ANESTHESIOLOGY

The Journal of

THE AMERICAN SOCIETY OF ANESTHETISTS, INC.

Volume 5 MAY, 1944 Number 3

PRODUCTION OF NEGATIVE PRESSURE IN THE RESPIRATORY TRACT BY CILIARY ACTION AND ITS RELATION TO POSTOPERATIVE ATELECTASIS * †

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THERE is voluminous literature on the subject of atelectasis. Coryllos and Birnbaum (1) reviewed the literature for 100 years back, and arrived at the conclusion that there is only one cause, namely: "bronchial obstruction with absorption of the air distal to the obstruction according to definite physical law." They expressed the belief that atelectasis, bronchopneumonia and lobar pneumonia are phases of the same thing, and vary in their manifestations according to the bacteria in the "plug." They wrote of "firmly fixed bronchial plugs."

Writing in 1942, de Takats, Fenn and Jenkinson (2) agreed substantially that the cause of atelectasis is obstruction by massive secretion. "Weakened respiratory force with accumulation of mucus from insufficient movement of cilia and suppressed cough is cause enough." They cited experiments in which bronchial constriction and production of excess mucus is caused reflexly by thoracic injury and visceral manipulation.

Van Allen and Adams (3) attempted to demonstrate the mechanism of atelectasis in experiments on 51 dogs. They destroyed a ring of bronchial epithelium by application made through a bronchoscope of strong silver nitrate. From the basis of these experiments they reached the following conclusions: atelectasis did not develop in a normal lung in the course of quiet respiration, but was favored by strained respiration and coughing; a valvular obstruction produced atelectasis faster than complete obstruction; the pent up air was probably absorbed by

* Read before the American Society of Anesthesiology and The Chicago Society of Anesthetists, Chicago, Illinois, February 18, 1944.

† This work has been aided by a financial grant from D. L. Tilderquist, M.D.

the blood. The investigators did not discover atelectasis in lobes which were found to be completely obstructed after several months; in fact such lobes floated when placed in water. Van Allen and Adams wrote of peristalsis and ciliary movement as the forces which normally remove secretion from the tract.

Churchill (4) expressed the belief that atelectasis is due to a combination of reduced respiratory force and obstruction.

Lee, Tucker and Clerf (5) produced atelectasis in dogs by instilling secretion which had been removed from a patient suffering from pulmonary collapse.

In summary, the current general opinion expressed in the literature seems to be that atelectasis is caused by obstruction of bronchi by firmly fixed masses of mucinous secretion which accumulates because of reduced respiratory force, and that the air entrapped beyond the obstruction is absorbed by the blood stream. Clinically, the condition can be prevented by deep breathing and coughing. This conception is doubtless largely true, but it does not give the ciliary mechanism the consideration which it seems to me to deserve. Ciliary action receives bare mention by only a few authors, who state that it is "weakened."

It seems to me that one can as well omit cardiac action from a discussion of the physiology and pathology of the circulatory system, or peristalsis from a discussion of the gastrointestinal tract, as to disregard ciliary action when speaking of the respiratory tract. In fact, a respiratory tract without ciliary action would be incompatible with life.

This conception of atelectasis leaves several questions unanswered. Why was there no atelectasis in the dogs in which the bronchi had been permanently closed? Why does deep breathing prevent atelectasis in man and produce it in dogs? Why, among asthmatic patients whose bronchi fill up with heavy mucus to the point of suffocation, does not atelectasis develop? Why should the ciliary action be weakened in surgical patients whose respiratory tracts are otherwise all right, especially those who are operated on under local or intravenous anesthesia? To what are these "plugs" of mucus "firmly fixed" since the entire mucinous lining is in continuous motion toward the pharynx? As a matter of fact, there are actually no plugs found through endoscopy or at necropsy. There is nothing there except some soft mucus which can readily be aspirated. Why doesn't this soft mucus slide down into the area of negative pressure beyond?

