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IMPLICATIONS OF INTERNAL LOADING TO BREATHING IN MAN

J. MEAD

Department of Physiology, Harvard University School
of Public Health, Boston, Mass., USA

I begin by classifying the motor acts involving the respiratory muscles in man:

I. Respiratory
Breathing — natural and unnatural
Phonation — speech, singing
Respiratory transients — coughing, sneezing, sighing, yawning

II. Non-respiratory (involving more than respiratory muscles)

Steady state, non-cyclic — maintainance of posture in various degrees of repose
Steady state, cyclic — rhythmic exertion, locomotion
Voluntary transients — special movements
Involuntary transients — in response to unanticipated loads
Gastro-intestinal transients — swallowing, vomiting, defecation

Breathing is the natural act by which lungs are ventilated. But natural breathing is rarely measured and little is known about it. Animals are commonly measured while anaesthetized and man while conscious, but in unnatural circumstances.

Phonation, when more or less continuous, replaces breathing. Ventilation during speech is somewhat more than is needed under resting conditions. Under chemical drive ventilation during speech increases, but about one-third as much per mm Hg rise in arterial PCO_2 as during breathing. Thus the control of ventilation during phonation is fairly

crude, but the two — phonation and ventilation — are most compatible during very modest exertion, the commonest circumstance for speech.

None of the transients has important implications to gas exchange. They may be superimposed on breathing (e.g. many simple voluntary movements), or interrupt breathing (e.g. weight lifting, swallowing) or augment ventilation (e.g. coughing, sneezing, sighing), but they are too short lived to have important infuences on the gas composition of the body.

The implications of steady state non-respiratory acts to gas exchange, although potentially great are largely unknown. Almost all studies are of unnatural breathing in subjects either resting with relatively high degrees of postural repose, or during exercise on treadmills or cycle ergometers. How well ventilation is maintained in various postures and in varying degrees of repose is not known — nor is the extent to which non-respiratory acts represent increased mechanical loads to breathing. Indeed it is somewhat dismaying to see how much more is known about the parts of the respiratory system, including the details of neural mechanisms, than is known about the function of the system as a whole.

In the instance of cyclic non-respiratory motor acts the entrainment of breathing with the non-breathing cyclic events is well recognized. A striking example is the race horse, who may be seen (on television, in weather cold enough so that each expiration is visible!) to breathe at his galloping frequency well in excess of 100 times a minute. Alternating movements between the two pairs of limbs, as in the galloping horse, the hopping rabbit and breast-stroke swimming man, with accompanying flexion and extension of the spine, must produce larger changes in lung volume than alternating movements between two limbs, as in walking. Indeed the functional significance of breathing frequency tending to be a sub-multiple of striding frequency in running man is not readily apparent.

Considered from the standpoint of control mechanisms it would appear that the body takes advantage of the relative freedom from instantaneous effects of volume change on blood and tissue chemistry to free up the breathing pattern. Thus breathing may be stopped or started reflexly, as in swallowing, or automatically, as when bracing to lift a load, or synchronized with other movements to its own advantage, as in the race horse. For the pattern *requirements* for gas exchange are very simple, and are completely expressed as the product of two variables, tidal volume and frequency. The same minute ventilation, the product of tidal volume and frequency, can be produced by an infinite variety of breathing pattern, and it would appear that the defense of

a particular wave form by some mechanism which preserves it in detail, would have no functional value as far as breathing is concerned.

But in contrast to breathing, many non-respiratory acts involving respiratory muscles must be comparatively rapid and accurate to be useful. The question repeatedly arises, to what extent do quick muscle responses, for example ones elicited by mechanical loading of the respiratory system, reflect non-respiratory mechanisms, where they are clearly necessary, and to what extent they are essentially respiratory in nature. It must be borne in mind that even respiratory rhythms may have mainly non-respiratory significance. Non-respiratory contractions of respiratory muscles are performed on a changing background of respiratory activity. It remains to be seen, for example, whether the respiratory rhythm of gamma discharge is basically respiratory, in the sense of its being a component of the motor act of breathing, non-respiratory, in the sense of keeping the muscle spindle properly tuned for non-respiratory events, or both.

In the remainder of this paper I present some respiratory responses of conscious human subjects to mechanical loading, in highly artificial circumstances, and discuss their relevance to natural breathing.

