

TABLE II.
Effect of Aureomycin on Growth of Normal Chicks on Various Diets.

Supplement	Wt at 3 wk						Commercial chick starter, g	P
	Diet I, g	P	Diet II, g	P	Diet III, g	P		
None	242(10)		223(9)		211(10)		195(10)	
50 mg aureomycin	273(10)	.05	263(10)	.05	240(10)	.05	226(10)	.02

P value calculated by the simple rank test using unpaired replicates.
No. of chicks in parentheses.

or certain other antibiotics will produce a growth stimulation greater than that obtained by vitamin B₁₂ alone. The activity of these compounds is presumably related in some way to their antibiotic activity. The lack of activity of intravenously administered aureomycin or penicillin is consistent with this hypothesis. However, the mode of action of these antibiotics on the intestinal flora remains to be determined. Moore *et al.* (7) have previously reported the stimulatory effect of streptomycin on the growth of the chick.

A number of source materials have been reported to possess growth-promoting activity greater than could be accounted for on the basis of their vitamin B₁₂ content (8-11).

7. Moore, P. R., Evenson, H., Luckey, T. D., McCoy, E., Elvehjem, C. A., and Hart, E. B., *J. Biol. Chem.*, 1946, v165, 437.

8. Hartman, A. M., Dryden, L. P., and Cary, C. A., *Proc. Am. Chem. Soc.*, Sept. 1949, p. 39A.

9. Carlson, C. W., Combs, G. F., Miller, R. F., Yacowitz, H., Norris, L. C., and Scott, M. L., *Proc. Am. Chem. Soc.*, Sept. 1949, p. 37A.

Since these natural materials are not known to contain any antibiotics, the relation of the effect of these materials to the growth stimulation induced by aureomycin is difficult to assess at this time. It may be possible that the factor present in the natural supplements and the factor presumably produced by the action of aureomycin in the intestinal flora of the chick are similar.

Summary. Aureomycin hydrochloride stimulates the growth of chicks when fed in the diet at levels as low as 25 mg per kilo. This effect is presumed to be an indirect one since certain other antibiotics manifest this same property. The relationship of this phenomenon to proposed new APF factors in certain natural materials is discussed.

10. Ansbacher, S., and Hill, H. H., *Proc. Am. Chem. Soc.*, Sept. 1949, p. 31A.

11. McGinnis, J., Stephenson, E. L., Levadie, B. T. H., Carver, J. S., Garibaldi, J. A., Ijichi, K., Snell, N. S., and Lewis, J. C., *Proc. Am. Chem. Soc.*, Sept. 1949, p. 42A.

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Alveolar Ventilation Studies Using the Mass Spectrometer.* (17794)

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In recent investigations the rate of intrapulmonary mixing of gases has been used as

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a measure of respiratory function. Cournand *et al.* examined the intra-alveolar mixing of tidal air by determining the concentration of nitrogen in an alveolar sample after the subject respired 100% oxygen for 7 minutes. Alveolar ventilatory insufficiency was as-

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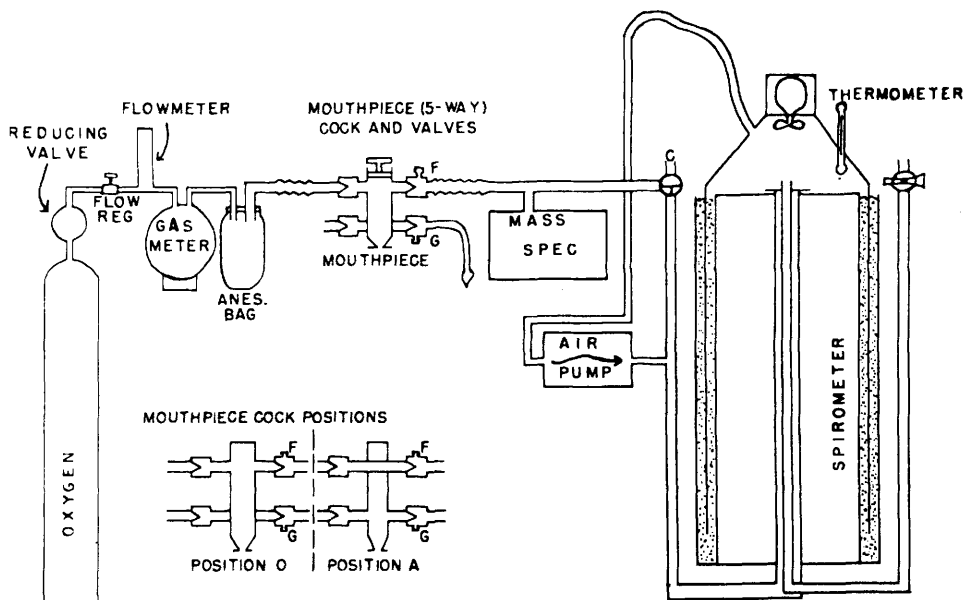


FIG. 1.