SOME RELEVANT PHYSIOLOGIC FACTS

Some rudimentary facts of physiology seem to bear on this subject. When the size of the thoracic cavity is increased by the inspiratory effort, a region of reduced air pressure is produced. Since this region is open to the out-of-doors, atmospheric pressure forces enough air into the chest to bring the pressure up again to that of the atmosphere. The

air flows down through the trachea, bronchi, and bronchioles, until it reaches the dead ends in the alveoli. These it picks up and carries along into the areas of reduced pressure, causing them to distend at the same time. The trachea and bronchi increase in diameter and length, and the lungs slide down the parietal pleura toward the abdomen. Expiration is accomplished by increasing the pressure within the thorax. Several factors enter into this procedure, such as the elasticity of the lungs, the weight of the relaxed thoracic wall, release of the abdominal organs by the diaphragm, and, when necessary, voluntary muscular contraction. The contained air flows out toward a lower pressure. The lungs rise and contract, and the air passages shorten and become narrower. The movements of the lungs and air tubes are purely passive. The volume of the lung at expiration may be readily doubled or trebled by deep inspiration. The diameter of the bronchi is said to vary as much as a third (6). Consider for a moment what the reduction in diameter of a cylinder by one-third means in terms of volume (fig. 1).

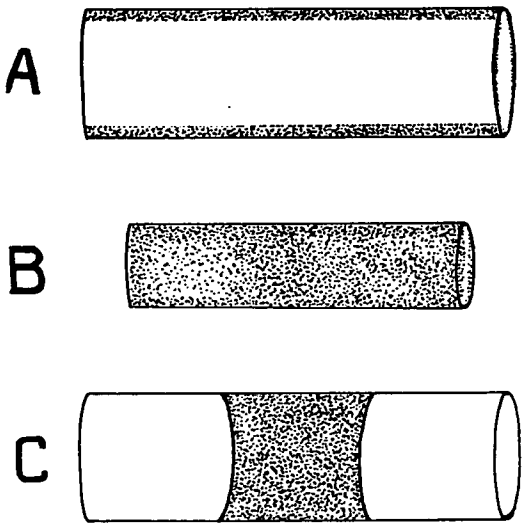

FIG. 1. Diagrammatic representation of how mucus might span the lumen of a bronchus, owing to changes in the length and diameter of the bronchus during respiration. Cylinders A and C measure 3 cm. in diameter, and 10 cm. in length, and contain a volume of about 71 cc. Cylinder B is one-fifth shorter, and one-third narrower, and contains only 25 cc. If cylinder A, containing a lining of mucus (as indicated by the stippling), should be reduced in size to that of B, and then reexpanded to its original size, as in C, the mucus would fill B, and might take a shape and position approximately as shown by the stippling in C. Something similar to this probably, takes place in the bronchi when an excessive amount of mucus is present.

The normal respiratory tract is lined with a thin film of mucus throughout its entire extent. This entire lining film is removed by ciliary action, perhaps one to three times each hour, and as often replaced by the mucus glands. The total volume of mucus normally present is extremely small since the film is exceedingly thin. It has been necessary in the course of some of the experiments here to be reported to obtain small quantities of respiratory mucus. It required fifty decapitated hens to produce about 2.00 cc. The entire respiratory tracts of twelve pigs when hung up for about an hour furnished, at the larynx, between 1 and 2 cc. In the same manner, it was possible to obtain about 1 cc. from the respiratory tracts of six cows.

Some physical characteristics of this respiratory mucus should be mentioned. It tends to extend across spaces, forming bubbles, diaphragms and threads. This is observed in the nose daily by rhinologists. It has a certain tensile quality and can be dragged for considerable distances. The cilia transport it readily, and seemingly can carry 100 times the normal load without difficulty. A normal ciliary mechanism would move the quantity and type of secretion found in atelectasis readily and with dispatch, if there were no other factors involved (7).

