6. The tests indicate that the pulse rate reduction would serve as a guide to the therapeutic action of digitalis in cardiac cases, and also as a guide to dosage.

7. Well dried and well kept digitalis leaf apparently does not lose much more than eight to ten per cent of its action within one year of time. This has been varified in other samples of digitalis. However, badly cured and badly kept leaf loses its strength rapidly.

8. A full strength infusion of digitalis leaf, when given in doses of 0.1 cc. per kilo of body weight, should cause an average percentage reduction in pulse rate of 10. There is, however, considerable individual variation in the rate of reduction as was shown in the tests above outlined.

It was intended to also note the influence of digitalis action on blood pressure but press of time did not allow this. In another year the tests will be repeated, including observations on blood pressure.

RESPIRATION TEST AS A POSSIBLE SUBSTITUTE FOR THE USUAL BASAL RATE DETERMINATIONS.*

BY ALBERT SCHNEIDER, M.D., PH.D.

The author presents that the breath-holding power or capacity, in seconds with lungs deflated, under basal rate conditions, yields results which harmonize closely with the results obtained by means of the metabolors.

Within recent years physicians have given much attention to what is generally known as the basal metabolism rate determinations. In a general way the basal rate of oxygen metabolism in the living tissues is the minimal rate or that rate of oxygen consumption which will just maintain life, which will just continue the vital functions. To the physician it means the lowest rate of metabolism which is obtainable under conditions which can be met in practice. In hospital practice, the patient whose basal metabolism is to be taken, is instructed to omit the evening meal, and the conditions for a good night's sleep are provided and the basal rate determination is made in the morning before any exercise has been taken and before the morning meal. In private practice these requirements cannot always be met. The trip to the office of the physician entails a certain amount of exercise, even though the most suitable conveyance is provided, with the result that the test made in no wise indicates a basal rate or anything approximating such a rate. It would appear desirable that for office-practice conditions a different method should be agreed upon so that the results by physicians engaged in general practice might in a measure harmonize.

The value of the basal rate tests are perhaps over-estimated. That the tests have considerable diagnostic value cannot be denied, and they are also of great value in dietetics. The results of the tests are perhaps of far greater interest and value to the physiologist, the pharmacologist and the dietitian, than they are to the practicing physician. It is also true that when physicians are better informed as regards diet and dieting in disease, they will be able to make better and more extended use of the metabolors.

* Scientific Section, A. PH. A., Philadelphia meeting, 1926.

The rate at which oxygen is consumed by the tissue cells depends upon a variety of factors. During exercises, after a meal, during emotional disturbances of an exciting nature and during fevers, the oxygen metabolism is greatly increased. Under conditions of health it reaches its lowest level after a prolonged period of rest and quietude, as for example after a night's sound sleep, with the omission of the evening meal. Under such rest conditions, the results of an army of observers have been summarized and recorded and we now have fairly reliable tables of basal metabolism averages. It was early noted that the normal metabolic rate is approximately proportional to the skin surface area, and again the surface area is known to be approximately proportional to height and body weight. It was furthermore noted that basal metabolism is quite uniformly influenced by age, by the atmospheric barometric pressure, and also by the atmospheric moisture. There are tables of corrections for the following:

1. Barometric pressure. Temperature.
2. Surface exposure of the body.
3. Height and weight.
4. Sex.
5. Amount and kind of food ingested.
6. Bodily state and condition.
7. Diseases, etc.

It is generally agreed by experienced metabolists that the basal rate should not fall more than ten per cent below the normal, nor rise much more than ten per cent above the normal (normal standards by DuBois) in health; so that +10 and —10 per cent may be considered the extreme ranges from the norm. One degree (F) of fever adds about 7.2 per cent to the metabolic rate, and any marked rise in the metabolic rate suggests fever.

The metabolic test, as made by means of any first class apparatus, depends upon the following:

1. Determining the volume of oxygen consumed (metabolized) in the body, after rest and abstinence from a meal or two, during one hour of time. The actual time of a test is as a rule not over six or seven minutes, but the oxygen consumption is figured per hour.

2. For making the test, a suitable apparatus is required, consisting of an oxygen tank, a soda-lime container for absorbing the CO_2 exhaled from the lungs, a recording device for indicating the amount of oxygen consumed each minute and each tenth of a minute, a barometer, record sheets.