Schematic diagram of apparatus used for nitrogen elimination test.

sumed to be present when this value was greater than 2.5%; this situation obtained in 97% of emphysematous patients(1). The time required for chemical nitrogen analysis in their studies limited the value of this pulmonary nitrogen clearance test, for but one point on the elimination curve was determined. Meneely and Kaltreider sought to resolve this difficulty with a catharometer(2). The analytical cell had, however, a marked lag period and therefore made the values relative rather than absolute. One of us, (A.O.C.N.), recently developed a portable mass spectrometer capable of continuous analysis of five different gases every 20 seconds with an accuracy of approximately 1%. This device is being used to test the efficiency of alveolar ventilation as evidenced by nitrogen elimination curves breathing 100% oxygen. With this instrument it is hoped that the above indicated limitations have been largely abolished.

1. Cournand, A., Baldwin, E. DeF., Darling, R. C., and Richards, D. W., *J. Clin. Invest.*, 1941, v20, 681.

2. Meneely, G. R., and Kaltreider, N. L., *J. Clin. Invest.*, 1949, v28, 129.

Method. With the subject in a sitting position, a 5 way valve is connected to a rubber mouthpiece and a conventional nose clip is applied. The diagrammatic representation of the valve and this set up are shown in Fig. 1. After an equilibration period breathing air, the valve is turned precisely at the end of a normal expiration, and the subject then inspires 100% oxygen from a partially inflated anesthetist's breathing bag. The expired mixture is discharged through the mass spectrometer and minute amounts are removed for analysis. The remainder of the expired gas flows into a 100 liter Tissot spirometer and the volume and temperature are recorded. When the mass spectrometer records a nitrogen concentration near equilibrium, the test is concluded and the subject is switched to breathing air. Values from this nitrogen regression curve are now plotted against the minute volume of the expired gas mixture, corrected to 37°C, saturated water vapor tension and standard barometric pressure.

Fig. 2 depicts a mass spectrometer record during a nitrogen elimination test in a normal individual. In this instance the nitrogen clearance was "complete" after 5 minutes of

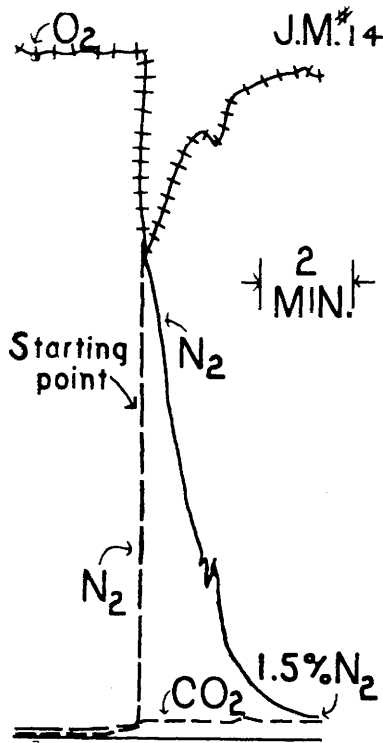


FIG. 2.
Mass spectrometer recording during a nitrogen elimination test on a normal individual.

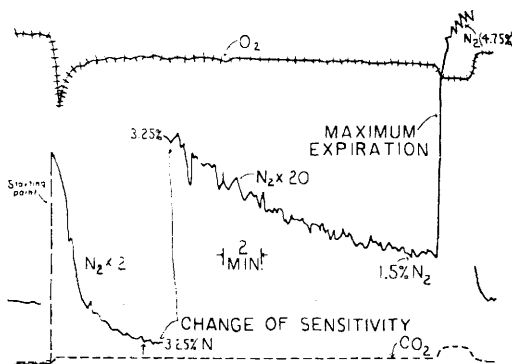


FIG. 3.
Mass spectrometer tracing of a nitrogen elimination test on an individual with marked emphysema. In this recording the sensitivity of the machine was changed during the test in order to determine at what point, if any, the curve leveled off.