A New Factor in the Conception of Atelectasis and the Experiments to Which It Led, with Comment

Another possible factor in the development of atelectasis occurred to me, which, if pertinent, might shed further light on the entire question of atelectasis. Consequently, I took a short vacation in a laboratory to test this possibility and did the following experiments:

Experiment 1.—A short section of trachea, taken from a freshly killed hen, was pinned horizontally to a small board, and a mass of mucus that had been collected from the respiratory tracts of several hens was introduced into the lower end. The mass was sufficient in size completely to occlude the lumen and it moved by ciliary action from the lower to the upper end in a few minutes.

Experiment 2.—The mucus then was recovered and again was introduced into the lower end. As soon as the mucus began to move, the trachea behind it was stoppered and was connected with a small water manometer, as in figure 2. Almost before the stopper could be secured a negative pressure began to develop (fig. 3). The pressure reached — 34 mm. of water in about eighteen minutes.

Experiment 2, repeated.—This experiment was repeated 18 times with similar results each time (table 1). A negative pressure developed behind the moving mass of mucus as the latter advanced. The further the mucus advanced, the more negative became the pressure, and the more negative the pressure became the more slowly the mass pro-

* These experiments were done at the University of Wisconsin, in the Department of Physiology, where Acting Dean Walter J. Meek made laboratory facilities, with assistance available to me.

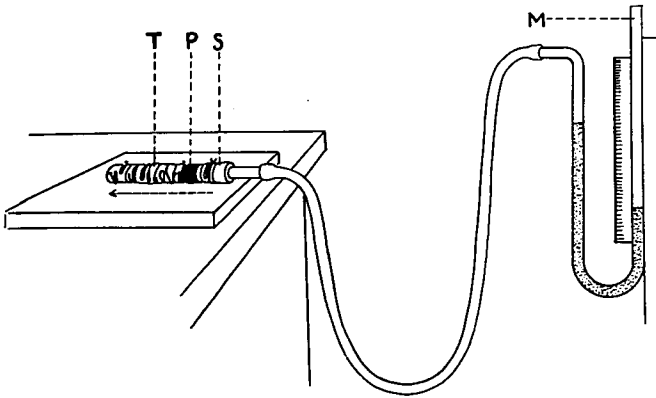

FIG. 2. Arrangement of section of excised trachea from a freshly killed hen, and of the water manometer, in the experiments demonstrating that negative pressure is produced by ciliary action. T—section of trachea. P—piston of mucus. S—stopper. M—water manometer.

gressed. Finally it came to a complete stop. The greatest negative pressure recorded was about — 40 mm. of water.

Comment.—This simple experiment seems to be the key to the development of atelectasis. Essentially a piston-cylinder action takes place. The mass of mucus motivated by cilia, acted as a moving piston within the cylindrical piece of trachea. The mucus was not "firmly fixed" when it came to a standstill. It was simply stopped by air pressure. The cilia can move large masses of mucus with no difficulty, but they cannot lift 15 pounds of atmospheric pressure with a piston of slippery

TABLE 1

MAXIMUM NEGATIVE PRESSURES OBTAINED IN THE EXPERIMENTS IN WHICH THE LOWER END OF THE TRACHEAL SECTION WAS STOPPERED AND CONNECTED WITH A WATER MANOMETER

Experiments in pressure changes produced by ciliary action in trachea of hen—pressure measured in mm. of water

Experiment	Maximum pressure change, mm.	Experiment	Maximum pressure change, mm.
1	— 17	11	— 16
2	— 33	12	— 13
3	— 16	13	— 16
4	— 12	14	— 15
5	— 14	15	— 4
6	— 20	16	— 12
7	— 19	17	— 14
8	— 5	18	— 20
9	— 5	19	— 40
10	— 11		