Whether the metabolor cylinder contains pure oxygen or a mixture of air and oxygen, is believed to be of little influence on the tests results, as the only gas taken out of the mixture during respiration is oxygen, the nitrogen contained being returned to the cylinder while the exhaled CO_2 is taken up by the soda-lime. It may also be assumed that the volume of the residual air in the lungs at the beginning of the test is about equal to the air residuum at the end of the test. Therefore, the volume reduction of the contents of the cylinder is equal to the volume of the oxygen consumed during the test. One test condition must always be met, namely the cylinder must have enough oxygen to supply the basal needs of the cells during the test. It is also believed to be important that the gases in the cylinder be well mixed before the test begins and during the test. Small electrically driven motor mixers are supplied with some machines for that purpose. Some authorities hold the opinion that the mechanical mixing is non-essential.

The following is the approximate composition of inspired and of expired air:

Constituents.	Inspired air.	Expired air.
Oxygen	20.96 vol. per cent	16.03 vol. per cent
Nitrogen	79.00 vol. per cent	79.00 vol. per cent
CO_2	0.04 vol. per cent	4.40 vol. per cent
Water vapor	Variable	Saturated

The volume of the air exhaled is somewhat less than the volume of the air inhaled, due to the fact that a portion of the oxygen absorbed is not returned as CO_2. The ratio of the CO_2 exhaled and the O absorbed is known as the "respiratory quotient," stated thus:

$$\frac{CO_2 \text{ exhaled}}{O_2 \text{ absorbed}} = \text{Respiratory quotient} = \frac{4.0 \text{ to } 4.5}{5} = 0.8 \text{ to } 0.9.$$

For class demonstration purposes a home-made metabolor may be constructed from a wet spirometer. Each student should be supplied with a book of instructions for using the metabolic apparatus. The instructions supplied by manufacturers will serve the purpose very well.

Some physicians question the clinical importance or value of the basal metabolism determinations and suggest that the results of the vital capacity and the breath-holding capacity tests give equally useful information regarding the oxygen metabolizing power of the blood and tissue cells. In fact it is as a rule recommended that at the termination of each metabolic rate test, the vital capacity be also taken, and in many of the metabolic rate appliances are equipped accordingly.

Naturally, the class-room tests, in which students serve as test subjects, are not made under clinical bed-side or hospital conditions and the results do not show the basal rate of oxygen consumption. Each student test requires five to seven minutes of time and three or four students should be tested at one laboratory period and the results compared and explained by the instructor. The demonstrations will give the student an introduction into the clinical use of the basal metabolism apparatus.

The following experimental observations are to be made by all of the students.

1. In the morning immediately upon rising and before any exercise of any kind has been taken, do the following; in the sitting posture:

(*a*) Determine the breath-holding capacity, in seconds, with lungs in maximum expansion.

(*b*) Determine the breath-holding capacity, in seconds, with lungs deflated to the maximum degree.

Do (*a*) and (*b*) three times at intervals of five minutes, always in the same sequence). Represent the average of (*a*) by F, and the average of (*b*) by E. (F for "full," and E for "empty.")

2. Immediately after completing (*a*) and (*b*), the vital capacity in (cubic inches or cc.) should be taken by means of the wet spirometer. Fill lungs to the maximum capacity and exhale into the wet spirometer, emptying lungs to the maximum degree. Since spirometers are not available at the home, the student should determine his vital capacity at the laboratory immediately upon arrival at the college, and before a morning meal has been taken. Ride to college and rest (lying down or sitting in chair) for 30 minutes at the laboratory before taking the vital capacity. Represent vital capacity by V.

In making the F tests, three distinct physical sensations are felt, as follows:

1. A feeling of discomfort due to the chest expansion. This feeling endures for from 10 to 15 seconds.

2. Feeling of comfort stage, as the chest pressure is lessened due to the absorption of O, reducing the volume of gas in the lungs. This sensation endures for 20 to 30 seconds.

3. Gradually the discomfort due to O hunger develops, which sensation increases in severity until it cannot be borne any longer and the chest is emptied.

In making the E test, the initial sensation (after maximum chest deflation) is one of comparative comfort, but this is soon followed (in from 10 to 20 seconds) by the rapidly increasing O hunger discomfort and ends in a deep inspiratory movement.

In the F and also E tests, the CO_2 of metabolic origin remains in the lungs, but it has not been determined what effect the gradually accumulating CO_2 may have on the respiratory exchange of O and CO_2. A small amount of the accumulating CO_2 is no doubt again absorbed into the circulation.

If V is high and F also high (in seconds), that indicates a normal condition and that the exchange of gases between blood and lungs (O and CO_2) is good or normal.