Since breathing frequency did not change in response to any of the loads, I will not mention it again; tidal volume is in these circumstances a measure of ventilation — the breathing output. As a further simplification, all responses will be considered under conditions of nearly constant chemical stimulation.

Figure 1 presents the average ventilatory response during mechanically assisted breathing by means of a servo-controlled respirator which

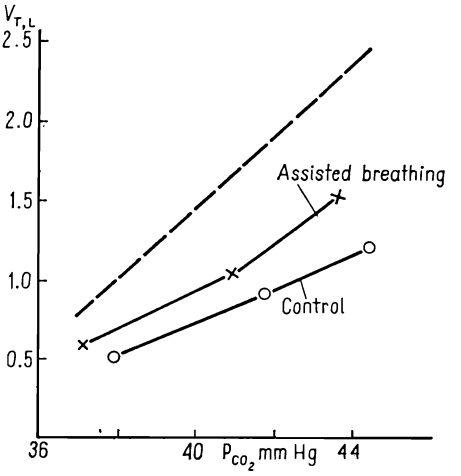

Fig. 1. For explanations *see* text.

took over the work of ventilating the lungs and left only the chest wall to be driven by the respiratory muscles. (The respirator accomplished this by developing a pressure at the mouth just sufficient to maintain pleural pressure constant relative to atmospheric. In so doing it developed all of the change in transpulmonary pressure required for each breath.) Despite this very substantial level of assistance — the lungs normally constitute more than half of the load of the respiratory muscles — tidal volume increased only modestly, at a given end-tidal PCO_2, suggesting that some mechanism was operating which tended to stabilize ventilation.

Figure 2*A* shows the amplitude of a rectified and filtered diaphragmatic EMG signal, sensed with an esophageal electrode, during assisted

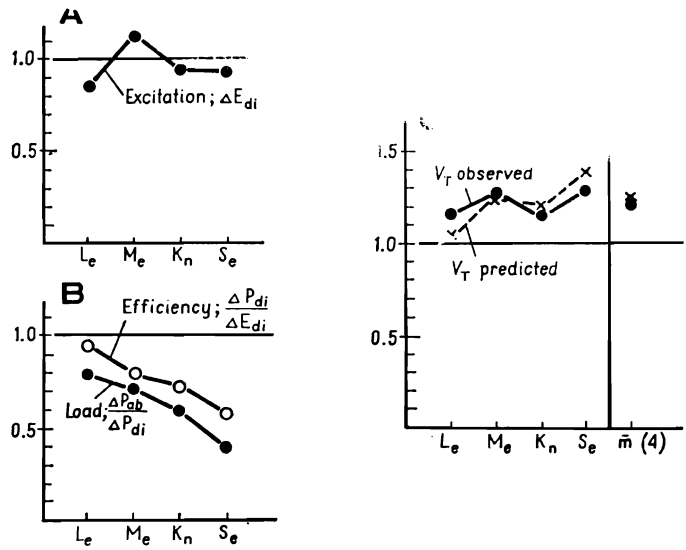

Fig. 2. For explanations *see* text.

breathing relative to the amplitude during unassisted breathing. Diaphragmatic excitation did not change systematically or significantly during assistance.

Figure 2*B* shows relative values for the change in diaphragmatic pressure load (solid circles), and diaphragmatic mechanical efficiency (open circles) for the same subjects. The total pressure load on the diaphragm is the sum of the pleural and abdominal pressure fluctuations. The load during assistance, when pleural pressure is constant, is simply the abdominal pressure swing. Mechanical efficiency was measured as the ratio of the change in transdiaphragmatic pressure to the amplitude of diaphragmatic excitation. As may be seen in the Figure, the

individuals with reduced mechanical efficiency also had the largest reduction in diaphragmatic pressure load.

Tidal volume would be expected to vary directly with the level of excitation and the mechanical efficiency, and reciprocally with load. Figure 2C shows the product of relative excitation, relative mechanical efficiency, and the reciprocal of the relative load. The relative tidal volume predicted on this basis corresponds quite closely with the observed relative tidal volume.