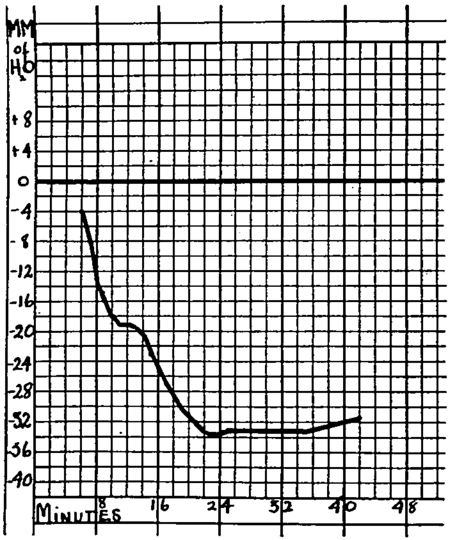

FIG. 3. Curve showing the fall in pressure in the closed space behind a mass of moving mucus in the section of hen's trachea illustrated in figure 2. The pressure fell 34 mm. of water in eighteen minutes.

mucus. When the pressure in front of the advancing mucus piston, minus the pressure behind it, became equal to the effective force which the cilia were able to apply, then the piston of mucus became stalled.

Experiment 3.—One experiment was continued for fifty minutes (fig. 4). The pressure in the manometer was maintained at the maximum for eight or ten minutes and then began to decrease. It finally returned to — 6 mm. from a maximum of — 14 mm. Meanwhile, the mucus began to appear at the unstoppered, cut end of the trachea, where it formed a thick ring. We removed the stopper, supposing that all of the mucus had already been transported, and that the pressure of — 6 mm. which still remained must be an effect of capillarity. The water in the manometer promptly equalized. When the trachea was inspected, it was found that a very thin, transparent diaphragm of mucus was still intact. This apparently had maintained the small pressure of — 6 mm.

The cilia obviously had not stopped working when the mucinous piston came to a standstill. They continued to exert traction, with the result that mucus was dragged away at the periphery and was carried away progressively toward the unstoppered end of the trachea in a thin

film (fig. 5). The volume of the piston was reduced in this manner thereby also reducing its thickness and strength. As it became thinner it could no longer maintain the maximum pressure, and sagged backward in the middle, thus reducing the negative pressure. This continued progressively until all of the mucus had collected in a thick ring at the unstoppered cut end of the trachea, and the negative pressure had practically disappeared. The wide variations in the curve shown in figure 4 are due to the effects of gravity. Gravity has a negligible effect on the flow of the normal thin film of mucus in the respiratory tract. However, when a large mass is present, gravity has a very considerable effect upon its movements. This also is doubtless a factor in atelectasis.

Experiment 4.—There remained a conceivable possibility that the air in the excised trachea used in the foregoing experiments might have

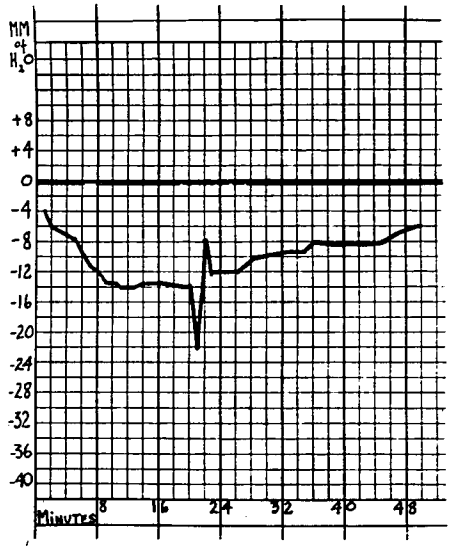

FIG. 4. Curve showing the fall in pressure in a hen's trachea behind a mass of mucus moved by ciliary action. After twenty-two minutes the pressure began to rise again, and, after fifty minutes, it had returned practically to atmospheric pressure. (Figure 5 indicates the change in the mass of mucus which caused the pressure to rise again.) The sudden marked changes in pressure, indicated by the two sharp points, occurred when the position of the trachea was changed from horizontal to vertical. At twenty-one minutes the trachea was held vertically, with the laryngeal end down, and with the cilia working in the direction of gravity. The pressure was noted and was found to have fallen 8 mm. more. At twenty-two minutes the trachea was held with the laryngeal end up, and with the cilia working against gravity. The pressure rose 5 to 6 mm.