100% oxygen inspiration. The asymptotic nature of the curve is due to the nitrogen excreted into the lungs from the blood, a very slow process. Fig. 3 in contrast shows the curve of an emphysematous individual. Note

that at the end of 20 minutes the clearance is still incomplete as demonstrated by the marked rise in the nitrogen value following a maximal expiration. In normal alveoli, which are virtually free of nitrogen, the rise after this maneuver is but a fraction of a per cent.

To avoid the errors imposed by changes in respiratory minute volume, all nitrogen elimination curves have been corrected to nitrogen clearance volume. This is by definition the quantity of diluting gas required to reduce the nitrogen content of the expired air to no more than 1% greater than the contaminant concentration of nitrogen in the diluting gas.

Eighteen clearance determinations were performed on 5 normal adult male students. Table I shows the results of multiple determinations on a single individual. The clearance volumes appear to be quite reproducible, with 4 liters the maximum deviation for one individual, and in the remainder duplicate tests agreed within 2.4 liters, a volume equivalent to 5 normal expirations. In comparing the different individuals, there is a maximum difference of 16.8 liters between 2 of the normal subjects. It is possible to correct this by correlation with total lung volume measurements(3).

The remaining portion of Table I shows the nitrogen clearance volumes of 3 patients with marked clinical pulmonary emphysema. A significant difference between the emphysematous individuals and the normal controls is apparent. The assumption that these patients are suffering from an inability to ventilate adequately the alveolar portions of their lungs seems valid.

Summary. A method of measuring alveolar ventilation utilizing a portable mass spectrometer to determine the rate of nitrogen elimination is described. This test was shown by repeated trials to be rather uniform for each of a group of normal individuals. The range of nitrogen clearance volumes among normal individuals appears to be related to differences in lung volume, and correction for this factor approximates the pattern of values

3. Miller, F., Hemingway, A., Nier, A. O. C., and Vareo, R., to be published.

TABLE I.
Nitrogen Clearance Data from 5 Control Subjects and 3 Patients with Marked Emphysema.

Subject	Condition	Height, cm	Body wt, kg	N ₂ clearance vol., l
D.	Normal	283	63.5	32.8 32.8 32. 32. 29.2 27.6 27.6 26.8 26. 22.8 22.8 22.8 20.4 20.4 17.6 17.3 16.8 16.
J.M.	"	268	66.0	116.
J.S.	"	260	59.2	120.
M.	"	280	75.0	160.
B.	"	280	77.4	
L.	Emphysema	280	63.5	
K.	"	264	61.0	
A.	"	264	77.5	

for those tested. Three cases of marked pulmonary emphysema are presented. The results from testing this group in a similar fashion indicate a prolongation of nitrogen

elimination in these patients as compared with the normal subjects.

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Cross Transfusion. II. Therapeutic Effect in Acute Mercury Nephrosis.* (17795)

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Recently, a safe and controllable method for cross transfusion and the instrument for this purpose have been described(1). The difficulties and dangers of earlier methods (2-7), which often caused the death of ex-

perimental animals, were encountered when the experiments were repeated by us. Briefly, the difficulties have been:

1. Sacrifice of an artery to obtain blood (2-7). This can be repeated only a few times in the same individual. It is also unsuitable because of the occurrence of arterial spasm, which often terminates the procedure, and because withdrawal of blood from an artery against a low resistance puts an additional load on the heart. Methods which alternately withdraw and administer blood often cause shock(3).

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2. Duncan, G. G., Tocantins, L., Cuttle, T. C., *Proc. Soc. Exp. Biol. and Med.*, 1940, v44, 196.

3. Green, H. D., *Rev. Scientific Instruments*, 1945, v16, 95.

4. Little, J. M., Green, H. D., Hawkins, J. E., *Am. J. Physiol.*, 1947, v151, 554.

5. Nyiri, W., *Arch. Exp. Path. Pharm.*, 1926, v115, 117.

6. Thalheimer, W., Solandt, D. Y., Best, C. H., *Lancet*, 1938, v235, 554.

7. Green, H. D., Bergeron, G. A., Little, M. J., and Hawkins, J. E., *Am. J. Physiol.*, 1947, v149, 112.