partial pressure difference between inspired tracheal air and end-expired tracheal air represents the retention of methoxyflurane in the body. The difference between end-expired air partial pressure and the partial pressure in arterial blood represents the sum of gradients between (1) end-expired tracheal gas and mean alveolar gas, (2) mean alveolar gas and mean pulmonary capillary blood, and (3) mean pulmonary capillary blood and arterial blood. The existence of a significant partial pressure difference between tracheal gas and alveolar gas can be expected on the basis of solution of methoxyflurane in the airway mucous film and tracheobronchial mucosa during inspiration, and wash-out during exhalation. An alveolar gas-pulmonary capillary blood tension difference might exist on the basis of failure to reach equilibrium due to slow diffusion. A pulmonary capillary-arterial gradient could be caused by venous admixture, or shunting. Existence of venous admixture was demonstrated in some patients by alveolar-arterial oxygen tension differences. The separation of the other two mechanisms is under continued study. An anesthetic partial pressure in blood of 0.66 mm. of mercury is in agreement with Ferguson's rule that the anesthetic partial pressure is approximately one-fortieth of the drug's vapor pressure at room temperature. (This investigation was supported by Public Health Service Research Grant NB 04212, from the National Institute of Neurological Diseases and Blindness, and Public Health Service Training Grant 5T1 GM-699 from the National Institute of General Medical Sciences.)

Effect of Isotonic Saline on the Alveolar Architecture. GARY L. HUBER and THEODORE N. FINLEY, M.D., *Department of Anesthesiology, University of Washington, School of Medicine, Seattle, Washington.* Washing the respiratory tree with saline is frequently employed clinically to remove excess secretions. We have studied the alveolar architecture and pulmonary surfactant following an isotonic saline lung wash. Marked ultrastructure changes in alveolar architecture were observed. *Methods:* The left lung was separated from the right lung in anesthetized dogs (pentobarbital 30 mg./kg.) by means of a modified Carlen catheter. Tracheal division was ascertained by direct vision. Continuous estimates of nonstatic pulmonary compliance of each lung were recorded on a Grass polygraph. The left lung was then filled, washed and emptied with 100 ml. volumes of isotonic saline. This was performed 5 times for a total volume of 500 ml., 450 ml. of which were recovered. Surface tension of the harvested wash and of extracts from minced wash (left) and unwashed (right) lung was measured on a modified Wilhelmy balance. Ten to 30 biopsy samples were taken *in vivo* from each lung and fixed in the inflated state by a variety of accepted procedures: (1) S-collidine buffered osmium fixation (Boatman, E. S. and Martin, H. B.: Amer. Rev. Resp. Dis. *88:* 779, 1963), (2) freeze-dry fixation (Chase, W. H.: Exp. Cell Res. *18:* 15, 1959), and (3) 4 per cent phosphate buffered formal-saline. Dehydration and embedding in Epon 812 was performed as described by Luft (Luft, J. H.: J. Biophys. Biochem. Cytol. *9:* 409, 1961). Two micra sections were cut from the epoxy embedded tissue, stained according to Richardson (Richardson, K. C. *et al.:* Stain Tech. *35:* 313, 1960) and surveyed with the light microscope. Selected areas from these blocks were further investigated by sectioning with a Porter-Blum I ultramicrotome and examined with an RCA EMU-2A electron microscope after staining with Millonig lead, uranyl acetate, osmium tetroxide, or platinum tetrabromide. Five dogs were allowed to survive for 24 hours post-washing before taking biopsies for EM and minced lung extracts for surface tension measurements. *Results:* Pulmonary surfactants was considered present if surface tension measured had a minimum value less than 15 dynes/cm. The surface tension of harvested wash and the extract from the unwashed side were considerably below 15 dynes/cm. Surface tension of the extract of the washed side was higher than on the unwashed side, and always above 15 dynes/cm. In the dogs sacrificed after 24 hours, pulmonary surfactant was absent in the washed lung. Pulmonary compliance was markedly decreased in the left lung after saline washing and remained so for 24 hours, while remaining unchanged in the unwashed lung. The left lung was usually filled with thick white foam. In those animals sacrificed immediately after washing, light microscopy