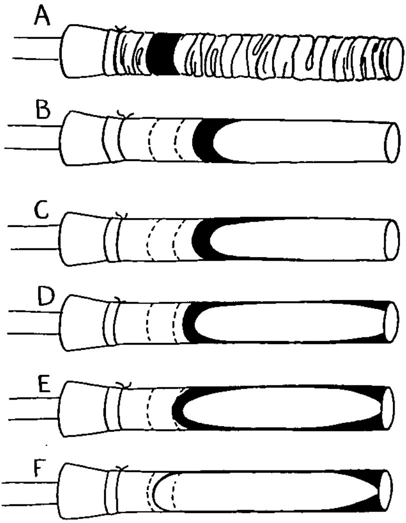

Fig. 5. A diagrammatic representation of the changes in the shape and position of the mass of mucus during the pressure change shown in figure 4. A, Position of mucus when stopper was introduced; B, mucus has advanced to the stalling point; C, the margins are advancing by ciliary action, while the main mass remains stationary, held by atmospheric pressure; D, E and F, progressive advance of the mucus in thin films to the unstoppered end of the trachea, where it collects in a ring. Meanwhile, the occluding diaphragm grows progressively thinner and weaker as its volume is reduced, and sags back toward the starting position, thus causing the pressure behind it to rise again.

The dotted lines in each sketch represent the position when the stopper was introduced.

been absorbed by the tracheal tissue, thus producing a reduced pressure. To determine whether this was so, another experiment was done in which the direction of the section of trachea was reversed. That is, the upper, or laryngeal, end was stoppered and was connected with a manometer. When the mucus was introduced at the lower end, and was carried upward by ciliary action, a positive instead of a negative pressure promptly developed (fig. 7). The pressure was maintained near the maximum for nearly an hour. It did not lessen, apparently because the mucus was carried against the stopper, and also against the end of the manometer tube, and was held there by ciliary action. This experiment shows that the negative pressure developed in the experiment was not due to absorption. No one would seriously argue that the air was absorbed behind the mass of mucus and excreted again in front of it. The experiment was repeated four times. The maximum pressure found was + 55 mm. (table 2).

Comment.—It now seems possible to formulate a conception of the development of atelectasis in which it is not even necessary to assume that nitrogen is absorbed into the bloodstream. It is not to be understood that these experiments prove that the air is not absorbed. They