That mechanical efficiency should vary with pressure loading is to be expected: the bigger the load reduction, the greater the degree and speed of shortening of the diaphragm, and the smaller the force (and hence diaphragmatic pressure) developed for a given level of excitation. Less easily explained are the large individual differences in loading and efficiency. We think that they have to do with the different ways the subjects chose to breathe in these unfamiliar circumstances. The two subjects with the smaller load changes were both highly experienced as respiratory test subjects, and proud of their ability to ignore the experimental situation! The other two were relative neophytes. We think that the former breathed in a more relaxed fashion than the latter two, with inspiratory, but little, if any, expiratory activity; while he less experienced subjects probably had phasic expiratory activity. The former had larger fluctuations in abdominal pressure than in pleural pressure before assistance and the lungs represented a smaller fraction of the total pressure load on the diaphragm. The other two subjects had comparatively small fluctuations in abdominal pressure, by virtue, we think, of phasic contractions of the abdominal muscles during expiration, which kept abdominal pressure from decreasing as much as it otherwise would, and relaxation during inspiration which limited the pressure rise. For them the lungs were a larger fraction of the diaphragmatic load before assistance, which resulted in greater shortening, and a greater fall in mechanical efficiency during assisted breathing.

But despite these real differences in the way the subjects breathed the ventilatory responses were nearly the same. This suggests that the force-length and force-velocity characteristics of the diaphragm may be particularly well suited for allowing the diaphragm to develop the same transpulmonary pressure at a given level of excitation in the face of changing abdominal loading. Certainly changes in abdominal loading must occur naturally with changes in position and posture. The relative stability of ventilation in the face of external loading probably reflects, as has been suggested, these intrinsic properties of contracting muscle. To this we would add the possibility that these same properties may

confer an even higher degree of stability under natural changes of load — namely abdominal loading when the load is more directly coupled to the contracting muscle.

Evidence for this is shown in Fig. 3*A*. Recently Drs. Sears, Green and I have been making measurements during external restrictions of breathing movements. This Figure shows tidal volume and diaphragmatic exci-

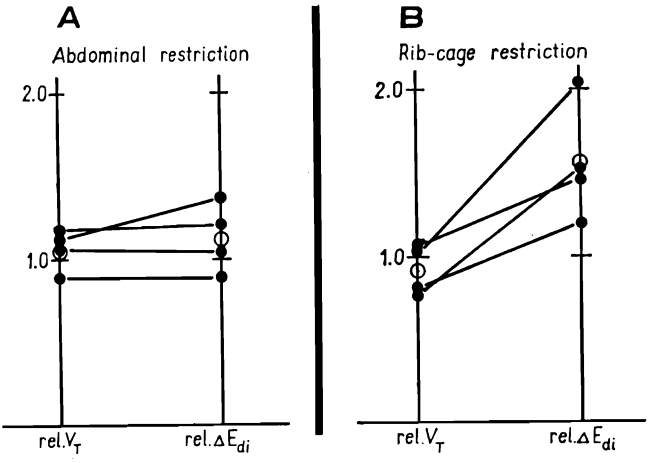

Fig. 3. For explanations *see* text.

tation when the abdomen is clamped front and back, compared to the unrestricted state. The subject sits with his back against a flat board, and abdominal excursions are limited by means of a block of wood, shaped to fit the contour of the abdomen anteriorly and held rigidly in place within a metal frame. The block is forced inward without impinging on either the rib-cage or pelvis until the end-expiratory level is reduced by about 5% of the vital capacity, VC, or somewhat less, and then fixed in place. This requires a substantial inward displacement of the abdominal wall and results in a distinct sensation of restricted abdominal excursion during inspiration. Nevertheless, as may be seen in the Figure, tidal volume and diaphragmatic excitation change little and non-systematically.

In contrast to abdominal loading, where the mechanical characteristics of the contracting diaphragm apparently effectively defend tidal volume, one would expect no such useful response, at least on the part of the diaphragm, when the rib-cage is restricted. For with restriction of the rib-cage, lung volume and pleural pressure would change less of a given level of excitation, and the diaphragm being thereby less loaded, would

shorten more and reduce its mechanical efficiency. We were interested to see what happened to diaphragmatic excitation in this circumstance, so we restricted the rib-cage in a similar way. The results are shown in Fig. 3*B*. Tidal volume was well defended, but in all four subjects diaphragmatic excitation increased substantially.