If V is high and F low (that is, the time in seconds short), that is an indication that the gas exchange (O and CO_2) is rapid and suggests increased tissue metabolism, as in fever, in hyper-thyroidism and in hyper-activity of the adrenals.

V low and F high (time in seconds long), suggests reduced metabolism, as in sub-normal temperature, in hypo-thyroidism and in adrenal insufficiency.

Exercise shortens the E period markedly, and conversely rest lengthens the period, up to a certain definite limit, after which it again shortens, as the tissue oxygen supply gradually becomes exhausted. The variations in the E time, due to personal differences in the self-imposed respiratory stress limitations, are also considerable, but this factor is of comparatively little consequence in individual determinations. The instructions to the subjects are to "hold on" to the limits of reasonable endurance or self-punishment, and to administer the same degree of self-punishment in all of the tests.

E high (in seconds) means a low or rather retarded or slow oxygen metabolism. As the oxygen metabolism increases, the E period decreases, but a short E period also indicates a low oxygen reserve in the system. During violent exercise, in high fevers, and after drug action (thyroid extract), the E period is greatly reduced. For adult males ranging in age from 25 to 30 years, and in weight from 150 to 160 pounds, the average period for E may be given as 25 seconds, provided the tests are made approximately under basal rate conditions, with an allowance of 10 to 30 per cent above and below that figure.

E is proportional to the available residual blood and tissue oxygen, and should therefore be and in all probability is proportional to the basal metabolism rate. E is therefore probably a measure of basal metabolism.

The relationship of V (vital capacity), F (breath-holding capacity with lungs expended), B (basal metabolism rate), and E (breath-holding capacity with lungs deflated), might be stated as follows:

$$V:F::B:E.$$

We may suppose the following example:

V = 5000 cc. of air.
F = 70 seconds.
B = 2000 cc. of oxygen per hour.
F = 28 seconds.

Another case might be:

V = 4000 cc.
F = 50 seconds.
B = 1200 cc.
E = 15 seconds.

or, the proportion could be stated as follows:

$$V:B::F:E.$$

E like B is influenced by barometric pressure, by height and weight, area of body surface, age and sex, and suitable corrections must be made for these factors. After a sufficient number of comparative tests shall have been made, it may then be possible to state E in terms relative to B, and we may then substitute the simple E test for the cumbersome, annoying and expensive metabolic rate determinations. The ratio of F to E is the vital or respiratory ratio, and normally F: : : 3:1.E A ratio of 2:1 would indicate a weak or low respiratory range, and a ration of 1.5:1, and less indicates a very serious respiratory disturbance. Certain drugs, as strychnine and digitalis, increase the ratio to 4:1 and even higher.

The following are some averages for E based on body weight (ages from 22 to 30):

190 lbs., E = 19 seconds.	150 lbs., E = 26 seconds.
180 lbs., E = 20 seconds.	135 lbs., E = 29 seconds.
170 lbs., E = 23 seconds.	130 lbs., E = 30 seconds.

F *increases* somewhat with age, at least in the age ranges from 20 to 35 years, while E. *decreases* in about the same ratio, but since advance in years also brings some increase in body surface area, such decrease in E may be essentially due to that factor rather than to any advance in years. Vital capacity is proportional to height rather than weight.

The percentage of CO_2 in normal air, in vitiated air, in air exhaled from the lungs after the tests above outlined, etc., may be determined by the Angus Smith method, as follows:

1. The required alkaline solution is prepared as follows: Dissolve exactly 2.409 Gm. of pure sodium carbonate (free from water of crystallization) in one liter of boiled distilled water. This is the stock solution and is to be kept in a well-filled bottle, tightly corked.

2. Each cc. of the stock solution will neutralize one cc. of CO_2. For making tests use about ten cc. of the stock solution, dilute to 100 cc., and add a drop or two of a neutral alcoholic solution of phenolpthalein. If the CO_2 content of a gas is high, and the gas container small, it may be desirable not to use the dilution of 1–10.

3. Use 1000-cc., or 500-cc. flasks, or even 250-cc. flasks, in special cases, fill with water, close with perforated rubber stopper, carrying an air intake tube which extends to the bottom of the container, and an outflow opening or tube. The air intake tube has a rubber tube with mouthpiece attached. Invert the water-filled container over water, and breathe into the intake tube until all of the water is replaced by the expired air; clamp off the intake rubber tube and plug the other opening with a piece of glass rod or closed tubing.