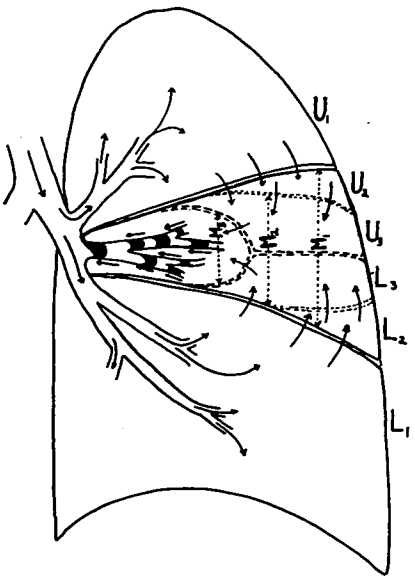

FIG. 6. Diagram representing the various steps in the production of postoperative pulmonary atelectasis. The middle lobe is the affected one. 1. An excess of secretion is formed in the lobe, the result of anesthesia, of reflex stimulation, or of a combination of these and other causes. 2. A series of occluding masses, or pistons of mucus, form across the lumen. A combination of circumstances enters into their formation, such as, force of inspired air, changes in diameter of the air passages during respiration, viscosity and volume of secretion, size of the air passages and so on. 3. The pistons move up the cylindrical air passages by ciliary action, each carrying a quantity of air. 4. As soon as the air pressure within the lobe begins to fall, the lobe shrinks by its own elasticity, and by pressure from surrounding lobes (M_1, M_2, M_3). 5. The surrounding lobes, carried by the force of inspired air, move into the space relinquished by the affected one (U_1, U_2, U_3 & L_1, L_2, L_3). The changes in position of the lobes, as well as their shrinkage and distention, are facilitated by the sliding motion of the lungs during respiration.

The advancing pistons of mucus rupture serially as they reach tubes of greater diameter and meet more forceful changes of air pressure. They then release the air bubbles which they have carried and continue on their course as mural films or masses. 6. Pressure in the affected lobe becomes so greatly negative that the mucus masses then present in the air passages come to a standstill against atmospheric pressure. These masses form the so-called firmly fixed mucus plugs referred to in the literature, but, actually, although they are static they are not fixed.

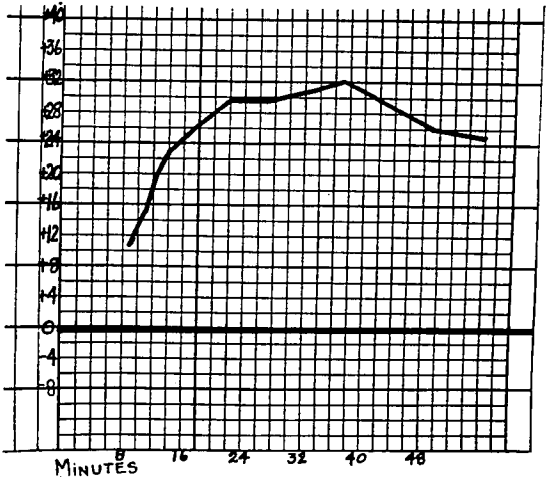

FIG. 7. Curve showing positive pressure produced in a section of trachea excised from a freshly killed hen. An occluding mass of mucus was introduced into the lower end, and the upper, or laryngeal, end was stoppered and connected with the manometer. This shows that the negative pressure found in the experiments illustrated in figures 2 and 3 was not the result of absorption of air by the tissues.

indicate nothing about absorption either pro or con but simply demonstrate that air can be removed more or less completely by another method. The steps are represented in figure 6 and would be repeated many times. One mucinous piston advancing up the bronchus would not produce collapse. There would have to be a succession of them, each carrying along a volume of air somewhat on the principle of a mercury vacuum pump. The pistons would continue to advance and be carried away as long as any considerable amount of air remained in the lobe. They would not come to a standstill until the pressure within the

TABLE 2

MAXIMUM POSITIVE PRESSURES OBTAINED IN THE EXPERIMENTS IN WHICH THE UPPER END OF THE TRACHEA WAS STOPPERED AND CONNECTED WITH A WATER MANOMETER

Experiments in pressure changes produced by ciliary action in trachea of the hen—pressure measured in mm. of Water

Experiment	Maximum pressure change, mm.
20	+ 32 at 37 m.
21	+ 40
22	+ 55
23	+ 23

lobe had fallen to such an extent that the effective power of the cilia had been overcome. This would not occur until the air in the lobe was exhausted and the lobe had collapsed.

I believe that some of the questions mentioned can be resolved more satisfactorily on the basis of this hypothesis than on the generally accepted one. The failure of the air to disappear from the lobes in the experimental dogs, in which the bronchi were permanently closed, might be explained on the basis of destruction of the ciliary mechanism which would otherwise remove it. This could also explain the difference in the effect of deep breathing in man, and the experimental dogs in which a ring of epithelium had been destroyed. The treatment with strong silver nitrate interrupted the continuity of the ciliary mechanism. The failure of atelectasis to develop commonly in asthmatics might well be due to the fact that in these patients the ciliary mechanism is largely destroyed, and the mucus is actually fixed to the walls. The vacuum pump action of the mucus would be absent under such circumstances.