A more natural instance of mechanical change which is unfavourable to diaphragmatic action is the shift in lung volume with posture. As one moves from the recumbent to the upright posture the force of gravity operating mainly on the abdominal contents, pulls the diaphragm downward, thereby increasing lung volume but simultaneously allowing the diaphragm to shorten more than it otherwise would at a given level of excitation. We have not measured diaphragmatic excitation in different postures, but we have measured it before and during a shift in mid position produced with a steady positive pressure of 10 cm H_2O at the mouth. In three of the subjects positive pressure breathing, PPB, resulted in an increase in end-expiratory lung volume of from 24 to 33% of VC. In one subject end-expiratory volume did not change. In the three subjects whose lung volumes increased, diaphragmatic excitation also increased. In the subject who resisted the pressure and kept end expiratory lung volume from shifting by active expiration, diaphragmatic excitation remained unchanged. When one of the other subjects was instructed to attempt to prevent any change in lung volume during PPB, which he did by active expiration, lung volume did not change, and diaphragmatic excitation decreased slightly. These results are shown in Fig. 4, the last example as a dashed line. It will be noted that none of these subjects showed a response to PPB of the kind occurring in *anaesthetized* animals, i.e. diaphragmatic inhibition.

I have given four examples of mechanical interventions in which ventilation has been fairly effectively defended. In two — assisted breathing and abdominal restriction — the mechanical event has been such as to alter the mechanical efficiency of the diaphragm so as to oppose the effect of the change on ventilation, and there has been no change in diaphragmatic excitation. In two — rib-cage restriction and positive pressure breathing — the event has been such as to alter diaphragmatic mechanical efficiency in a direction to further impair ventilation, and in both instances diaphragmatic excitation increased. (It perhaps should be reiterated at this point that these changes in excitation occurred without change in chemical stimulus.)

What produces the change in excitation when it occurs? Is it a conscious response to some sensation of a reduction in tidal volume or of an increased effort required to breathe? Certainly both during rib-cage restriction and positive pressure breathing subjects are aware of difficult

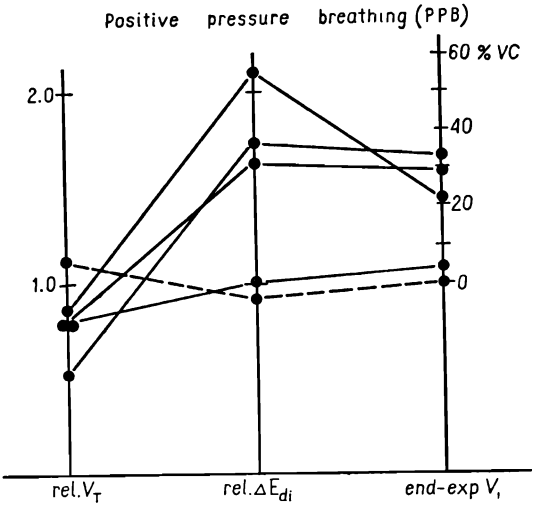

Fig. 4. For explanations *see* text.

breathing. An observation made during the course of the experiments with assisted breathing is pertinent. Commonly the subjects reported when the assistance was stopped that they were suddenly aware that breathing had become somewhat difficult; the return to normal conditions was sensed as abnormal. This sensation passed off in less than a minute. But the ventilatory response had occurred immediately, and it showed no change as the sensation of impaired breathing wore off. Furthermore in the subjects whose diaphragmatic excitation was measured there was no change in the amplitude of excitation in this period of altered sensation. In this example consciousness of increased difficulty in breathing was not accompanied by any change in excitation.

A further suggestion that the response during rib-cage restriction and pressure breathing is not simply a conscious one is the finding of Grassino et al. that subjects who breathed air while exposed to positive pressure (in this instance by lowering the pressure around the body in a chamber from which the head of the subject protruded through a collar) sufficient to increase lung volume approximately 28% of VC (mean pressure +17 cm H_2O), had no significant change in tidal volume or frequency, and no change in end-tidal, and inferentially arterial PCO_2. (Average end-tidal PCO_2 of nine subjects was 40.7 mm Hg before pressure breathing and 41.0 during pressure breathing.) A. E. Grassino (personal communication) has estimated that diaphragmatic excitation must have increase 2–3 fold during pressure breathing — basing these estimates on observations of the relationship between transdiaphragmatic pressure and excitation at different lung volumes. It seems unlikely

that such large increases in excitation produced with conscious effort could have resulted in such excellent control of arterial PCO_2.