4. Enough of the test solution (diluted or not diluted as may be required) is introduced into the flask or container to just neutralize the liquid after thorough shaking. Add small quantities of the test solution at a time, shake thoroughly, and continue this operation until the solution no longer becomes decolorized and remains faintly pink. The solution is now neutral or nearly so. Carefully measure the volume of the solution added.

5. The number of cc. of the solution added multiplied by the dilution factor, multiplied by 100, and divided by the number of cc. of the container, minus the amount of the solution added gives the per cent of CO_2 in the air tested. Examples:

1. $$\frac{4.5 \times 0.1 \times 100}{500 - 4.5} = 0.09 \text{ per cent of } CO_2.$$

2. $$\frac{2 \times 0.1 \times 100}{500 - 2} = 0.04 \text{ per cent of } CO_2.$$

3. $$\frac{43 \times 100}{400 - 43} = 12.04 \text{ per cent of } CO_2.$$

4. $$\frac{9 \times 0.1 \times 100}{1200 - 9} = \frac{90}{1191} = 0.0755 \text{ per cent of } CO_2.$$

Laboratory tests made show that there is a rapid increase in the CO_2 content of air retained or held in the lungs for a time, up to a maximum of about 12 per cent. It has long been known that the CO_2 content of the air exhaled from the lungs, in the ordinary or normal or average respiratory act, of one and the same person, is and remains fairly constant. It is also known that this CO_2 content varies within a limited degree (within one per cent) in different persons. With one person the CO_2 volume of expired air may be fairly constantly 4.3 per cent, with another person 4.45, with another, 4.26, etc. There are indications that the percentage of CO_2 in lung air is in proportion to the time lapse between the end of the inspiratory movement and the beginning of the expiratory movement and also proportional to the number of respirations per minute. These intervals and respiratory rates vary in different persons, and as a result there is a personal difference in the CO_2 content of the expired air. The following are some of the results of CO_2 determinations of air held in the lungs as long as possible, as in the F and E tests:

11.43 per cent CO_2.	13.00 per cent CO_2.
12.04 per cent CO_2.	12.30 per cent CO_2.
11.80 per cent CO_2.	11.80 per cent CO_2.

The following tables are intended as guides and suggestions to other investigators. Unquestionably with the accumulation of data, it will be found necessary to alter the tentative values indicated in the tables.

TABLE I.—EXAMPLES OF DATA USED IN THE RESPIRATION TESTS.

Age (years).	Weight (pounds).	Height (inches).	V. C. (cu. in.).	F (sec.).	E (sec.).	*1. Basal requirement (calories).	*2. Area (sq. m.).	*3. P-M.
38	160	69	258	58	20	1790	1.86	.....
35	140	67 1/2	213	50	20	1630	1.70	32.40
32	162	72	268	46	22	1800	1.95	.....
30	150	68	272	120	29	1680	1.82	34.50
29	180	71 1/2	250	75	25	1870	2.00	.....
25	130	65 1/2	218	65	31	1640	1.63	34.40
23	185	72	268	63	33	1970	2.04	30.00
22	147	69 1/2	245	66	37	1690	1.72	34.00
21	158	67	274	95	30	1690	1.82	36.30
20	144	69 1/2	244	80	35	1710	1.80	29.00

*1 The values determined by means of the Mayo chart.

*2 Values obtained by means of the DuBois chart.

*3 P-M = physico-mental efficiency rating index. Figures based on the measurements and determinations as explained in another report.

TABLE II.—GIVING THE NORMAL VALUES FOR E, IN SECONDS, ACCORDING TO SEX, AND AGES FROM 20 TO 60 YEARS.

Age (male).	E. in seconds.	Age (female).
60 to 70	15	50 to 60
50	14	45
50	15	40
45	16.5	35
40	18.5	30
35	21	25
30	23	20
25	25	..
20	28	..

TABLE III.—INDICATING CORRELATION OF E TO SURFACE AREA OF BODY.

Area (sq. m.) high.	E. in seconds.		Area (sq. m.) low.
2.20	24	33	1.77
2.01	20	28	1.75
2.00	13	28	1.75

TABLE III.—(*Continued*).

Area (sq. m.) high.		E. in seconds.			Area (sq. m.) low.
1.95		22	40		1.75
2.00		25	31		1.70
2.05		25	30		1.70
1.90		23	30		1.70
1.93		26	24		1.75
2.10		28	21		1.66
1.90		28	24		1.74
2.02	Averages	23.4	28.9	Averages	1.73

TABLE IV.—TENTATIVE AVERAGE VALUES FOR E ACCORDING TO AGE, SEX AND SURFACE AREA, WITH PERCENTAGES BELOW AND ABOVE A PROPOSED NORMAL.

