular injury. J. Physiol. 191 (1967) 591–609

2 *Clermont, H.G., J.T. Adams, J.S. Williams:* Source of a lysosomal enzymes and phosphatase in hemorrhagic shock. Ann. Surg. 175 (1972) 19–25

3 *Vesell, E.S., M.P. Feldman, E.D. Frank:* Plasma lactic dehydrogenase activity in experimental

hemorrhagic shock. Soc. Exp. Biol. Med. 101 (1959) 644–648
4 *Wacker, W.E.C., P.J. Snodgrass:* Serum LDH activity in pulmonary embolism diagnosis. JAMA 174 (1960) 2142
5 *Manzoli, U., R. Penneys:* Serum enzyme activities of glutamic oxaloacetic transaminase, lactic dehydrogenase and isometric dehydrogenase, following embolization of the dog limb. Am. J. Cardiol. 8 (1961) 829–834
6 *Meyers, J.R., J.S. Meyers, A.W. Baue:* Does human shock damage the lung? J. Trauma 13 (1973) 509–519
7 *Staub, N.C., R.D. Bland, K.L. Brigham,* et al.: Preparation of chronic lung lymph fistulas in sheep. J. Surg. Res. 19 (1975) 315–320
8 *Doumas, B.T., H.G. Biggs:* Determination of serum albumin. In: Standard Methods of Clinical Chemistry. Acad. Press, New York 7, pp. 175–188
9 *Cabaud, P.G., F. Wroblewski:* Colorimetric measurement of lactic dehydrogenase activity of body fluids. Am. J. Clin. Pathol. 30 (1958) 234–236
10 *Moss, G.S., T.K. DasGupta, B. Newson,* et al.: Morphologic changes in the primate lung after hemorrhagic shock. Surg. Gynecol. Obstet. 122 (1966) 751–761
11 *Hillen, G.P., W.D. Grisford, C.G. Jensen:* Pulmonary changes in treated and untreated hemorrhagic shock. Am. J. Surg. 122 (1971) 639–649
12 *Demling, R.H., S.L. Selinger, R.D. Bland, N.C. Staub:* Effect of acute hemorrhagic shock on pulmonary microvascular fluid filtration and protein permeability in sheep. Surgery 77 (1975) 512–519
13 *Wilson, J.W., N.B. Ratliff, D.B. Havel:* The lung in hemorrhagic shock. I. In vivo observations of the pulmonary microcirculation in cats. Am. J. Pathol. 58 (1969) 337
14 *Smith, N.T.:* Circulatory effects of modern anesthetic agents. In: Modern Inhalation Anesthetic Agents. Ed. *Chenoweth, M.B.* Heffters Handbook of Experimental Pharmacology. Berlin, Springer-Verlag 30 (1972) 149–241
15 *Hovig, T., A. Nicolaysen, G. Nicolaysen:* Ultrastructural studies of the alveolar-capillary barrier in isolated plasma-perfused rabbit lungs. Effects of EDTA and of increased capillary pressure. Acta Physiol. Scand. 82 (1971) 417–432
16 *Hyde, D.M.:* A freeze-fraction study of oxone-induced morphological changes in primate lung. Proceed. Electron Microscopy Soc. Am. 31 (1973) 394–395
17 *Staub, N.C., T.R. Vaughn, Jr., A.J. Erdmann, III,* et al.: Evidence for high efficiency and sensitivity of the lungs lymph pump in unanesthetized sheep. Microvasc. Res. 4 (1972) 431
18 *Staub, N.C.:* Steady state pulmonary transvascular water filtration in unanesthetized sheep. Circulation Res. 28 (1971) 135–139
19 *Wroblewski, F., J.S. LaDue:* Lactic dehydrogenase in blood. Proc. Soc. Exp. Biol. Med. 90 (1955) 210–213
20 *Berman, I.R., R.V. Moseley, P.B. Lamborn, K. Sleeman:* Thoracic duct lymph in shock: gas exchange acid base balance and lysosomal enzymes in hemorrhagic and endotoxin shock. Ann. Surg. 169 (1969) 202–209
21 *Glenn, T.M., A.M. Lefer:* Protective effect of thoracic lymph diversion in hemorrhagic shock. Am. J. Physiol. 219 (1970) 1305–1310

*Robert H. Demling, M.D., University of Wisconsin Hospitals, Department of Surgery, 1300 University Avenue, Madison, Wisconsin 53706*