If the response is reflex in nature, what might the receptor mechanism be? One possibility is than it has to do with diaphragmatic tension. At a given level of excitation the shorter the diaphragmatic fibres the lower the tension. In both circumstances where diaphragmatic excitation increased, diaphragm shortening was also greater. This suggests that the combination of rib-cage restriction and positive pressure breathing should produce greater diaphragmatic shortening, and greater excitation than PPB alone. Furthermore the combination of abdominal restriction and PPB should produce less diaphragmatic shortening and a smaller increase in excitation than PPB alone.

Figure 5*A* shows diaphragmatic excitation under the three conditions: PPB alone, PPB together with abdominal restriction, and PPB with rib-cage restriction. No consistent relationship is apparent. But this

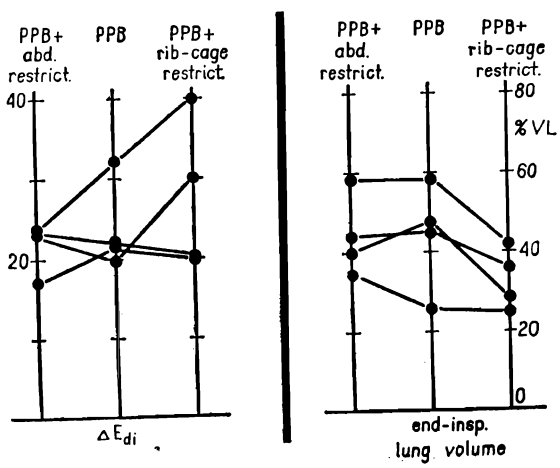

Fig. 5. For explanations *see* text.

comparison leaves out of consideration the influence of restriction on the lung volume shift associated with PPB. To the extent that the restriction limits the volume increase, it should also limit diaphragmatic shortening. Figure 5*B* shows the end-inspiratory lung volume expressed relative to the control end-expiratory level, FRC (The volume units are observed volumes divided by the vital capacity $\times$ 100, i.e. % VC.) Whereas abdominal restriction had comparatively little influence on end-inspiratory volume, rib-cage restriction did.

We have taken the volume changes secondary to restriction into account by plotting diaphragmatic excitation against end-inspiratory

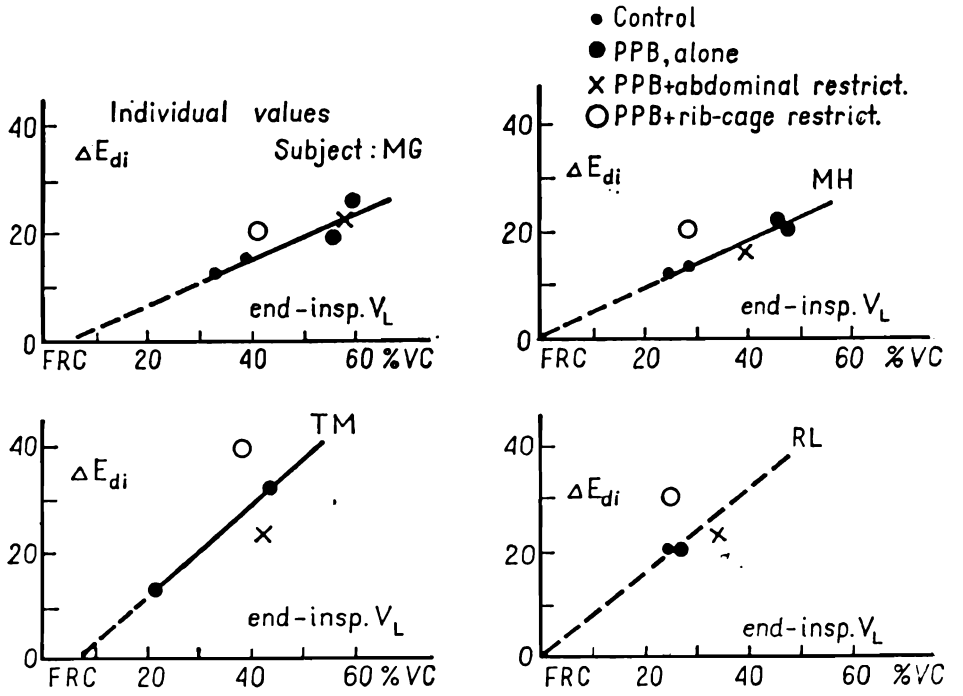

Fig. 6. For explanations *see* text.