The development of atelectasis in patients operated on under local anesthesia and whose respiratory tracts were normal can be understood readily. The cilia remain normally active and produce atelectasis by their very activity. It is necessary that an abnormally great quantity of mucus be present, but this is always the case. It seems to be produced reflexly through visceral manipulation. The mucus "plugs" are not fixed in the usual sense; they have simply been stopped by air pressure against which the cilia are unable to advance them. The mucus in the air passages does not slide down because the cilia maintain it in position, even in the presence of considerable negative pressure. Given time, the cilia might drag the mucus past the column of air which obstructs it. However, in atelectatic patients, the mucus is probably produced as fast as the cilia can remove it.

Doubtless absorption of air from obstructed lobes plays a part in the development of atelectasis, but the piston cylinder action of mucus and cilia probably also plays a role. We have demonstrated negative pressure up to 65 mm. of water (8) in the frontal sinus of the dog, as produced by ciliary action, and in this instance it does not seem likely that absorption could have been effective to any extent.

SUMMARY AND CONCLUSIONS

It has been demonstrated experimentally that ciliary power acting on masses of occluding mucus can produce negative pressure in both the upper and lower parts of the respiratory tract. Steps in the production of postoperative pulmonary atelectasis seem to be about as follows: (1) production of an excessive amount of secretion; (2) formation of occluding masses in the air passages partly because of reduced respiration through splinting of diaphragm, pain, and so on, and because the patient lies quietly in one position; (3) movement of a succession of these masses upward in the tract by ciliary action; (4) removal of a quantity

of air by each of these masses, somewhat on the principle of a mercury vacuum pump; (5) progressive shrinkage of the affected lobes as air is removed; (6) compensatory distention of neighboring lobes; (7) production of considerable negative pressure within an affected lobe when the contained air has been exhausted; (8) immobilization of the mucus in the bronchus by atmospheric pressure.

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REFERENCES

1. Corylios, P. N., and Birnbaum, G. L.: Syndrome of Pneumococcic Bronchial Obstruction: Experimental Production of Atelectasis or Lobar Pneumonia with Human Pneumococcic Sputum; Suggestion for Preventive and Therapeutic Treatment, Arch. Int. Med. 51: 290–323 (Feb.) 1933.
2. de Takats, Geza; Fenn, G. K., and Jenkinson, E. L.: Reflex Pulmonary Atelectasis, J. A. M. A. 120: 686–690 (Oct. 31) 1942.
3. Van Allen, C. M., and Adams, W. E.: Mechanism of Obstructive Pulmonary Atelectasis, Surg., Gynec. & Obst. 50: 385–396 (Feb.) 1930.
4. Churchill, E. D.: Pulmonary Atelectasis with Especial Reference to Massive Collapse of the Lung, Arch. Surg. 11: 489–518 (Oct.) 1925.
5. Lee, W. E.; Tucker, G., and Clerf, L. H.: Post-operative Pulmonary Atelectasis, Ann. Surg. 88: 6–14 (July) 1928.
6. Heinbecker, Peter: A Method for the Demonstrations of Calibre Changes in the Bronchi in Normal Respiration, J. Clin. Investigation 4: 459–469 (Oct.) 1927.
7. Hilding, Anderson: The Physiology of Drainage of Nasal Mucus. III. Experimental Work on the Accessory Sinuses, Am. J. Physiol. 100: 664–670 (May) 1932.
8. Hilding, A. C., and Essex, H. E.: To be published.

COMING EXAMINATIONS

The Part II (Oral) Examinations for certification by the American Board of Anesthesiology, Inc., will be held in Chicago, June 9, 10, and 11, 1944. Paul M. Wood, M.D., 745 Fifth Avenue, New York 22, N. Y., Secy.