Females, yrs.	44–40	39–30	29–25	24–18	.....	.....
Males, yrs.	50–45	44–40	39–35	34–30	29–25	24–20
			In seconds			
Normal, E	15	18	20	23	26	28
E, in seconds, found						
10	−33	(± 30 per cent is within the normal)				
11	−26	−39				
12	−20	−33	−40			
13	−13	−28	−33			
14	− 6	−22	−30	−39		
15	0	−17	−22	−34	−40	
16	+ 6	−11	−20	−30	−36	
17	+13	− 5	−15	−26	−32	
18	+20	0	−10	−21	−28	−35
19	+26	+ 5	− 5	−17	−24	−32
20	+33	+11	0	−13	−20	−28
21	+40	+17	+ 5	− 8	−16	−25
22	+46	+22	+10	− 4	−12	−21
23	+53	+28	+15	0	− 8	−18
24		+33	+20	+ 4	− 4	−14
25		+39	+22	+ 8	0	−10
26			+30	+13	+ 4	− 7
27			+33	+17	+ 8	− 3
28			+40	+21	+12	0
29				+26	+16	+ 3
30				+30	+20	+ 7
31				+34	+24	+10
32				+39	+28	+14
33					+32	+18
34					+36	+21
35					+40	+32
36						+35

The following is a summarization of the results of the tests and observations above outlined:

1. The indications are that E, in seconds, is a measure of the reserve tissue oxygen metabolism. It is a measure of the rate as well as of the amount of tissue oxygen metabolism.

2. The values for E apparently harmonize with the values of the basal rate metabolism tests. The indications are that the E test may be substituted for the far more difficult and expensive metabolor tests now employed by physicians.

3. The following factors and influences shorten the time of E, in seconds.

(*a*) Increase in body surface area.
(*b*) Exercise. The time in seconds decreases rapidly with increase in physical exercise.
(*c*) E, in seconds, decreases with advance in years.
(*d*) Sex. Time is considerably shorter for women.
(*e*) Fevers. Time in seconds decreases in proportion to the increase in body temperature.
(*f*) The time in seconds for E, is reduced to the maximum degree as basal rate conditions are approached.
(*g*) Reduction in food supply and starvation shortens the time in seconds.
(*h*) Thyroid gland medication shortens the time in seconds.
(*i*) Contrary to expectations, small doses of alcohol shorten the time in seconds considerably. Further tests should be made.
(*j*) High altitudes.

4. Factors and influences which apparently increase the time of E, in seconds:

(*a*) Food. The time in seconds is markedly increased after a meal.
(*b*) Rest, after exercise. (See *b*, above.)
(*c*) Low barometric pressure.
(*d*) Mental depression.
(*e*) Phlegmatic temperament. The indications are that a so-called phlegmatic temperament is the result of a reduction in the rate of tissue oxygen consumption.
(*f*) Time in seconds is apparently increased in those having sub-normal temperatures.

5. The CO_2 content of respiratory air is in proportion to the time that the air is held in the lungs, until a maximum increase is reached. The maximum CO_2 content of expired air in the tests for F and E, as above outlined, is about 12 per cent.

6. Thirty per cent above and thirty per cent below the average may be considered a normal range. These percentage ranges may prove too extreme as additional data are brought into the calculations.

7. There appears to be a correlation between E and the physicomental rating, but the evidence is as yet inconclusive.

THE EARTHWORM METHOD FOR TESTING SANTONIN AND RELATED ANTHELMINTICS.*

BY ALBERT SCHNEIDER, M.D., PH.D.

The author describes a modification of the Trendelenburg method. The rating of the anthelmintics is based on the spasm producing properties of the drug, and not upon its toxic action.

Santonin appears to have a specific action on the common earthworm or rainworm (*Lumbricus terrestris*), causing the muscular tissue to undergo a tonic as well as clonic spasmodic contraction which endures for long periods of time. Other species of earthworms and also intestinal ascarids and the leeches, react in a similar manner. The spasm-inducing action is due to the lactonic nature of the drugs, not being elicited by the sodium salts with santonic acid nor by the oxides, hydrates, or the chlorides of santonin and of related lactone compounds. This action is also produced by lactonic derivatives of santonin, by uncombined cumarin and by oil of chenopodium, and by other substances having anthelmintic prop-

* Scientific Section, A. PH. A., Philadelphia meeting, 1926.