lung volume. As shown in Fig. 6, all four subjects had a greater increase in excitation when the rib-cage was restricted during PPB then we estimate PPB alone would have produced at the same lung volume. Abdominal restriction had less influence on lung volume and a smaller influence on excitation as well. It is of interest that in the three subjects who had substantial shifts in volume during PPB, excitation increased nearly in direct proportion to end-inspiratory volume, as illustrated by the linear extrapolation close to the origin. This is the basis of the dashed line in the instance of the subject, RL, whose end-inspiratory volume did not shift during PPB.

These results are consistent with a reciprocal relationship between diaphragmatic excitation and tension. Diaphragmatic tension could be "sensed" either within the diaphragm itself, e.g. by tendon organs, or by receptors in that portion of the rib-cage directly influenced by diaphragmatic tension. The latter possibility is in line with the intercostal phrenic reflexes described by Euler.

I may mention some other possible receptor mechanisms. Lung volume per se, and rib-cage volume per se change in opposite directions during PPB as compared to rib-cage restriction, so slow adapting stretch

receptors in these structures are ruled out. On the other hand the volume changes of both lungs and rib-cage are limited both during PPB and rib-cage restriction, so receptors sensitive to volume change, e.g. quick adapting stretch receptors, either of the lungs or rib-cage are candidates.

Finally, how do these findings relate to natural breathing? The intrinsic properties of the respiratory muscles, and in particular their force-length characteristics, stabilize ventilation in the face of moderate changes in overall mechanical load such as occur naturally when one switches from nose to mouth breathing. This represents approximately a halving of flow-resistance and is quite comparable to the change in load produced by us with the servo-respirator. The intrinsic properties of the diaphragm are particularly effective in defending ventilation when the motion of the abdominal wall is restricted. Indeed the diaphragm's ability to lower pleural pressure and thereby ventilate the lung seems to be substantially independent of influence from abdominal pressure. Since the abdominal muscles take part in many non-respiratory motor acts this independence is undoubtedly important in natural breathing.

But in two other naturally occurring circumstances these same intrinsic properties of the diaphragm are a mechanical liability. When the rib-cage is restricted, for example by non-respiratory contraction of intercostal muscles during weight bearing, the diaphragm shortens more and develops less force for a given level of excitation. Similarly when the mean lung volume, around which breathing takes place, is increased, as occurs when one assumes the upright posture, the mean length of the diaphragmatic muscle fibres is decreased, and so also the force that they develop at a given level of excitation. It these situations there appears to be an automatic and highly appropriate adjustment of excitation. We have seen that ventilation may be completely defended in circumstances requiring a two- to threefold increase in excitation.

In summary, substantial changes in internal loading of the respiratory system occur naturally. The diaphragm in particular is admirably suited to cope with some of these on its own. For others it needs help, which it appears to get reflexly without recourse to higher centres, but which may to some extent be consciously guided; at least the last possibility has not been ruled out.

Note from the Author

The experimental results described herein will be published in detail elsewhere. Two manuscripts concerning work carried out in the Department of Physiology, Harvard University School of Public Health, have been prepared: ***Ventilatory responses to*** CO_2 ***during mechanically assisted breathing,*** by R. H. Kellogg, J. Mead, D. E. Leith and K. Konno, and ***Mechanisms of response during mechanically assisted***

breathing, by J. Mead, T. A. Sears, R. T. Knudson and M. Goldman. The studies of positive pressure breathing and of restriction of the chest wall were done in the Department of Neurophysiology of the Institute of Neurology, The National Hospitals for Nervous Diseases, Queen Square, London, by M. Green, T. A. Sears and J. Mead. The results of Grassino et al. are from a manuscript entitled *Effects of hyperinflation of the thorax on the ventilatory response to* CO_2, by A. E. Grassino, G. E. Lewinsohn and J. M. Tyler. This work was done in the Pulmonary Division of the Medical Service, Lemuel Shattuck Hospital, Department of Public Health, Commonwealth of Massachusetts, and in the Department of Physiology, Harvard School of Public Health, Boston.

J. MEAD, Department of Physiology, Harvard University School of Public Health, Boston, Massachusetts, USA.