showed a removal of normally present cellular elements (macrophages, extravated red and white blood cells) from the alveolar spaces on the washed side but not on the unwashed side. Widespread dilation of capillaries and arterioles was seen only on the washed side. Electron microscopy revealed epithelial cell fragmentation, increased vesiculation and disruption, interstitial edema and basement-membrane alteration, swelling of macrophage inclusion bodies, markedly dilated and vesiculated capillaries, and other cellular damage. In the dogs sacrificed 24 hours post-wash, microscopy revealed in the saline-treated lung massive congestion, atelectasis, alveolar cell disruption, cell debris, and hyaline membranes. *Summary:* Isotonic saline is destructive to the normal alveolar architecture. This culminates in transudation of fluid into the alveolar spaces. A search is being undertaken to find a more physiological solution with which to wash the respiratory passages. (Supported by USPHS Grant HE-07550-01.)

Circulatory and Respiratory Response to Tilt With Pentazocine (Win 20, 228), Droperidol (R4749), Droperidol-Fentanyl (Innovar), and Methotrimeprazine in Normal Healthy Male Subjects. JACOB S. ISRAEL, M.D., GRACE T. JANSEN, M.D., and ALLEN B. DOBKIN, M.D., *Department of Anesthesiology, State University of New York, Upstate Medical Center, Syracuse, New York.* Pentazocine, droperidol, Innovar (a 50:1 droperidol-fentanyl mixture) and methotrimeprazine are drugs with potential use in anesthesia. (Dobkin, A. B.: Canad. Anaesth. Soc. J. *11*: 252, 1964). *Method:* The responses to tilt and the subjective and respiratory effects of these drugs were determined when administered in a therapeutic dose to 19 healthy male subjects. Blood pressure and pulse rate were measured at regular intervals during the control tests, first with the subject supine on an operating room table. After 15 minutes, respiratory minute volume was measured and the subject was gradually tilted to 60°. He was kept in this position for a further 15 minutes, then returned to the supine position. Then either pentazocine 30 mg. (17 tests, 10 volunteers); droperidol 3 mg. (17 tests, 10 volunteers); Innovar—2.5 mg. droperidol and 0.05 mg. fentanyl—(17 tests, 10 volunteers) or methotrimeprazine 10 mg. (16 tests, 8 volunteers) was injected intravenously. The same procedure was then carried out as in the control period. Any side effects were noted during and after each test and the subjects were requested to report any discomfort during the following 24 hours. They were also queried as to specific disorders. If there was an extreme fall in blood pressure or fainting during the tilt, or a desire to discontinue the experiment, the table was returned to the horizontal position and the test was terminated. There was at least one day between each test. (Dobkin, A. B., Keil, A. M., and Wong, G.: Anaesthesia *16:* 160, 1961; Dobkin, A. B., and Criswick, V. G.: ANESTHESIOLOGY *22:* 398, 1961; Dobkin, A. B. and Criswick, V. G.: Canad. Anaesth. Soc. J. *8:* 387, 1961.) *Results:* Appreciable hypotension was observed in 1 of 24 pentazocine tests, 4 of 17 droperidol tests, 12 of 22 Innovar tests and 12 of 16 methotrimeprazine tests. The following symptoms were elicited from the subjects the day after they were given pentazocine: dizziness in 9; a drunken feeling, restlessness, nausea and perspiration in 7; muscle weakness in 5; blurred vision in 4; tremors in 3; sleep disturbance, slurred speech, confusion, twitching muscles, dry mouth, stuffy nose, diarrhea, and redness of veins, each in 2; and muscle pains in 1 subject. After droperidol, 15 subjects had symptoms of drowsiness, 9, of restlessness; 7, of sleep disturbance; 3, perspiration, dry mouth, stuffy nose and dizziness; 2, stiffness and urinary disturbance, and 1 each of drunkenness, incoordination of muscles, slurred speech, confusion, faintness and muscle pains. After Innovar, 18 subjects were drowsy; 14 reported marked restlessness; 10, muscle weakness; 7, stiffness; 6, sleep disturbance, a drunken feeling and dizziness; 5, twitching muscles; 4, dry mouth and stiffness; 3 noted constipation, confusion and perspiration; 2 had tremors and incoordination of muscles; and 1 volunteer each had blurred vision, diarrhea, nausea, faintness and slurred speech. Those given methotrimeprazine reported as follows: 12 had a stuffy nose; 7, muscle weakness; 4 each—drunkenness, restlessness, dizziness and blurred vision; 2, tremors; and 1 each experienced stiffness, slurred speech, twitching muscles, faintness,